- Cardiovascular –system [introduction]
- Heart: with in about three weeks after conception the heart of developing embryo starts to function. it is the first organ to become functional at this time when the human embryo is only a few millimeters long.
- Through out an average life span the heart contract never stopping except for fraction of a second to fill between beats

- The circulatory –system has three basic components:
- 1.the heart : serves as the pump that impart pressure to the blood to establish the pressure gradient needed for blood to flow to the tissues .blood like all liquids flows down a pressure gradient from an area of higher pressure to an area of lower pressure.

- 2. the blood vessels serve as passage ways through which blood is directed and distributed from the heart to all parts of the body and subsequently returned to the heart.
- 3. blood is the transport medium within which materials being transported long distance in the body such as O2,CO2,nutrient,waste electrolytes, and hormones.

- The heart is a dual [two] pump:
- Even though anatomically the heart is a single organ the right and left sides of the heart function as two separate pumps.
- Both sides of the heart simultaneously pump equal amounts of blood .the volume of O2 poor blood being pumped to the lungs by the right side of the heart soon becomes the same volume of O2 –rich blood being delivered by the left side of the heart

- In pulmonary –circulation all the blood flows through the lungs.
- The systemic circulation may viewed as a series of parallel pathways .part of the blood pumped out by the left ventricle goes to the muscles, part to the kidneys, part to the brain and so on . Thus the out –put of the left ventricle is distributed so that each part of the body receives a fresh blood supply, the same arterial blood does not pass from organ to organ.

- The pulmonary –circulation is a low pressure ,low resistance system. Where as the systemic circulation is high pressure ,high resistance system

- Pressure: is the force exerted on the vessel walls by the blood pumped into the vessels by the heart.
- Resistance : is the opposition to blood flow ,largely caused by friction between the flowing blood and the vessel wall.

- Blood flows through the heart in one direction from veins to atria to ventricles to arteries.
- The presence of four [4] one –way valves ensure this unidirectional flow of blood.
- The valves are positioned so that they open and close passively because of pressure gradiend similar to one-way door.

- Forward pressure gradient[that is a greater pressure behind the valves] forces the valves open much as open a door by pushing on one side of it. Where as a backward pressure gradient [that is a greater pressure in front of the valves]forces the valve closed just as you apply pressure to the opposite of the door to close it.

- Fibrous-skeleton of the valves:
- Four interconnecting rings of dense connective tissue provide a firm base for attachment of the four heart valves. The function of fibrous skeleton is to separate the atria from the ventricles ,it also provides a fairly rigid structure for attachment of the cardiac muscle.

- The atrial muscle mass is anchored above the rings and the ventricular muscle mass is attached to the bottom of the rings.

- The inlet valve to the ventricles[atrio-ventricular valves] and the outlet valves from the ventricles[the semi lunar –valves] all lie on the same plane through the heart . This relationship comes about because the heart forms from a single tube that bends on it self and twists on its axis during embryonic development.

- Heart muscle[myocardium]
- The myocardium consist of interlacing bundles of cardiac muscle fibers arranged spirally around the circumference of the heart. the spiral arrangement is due to the hearts complex twisting during development . As a result of this arrangement when the ventricular muscle contracts and shorten, the diameter of the ventricular chambers is reduced while the apex

- Is simultaneously pulled upward toward the top of the heart in rotating manner ,this exerts a wringing effect efficiently exerting pressure on the blood within the enclosed chambers and directing it upward toward the openings of the major arteries that exit at the base of the ventricles.
- The individual cardiac muscle cells are interconnected to form branching fibers with

- Adjacent cells joined end to end at a specialized structures known as intercalated discs . Within an intercalated disk there are two types of membrane junctions.
- A. desmosomes .B. Gap –junctions
- Desmosomes is type of mechanical junction that hold cells together.
- Gap –junction if formed when the opposing

- Membranes approach each other very closely to form gap junctions which are areas of low electrical resistance that allow action potential to spread from one cardiac cell to adjacent cells. Some cardiac muscle cells can generate action potential without any nervous stimulation . When one of the cardiac cells spontaneously undergoes an action potential the electrical impulse spreads to all the other

- Cells that are joined by gap junctions in the surrounding muscle mass so that they become excited and contract as a single functional syncytium. The atria and the ventricles each form a functional syncytium and contract as separate units. The synchronous contraction of the muscle cells that make up the walls of each of these chambers[atria and ventricles] produce the force needed to eject the enclosed blood.

- No junction join the atria and ventricular contractile cells and further more the atria and ventricles are separated by the electrically non conductive fibrous skeleton that surrounds and support the valves . However an important specialized conductive system facilitates and coordinates transmissions of electrical excitation from the atria to the ventricles to ensure synchronization between atrial and ventricular pumping

- Because of both the syncytial nature of cardiac muscle and the conduction system between the atria and ventricles an impulse spontaneously generated in one part of the heart spreads through out the entire heart . Therefore unlike skeletal muscle when graded contractions can be produced by varying the number of muscle cells contracting within the muscle [recruitment of motor units] either all

- The cardiac muscle fibers contract or none do.
- A half hearted contraction is not possible .
- Cardiac muscle contraction is graded by varying the strength of contraction of all the cardiac muscle cells

- Electrical –activity of the heart
- Contraction of cardiac muscle cells to eject blood is triggered by action –potentials sweeping across the muscle membranes.
- The heart contracts or beats rhythmically as result of action –potentials that it generate by itself a property called auto-rythmicity .
- There are two specialized types of cardiac muscle cells:

- 1. contractile –cells which are 90% of the cardiac muscle cells do the mechanical work of pumping. These working cells normally do not initiate their own action-potentials.
- 2. auto-rhythmic cells do not contract but instead are specialized for initiating and conducting the action –potentials responsible for contraction of the working cells.

- Auto-rhythmic cells do not have resting membrane potential instead they display pace maker activity that is their membrane potential slowly depolarizes or drifts between action –potentials and threshold is reached at which time the membrane fires or has an action potential.
- An auto-rhythmic cell membranes slow drift to threshold is called the pace-maker potential.

- Through repeated cycles of drift and fire these auto-rhythmic cells cyclically initiate action – potentials which then spread throughout the heart to trigger rhythmic beating without any nervous stimulation.
- Complex interaction of several different ionic mechanism are responsible for the pace-maker potential .

- The most important changes in ionic movement that give rise to the pace-maker potential are:
- 1. a decreased outward K current coupled with a constant inward Na current.
- 2. an increased inward Ca current.

- The initial phase of the slow depolarization to threshold is caused by a cyclical decrease in the passive outward flux of K+ superimposed on a slow unchanged inward leak of Na+.
- In cardiac auto-rhythmic cells permeability to K+ does not remain constant between action potential as it does in nerve and skeletal muscle cells. Instead membrane permeability to K+ decrease between action potentials because K+ channels slowly close at negative potential.

- This slow closure gradually diminished the outflow of positive potassium ions down their concentration gradient. also unlike nerve and skeletal muscle cells cardiac auto rhythmic cells does not have voltage gated Na+ channels instead they have channels that are always open and thus permeable to Na+ at negative potentials. As a result a small passive influx of Na+ continue unchanged at the same

- Time the rate of K+ efflux slowly decline thus the inside gradually becomes less negative that is the membrane gradually depolarizes and drifts toward threshold.
- In the second half of the pace maker potential a transient Ca+ channel[T-type channel] one of two types of voltage –gated Ca+ channel opens. As the slow depolarization proceed this channel is opened before the membrane reaches threshold.

- The resultant brief influx of Ca+ further depolarizes the membrane bringing it to threshold. Once threshold is reached the rising phase of the action potential occurs in response to activation of longer –lasting voltage –gated Ca+ channel[L-type Ca+channel] and subsequently large influx of Ca+. The Ca+ - induced rising phase of a cardiac pace maker cell differs from that in nerve and skeletal muscle cells where Na+ influx rather than Ca+ influx swings the potential in the positive direction.

The falling phase is due as usual to the K+ efflux that occurs when K+ permeability increases as a result of activation of voltage gated K+ channels .after the action potential is over slow closure of these K+ channels initiates the next slow depolarization to threshold

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- The sinoatrial –node is the normal pace maker of the heart .it discharge 70-80 action potential per minute .
- The specialized non contractile cardiac cells capable of autorhythmicity form 1% of the heart muscle. they are as follow:

- 1. the sino-atrial node [SA-node] discharge 70-80 per minute.
- 2. atrio-ventricular node [AV-node] discharge 40-60 per minute .
- 3. the bundle of His [atrio ventricular bundle]
  4. Purkinje fibers .
- Discharge rate of bundle of His and Purkinje fibers 20-40 per minute.

- The heart cells with the faster rate of action potential initiation are localized in the S-A node . Once an action potential occur in any cardiac muscle cell it is propagated throughout the rest of myocardium via gap junctions and the specialized system.
- Therefore the S-A node which normally has the fastest rate of autorhythmicity at 70-80 action potential per minute drives the rest of

- The heart at this rate and thus is known as the pace-maker of the heart. That is the entire heart becomes excited ,triggering the contractile cells to contract and the heart to beat at the pace or the rate set by S-A node autorhythmicity normally at 70-80 beats per minute.

- The other auto rhythmic tissues can not assume their own naturally slower rates because they are activated by action potentials originated in the S-A node before they can reach threshold at their own slower rhythm.

- The spread of action potential is coordinated to ensure efficient pumping . Once initiated in the S-A node an action potential spreads throughout the rest of the heart .
- For efficient cardiac function the spread of excitation should satisfy three criteria

- 1. atrial excitation and contraction should be complete before the onset of ventricular contraction . The atria must become excited and contract before ventricular excitation and contraction. During a normal heart beat atrial contraction occurs about 160 msec[.,016] before ventricular contraction.

- Excitation of cardiac muscle fibers should be coordinated to ensure that each heart chamber contracts as a unite to pump efficiently . If the muscle fibers in a heart chamber become excited and contracted randomly rather than contracting simultaneously in a coordinated fashion they would be unable to eject blood .

- A smooth uniform ventricular contraction is essential to squeeze out the blood.
- Contraction of isolated cardiac muscle fibers is not successful in pumping blood .such random uncoordinated excitation and contraction of the cardiac cells is known as fibrillation.

- The pair of atria and pair of ventricles should functionally coordinated so that both members of the pair contract simultaneously this coordination permits synchronized pumping of blood into the pulmonary and systemic circulation.

- Atrial –excitation
- An action potential originating in the S-A node spread rapidly throughout both atria primarily from cell to cell via gap junction ,in addition several poorly delineated specialized conduction pathways spreads up conduction of the impulse through the atria

- Inter-atrial –pathway : extends from the S-A node within the right atrium to the left atrium. this pathway rapidly transmits the action potential from the S-A node to the pathways termination in the left atrium . A wave of excitation can spread across the gap junctions throughout the left atrium at the same time excitation is similarly spreading throughout the right atrium this ensure that atria become depolarized to contract simultaneously.

- Inter- nodal pathway :
- Extends from the S-A node to the A-V node . The A-V node is the only point of electrical contact between the atria and ventricles because atria are separated by non conductive fibrous tissue. The inter-nodal conduction pathway directs the spread of an action potential originating at the S-A node to the A-V node to ensure sequential contraction of the ventricles following atrial

- Contraction .hastened by this pathway the action potential arrives at the A-V node within 30 msec af the S-A node firing.

- The action potential is conducted relatively slowly through the A-V node . This slowness is advantageous because it allows time for complete ventricular filing . The impulse is delayed about 100 mesc[the A-V nodal delay]which enables the atria to become completely depolarized and to contract emptying their contents into the ventricles before ventricular depolarization and contraction occur.

- Ventricular –excitation:
- After the A-V nodal delay the impulse travels rapidly down the septum to the right and left branches of the bundle of His and throughout the ventricular myocardium via the purkinje fibers. The network of fibers in this ventricular conduction system is specialized for rapid propagation of action potentials .

- its presence hastens and coordinates the spread of ventricular excitation to ensure that the ventricles contract as a unit. The action potential is transmitted through the entire purkinje fiber system within 30 msec.
- Although this system carries the action potential rapidly to a large number of cardiac muscle cells it does not terminate on every cell. The impulse quickly spreads from the

- Excited cells to the rest of the ventricular muscle cells by means of gap junctions. Purkinje fibers can transmit an action potential six times faster than the ventricular syncytium of contractile cells could. If the entire ventricular depolarization process depends on cell to cell spread of the impulse via gap junctions the ventricular tissue immediately next to the A-V node would become excited and contract before the impulse have even passed to the heart apex this of course would not allow efficient pumping.

- Rapid conduction of the action potential down the bundle of His and its swift diffuse distribution throughout the purkinje network lead to almost simultaneous activation of the ventricular myocardial cells in both ventricular chambers which ensures a single ,smooth,coordinated contraction that can efficiently eject blood into both the systemic and pulmonary circulation at the same time.

- Action –potential of contractile muscle cells:
- Unlike the membrane of autorhythmic cells the membrane of contractile cells remains essentially at rest at about -90 mV until excited by electrical activity propagated from the pace-maker of the heart.

- Components of action potential of contractile cell:
- 1. rising –phase of action potential up to +30mV as a result of activation of voltage –gated Na+ channels and Na+ subsequently rapidly entering the myocardial cell.
- 2. plateau-phase is maintained by two voltage –dependent permeability changes .these are the activation of slow L-type Ca+ channels

- And marked decrease in K+ permeability in the contractile cell membrane.
- 3. the rapid falling of the action –potentials results from inactivation of the Ca+ channels and delayed activation of voltage –gated K+-channels. so the return to its resting level as the K+ leaves the cell

- Calcium entry from ECF induces a much larger Ca+ release from the sarcoplasmic reticulum:
- In cardiac contractile cells the L-type Ca+ channels lie primarily in the T-tubule. these voltage-gated channels open during a local action potential thus calcium diffuses into the cytosol from the ECF across the T tubule membrane during a cardiac action potential.

- This entering Ca+ triggers the opening of nearby Ca+ release channels in the adjacent lateral sac of the sarcoplasmic reticulum.
- By means of this so called Ca+-induced Ca+ release Ca+ entering the cytosol from the ECF induces a much larger release of Ca+ into the cytosol from the intecelluar stores. The resultant local bursts of Ca+ sparks from the sarcoplasmic reticulum collectively increase the cytosolic Ca+pool sufficiently to turn the contractile machinary.

- Ninety percent of the Ca+ needed for muscle contraction comes from the sarcoplasmic reticulum. This extrasupply of Ca+ coupled with slow Ca+ removal process is responsible for the long period of cardiac contraction which last about three times longer than the contraction of a single skeletal muscle fiber[300msec compared to100mesc] this increased contractile time ensures adequate time to eject the blood from the heart.

- Mechanism of contraction in cardiac contractile cell:
- 1. action –potential in cardiac cell travel down T-tubule.
- 2. entry of small amount of Ca+ from ECF which leads to release of large amount of Ca+ from sarcoplasmic reticulum.
- 3. increase cytosolic Ca+.this will lead to.

- 4. Troponin-tropomyosin complex in thin filaments pulled aside which lead to.
- 5. cross-bridge cycling between thick and thin filaments which leads to.
- 6. thin filament slide inside between thick filament which cause
- 7.contraction of cardiac muscle.

- In skeletal muscle sufficient Ca+ is always released to turn on all the cross bridges .
- In cardiac muscle the extent of cross-bridge activity varies with the amount of cytosolic Ca+. Various regulatory factors can alter the amount of cytosolic Ca+.

- Effect of elevated K+ ion on the heart :
- Normally there is substantially more K+ inside the cells than in the ECF . But with elevated ECF K+ levels this gradient is reduced . Associated with this change is a reduction in resting membrane potential [that is the membrane is less negative on the inside than normal because less K+ leaves].among the consequences is tendency to develop ectopic foci ,prolongation in conduction ,weak cardiac muscle as well as cardiac arrhythmias.

- Effect of ECF Ca+ on the heart :
- Elevated ECF calcium concentration augments the strength of cardiac concentration by prolonging the plateau phase of action potential and by increasing the cytosolic concentration of Ca+ contraction tend to be of longer duration with little time to rest between contraction . Calcium channel blockers block Ca+ influx during an action potential reducing the force of cardiac contraction. other drugs such as digitalis increases cardiac contractility by inducing accumulation of cytosloic Ca+.

- Cardiac muscle has along refractory period that lasts about 259msec because of the prolonged plateau phase of the action potential . This is almost as long as the period of contraction initiated by the action potential , a cardiac muscle fiber contraction average about 300msec.consequently cardiac muscle can not be restimulated until contraction is almost over precluding summation of contractions and tetanus of cardiac muscle.

- This is a valuable protective mechanism because the pumping of blood requires alternate period of contraction [emptying] and relaxation [filling] a prolonged tetanic contraction would prove fatal ,the heart chambers could not be filled and emptied again.

- The chief factor responsible for the long refractory period is inactivation during the prolonged plateau phase of the Na+ channels that were activated during the initial Na+ influx of the rising phase . Not until the membrane recovers from this inactivation process [when the membrane has already repolarized to resting] can the Na+ channels be activated once again to begin another action potential

- Electro-cardiography [ECG]
- The electrical currents generated by cardiac muscle during depolarization and repolarization spread into tissues around the heart and conducted through the body fluids . A small part of this electrical activity reaches the body surface where it can be detected using recording electrodes the record produced is called electro –cardiograph or ECG

- Three important points when considering what an ECG represents:
- 1. an ECG is a recording of that part of the electrical activity induced in body fluids by the cardiac impulses that reaches the body surface not a direct recording of the actual electrical activity.

- 2. The ECG is a complex recording representing the overall spread of activity throughout the heart during depolarization and repolarization. It is not a recording of a single action potential in a single cell at a single point in time . The record at any given time represents the sum of electrical activity in all the cardiac muscle cells some of which may be undergoing action potential while others may not be activated. For example immediately

- After the S-A node fires the atrial cells are undergoing action potential while the ventricular cells are still at resting potential . At a later point the electrical activity will have spread to the ventricular cells while the atrial cells will be repolarizing . Therefore the overall pattern of cardiac electrical activity varies with time as the impulse passes throughout the heart.

- 3. the recording represents comparisons in voltage detected by electrodes at two different points on the body surface not the actual potential . For example the ECG does not record a potential at all when the ventricular muscle is either completely repolarized or completely depolarized , both electrodes are viewing the same potential so no difference in potential between the two electrodes is recorded.

- Parts of ECG:
- 1. P-wave represents atrial depolarization.
- 2. QRS – complex represents ventricular depolarization.
- 3. T- wave represents ventricular repolarization.

- Some important point concerning ECG:
- 1. firing of the S-A node does generate enough electrical activity to reach the body surface so no wave is recorded for S-A nodal depolarization.
- 2. in normal ECG no separate wave for atrial repolarization is visible .the electrical activity asssociated with atrial repolarization normally occurs simultaneously with ventricular depolarization and is masked by the QRS complex.

- 3. the p-wave is much smaller than the QRS complex because the atria have a much smaller muscle mass than the ventricles and consequently generate less electrical activity.
- 4. at the following three points in time no net current flow is taking place in the heart musculature so the ECG remains at baseline.

- A. during the A-V nodal delay this delay is represented by the interval of time between the end of P-wave and the onset of QRS. This segment of the ECG is called PR segment .current is flowing through the A-V node but the magnitude is too small for the ECG electrode to detect.
- B. when the ventricles are completely depolarized and the cardiac contractile cells are undergoing the plateau phase of their action potential before they repolarize represented by the S-T segment. This segment lies between QRS and T –wave it coincides with the time during which ventricular activation is complete and the ventricles are contracting and emptying.

- C. when the heart muscle is completely repolarized and at rest and ventricular filling is taking place after the T-wave and before the next P-wave .this period is called the TP interval.

Because electrical activity triggers mechanical activity abnormal electrical patterns are usually accompanied by abnormal contractile activity of the heart.

- Atrial-flutter:
- Is characterized by a rapid but regular sequence of atrial depolarization at a rates between 200 and 380 beats per minute.
- Atrial –fibrillation:
- Is characterized by rapid irregular uncoordinated depolarization of the atria with no definite P – wave. Because impulses reach the A-V node erratically the ventricular rhythm is also irregular.

- The QRS complex are normal in shape but occur sporadically . Variable length of time between ventricular beats are available for ventricular filling . Some ventricular beats come so close together that little filling can occur between beats . When less filling occurs the subsequent contraction is weaker . In fact some of the ventricular contractions may be too weak to eject enough blood to produce a palpable wrist pulse.

- In this situation if the heart rate is determined directly either by the apex beat or via the ECG and the pulse rate is taken concurrently at the wrist the heart rate will exceed the pulse rate . Such a difference in heart rate and pulse rate is known as a pulse deficit.
- Normally the heart rate coincides with the pulse rate because each cardiac contraction initiate a pulse wave as it eject blood into the arteries.

- Ventricular- fibrillation: is a very serious rhythmic abnormality in which the ventricular musculature exhibits uncoordinated chaotic contractions . Multiple impulses travel erratically in all directions around the ventricles . The ECG tracing in ventricular fibrillations is very irregular with no detectable pattern or rhythm when contraction are so disorganized the ventricle are ineffectual as pumps.

- If circulation is not restored in less than four minutes through external cardiac compression or electrical defibrillation irreversible brain damage occurs and death is imminent.
- Heart –block:
- Arises from defects in the cardiac conducting system .the atria still beat regularly but the ventricles occasionally fail to be stimulated and thus do not contract following atrial contraction.

- Impulses between the atria and ventricles can be blocked to varying degrees . In some forms of heart block only every second or third atrial impulse is passed to the ventricles this known as 2:1 or 3:1 block which can be distinguished from 2:1 or 3:1 rhythm associated with atrial flutter by the rates involved . In heart block the atrial rate is normal but the ventricular rate is considerably below normal . Where as

- In atrial flutter the atrial rate is very high in accompaniment with a normal or above normal ventricular rate.
- Complete heart block is characterized by complete dissociation between atrial and ventricular activity with impulses from the atria not being conducted to the ventricles at all . The S-A node continue to govern atrial depolarization but the ventricles generate their own impulses

- at a rate much slower than that of the atria . On the ECG the P-wave exhibit a normal rhythm ,the QRS and T-waves also occur regularly but much more slowly than the P-wave and completely independent of P-wave rhythm. Because atrial and ventricular activity is not synchronized waves for atrial repolarization may appear no longer masked by the QRS complex.

- The mechanical events of the cardiac cycle:
- Contraction, relaxation and the resultant changes In blood flow through the heart are brought about by the rhythmic changes in cardiac activity.
- The heart alternately contracts to empty and relaxes to fill with blood.

- The cardiac cycle consists of alternate periods of:
- A. systole means contraction and emptying.
- B. diastole means relaxation and filling.

Contraction results from the spread of excitation across the heart.

Relaxation follows the subsequent repolarization of the cardiac musculature. the atria and ventricles go through separate cycles of systole and diastole.

- Mid-ventricular diastole
- During most of ventricular diastole the atrium is still also in diastole . This stage corresponds to the T-P interval on the ECG[the interval after ventricular repolarization and before another atrial depolarization].
- Because of the continuous inflow of blood from the venous system into the atrium atrial pressure slightly exceeds ventricular pressure even though both chambers are relaxed.

- Because of this pressure differential the A-V valve is open and blood flows directly from the atrium into the ventricle throughout ventricular diastole . As a result of this passive filling the ventricular volume slowly continues to rise even before atrial contraction takes place

- Late-ventricular diastole
- Late in ventricular diastole the S-A node reaches threshold and fires . The impulse spread throughout the atria which appears in the ECG as the P-wave . Atrial depolarization brings about atrial contraction rising the atrial pressure and squeezing more blood into the ventricle. Throughout atrial contraction atrial pressure still slightly exceeds ventricular pressure so the A-V valve remains open.

- Ventricular diastole ends at the onset of ventricular contraction by this time atrial contraction and ventricular filling are completed. The volume of blood in the ventricle at the end of diastole is known as the end-diastolic volume [EDV]. Which average about 135ml . No more blood will be added to the ventricle during this cycle.

- Therefore the end –diastolic volume is the maximum amount of blood that the ventricle will contain during this cycle.

- Ventricular-excitation and onset of ventricular systole:
- After atrial excitation the impulse travels though the A-V node and specialized conduction system to excite the ventricle. By the time ventricular activation is complete atrial contraction is already over. The QRS complex represents this ventricular excitation which induces ventricular contraction. the ventricular pressure sharply increases after the QRS complex signaling the onset of ventricular systole.

- The slight delay between the QRS complex and the actual onset of ventricular systole is the time required for the excitation-contraction coupling process to occur. As ventricular contraction begins ventricular pressure immediately exceeds atrial pressure . This backward pressure differential forces the A-V valve close

- After ventricular pressure exceeds atrial pressure and the A-V valve has closed .to open the aortic valve the ventricular pressure must continue to increase until it exceeds aortic pressure. Therefore after closing of the A-V valve and before opening of the aortic valve is a brief period of time when the ventricle remains a closed chamber. Because all valves are closed no blood can enter or leave the ventricle during this time.

- This interval is termed the period of iso-volumetric ventricular contraction [iso-volumetric means constant volume and length]. Because no blood enter or leaves the ventricle the ventricular chamber stays at constant volume and the muscle fibers stay at constant length. During iso-volumetric ventricular contraction ventricular pressure continues to increase as the volume remains constant.

- Ventricular –ejection
- When ventricular pressure exceeds aortic pressure the aortic valve is forced open and ejection of blood begins.
- The amount of blood pumped out of each ventricle with each contraction is called the stroke volume

- The aortic pressure rises as blood is forced into the aorta from the ventricle faster than blood is draining off into the smaller vessels at the other end. The ventricular volume decreases substantially as blood is rapidly pumped out. Ventricular –systole include both:
- 1. the period of iso-volumetric contraction.
- 2.the ventricular ejection phase.

- End of ventricular systole:
- The ventricle does not empty completely during ejection. Normally only about half the blood within the ventricle at the end of diastole is pumped out during the subsequent.
- The amount of blood left in the ventricle at the end of systole when ejection is complete is the end-systolic volume [ESV] which average about 65ml .

- This is the least amount of blood that the ventricle will contain during this cycle .
- Systolic –volume= end diastolic volume- end systolic volume.
- S-V= EDV-ESV
- Stroke volume=135-65=70ml

- Ventricular repolarization and onset of ventricular diastole:
- The T-wave signifies ventricular repolarization at the end of ventricular systole . As the ventricle starts to relax on repolarization ventricular pressure falls below aortic pressure and the aortic valve closes . Closure of the aortic valve produces a disturbances or notch on the aortic pressure called dicrotic notch.

No blood leaves the ventricle during this cycle because the aortic valve has closed .when the aortic closes the A-V valve is not yet open because ventricular pressure still exceeds atrial pressure .so no blood can enter the ventricle from the atrium .therefore all the valves once again closed for a brief period of time known as iso-volumetric ventricular relaxation. the muscle fiber length and chamber volume remain constant .no blood leaves or entrs as the ventricle continues to relax and the pressure steadily falls.

- When ventricular pressure falls below atrial pressure the A-V valve opens and ventricular filling occurs again. Ventricular diastole include both the period of :1.iso-volumetric ventricular relaxation.2. the ventricular filling phase .
- Atrial repolarization and ventricular depolarization occur simultaneously so the atria are in diastole are in diastole throughout ventricular systole. Blood continues to flow from the pulmonary veins into the left atrium .as this incoming blood pools in the atrium atrial pressure rises continously.

- When the A-V valve opens at the end of ventricular systole blood that accumulated in the atrium during ventricular systole pours rapidly into the ventricle . Ventricular filling thus occurs rapidly because of the increased atrial pressure resulting from the accumulation of blood in the atria .then ventricular filling slows down as the accumulated has already been delivered to the ventricle and atrial pressure starts to fall. During this period of reduced filling blood continue to flow from the pulmonary veins into the left atrium and through the open A-V valve into the left ventricle.

- During late ventricular diastole when the ventricle is filling slowly the S-A node fires again and the cardiac cycle starts over.
- When the body at rest one complete cardiac cycle lasts 800msec with 300msec devoted to ventricular systole and 500msec taken up by ventricular diastole. significantly much of ventricular filling occurs early in diastole during the rapid filling phase

- During times of rapid heart rate diastole length is shortened much more than systole length . Because much of ventricular filling occurs early in diastole during the rapid filling phase filling is not seriously impaired when diastolic time is reduced as a result of an increase in heart rate.
- Normally ventricular rate do not exceed 200beats per minute because the relatively long refractory period of the A-V node will not allow impulses to be conducted to the ventricles more frequently than this.

- Heart –sounds:
- 1. first –heart sound is low pitched soft and relatively long ,sound like lub.
- 2. second heart sound has a higher pitch and is shorter and sharper often said to sound like dup.
- The first heart sound is associated with closure of the A-V valves where as the second heart sound is associated with closure of the semi lunar valves.

- Opening of valves does not produce any sound .
- The sounds are caused by vibrations setup within the walls of the ventricles and major arteries during valve closure not by the valves snapping shut.
- Because the A-V valves close at the onset of ventricular contraction when ventricular pressure exceeds atrial pressure the first heart sound signals the onset of ventricular systole.

- The semi lunar valve close at the onset of ventricular relaxation as the left and right ventricular pressures falls below the aortic and pulmonary artery pressures respectively.
- The second heart sound therefore signals the onset of ventricular diastole.
- The pouring of blood from atrium toward ventricle during mid-diastole produce sound called third heart sound.
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- Atrial contraction during late diastole push additional blood to the ventricle which is already contain blood this pouring of blood produce a sound called fourth heart sound.
- So the second, third and the fourth heart sounds all occurs in diastole

- Murmurs : are abnormal sounds due to turbulence of blood flow.
- Stenotic valve is stiff narrowed valve that does not open completely . Blood must be forced through the constricted opening at tremendous velocity resulting in turbulence that produce an abnormal whistling sund similar to the sound produced when you force air rapidly through narrowed lips to whistle.

- Insufficient or incompetent valve:
- Is the one that can not close completely usually because the valve edges are scarred and does not fit together properly. Turbulence is produced when blood flows backward through the insufficient valve and collides with blood moving in the opposite direction creating a swishing ao gurgling murmur.

- Such backflow of blood is known as regurgitation . An insufficient heart valve is often called a leaky valve because it lets blood leaks back through at a time when the valve should be closed.
- Murmur between the first and second heart sound LUP-murmur-dup is a systolic murmur.

- Diastolic –murmur occurs between the second and first heart sound LUP-DUP murmur.
- The sound of the murmur characterizes it as either a stenotic [whistling] murmur or an insufficient [swishy] murmur.

cardiac –output: is the volume of blood pumped by each ventricle per minute.

Cardiac –output depends on the heart rate and the stroke volume.

Cardiac-output= heart rate X stroke volume =5 liters.

- Because the body's total blood volume averages 5 liters each half of the heart pumps the equivalent of the entire blood volume each minute. In other words each minute the right ventricle normally pumps 5 liters of blood through the lungs and the left ventricle pumps 5 liters through the systemic circulation.

- During exercise cardiac- out put increase to 20 to 25 liters per minute and out-put as high as 40 liters per minute have been recorded in trained athletes during heavy endurance type exercise.
- Cardiac –reserve= maximum volume of blood the heart can pump per minute– cardiac out-put at rest.

- So the cardiac reserve is the difference between the cardiac out-put at rest and the maximum volume of blood the heart can pump at exercise.

- Heart rate:
- Is determined primarily by autonomic influences on the S-A node .
- Membrane potential of the S-A node is due to a complex interplay of ion movements involving a reduction in K+ permeability , a constant Na+ permeability and an increased Ca+ permeability . When the S-A node reaches threshold an action potential is initiated that spreads throughout the heart.

- Para-sympathetic nerve to the heart [the vagus] primarily supplies the atrium especially the S-A node and A-V nodes . Para-sympathetic innervations of the ventricle is sparse.
- The cardiac sympathetic nerves also supply the atria including the S-A and A-V node and richly innervate the ventricle as well.

- Both the para-sympathetic and sympathetic nervous system bring about their effects on the heart by altering the activity of the cyclic AMP second messenger system in the innervated cardiac cells.
- Acetyl-choline released from the vagus nerve bind to a muscarinic receptor and is coupled to an inhibitory G protein that reduces activity of the cyclic AMP pathway.

- Sympathetic neurotransmitter norepinephrine binds with a Beta 1 adrenergic receptor and is coupled to a stimulatory G protein that accelerates the cyclic AMP pathway in the target cells

- Effect of para-sympathetic stimulation on the heart:
- Acetyl choline released on increased para-sympathetic activity increases the permeability of the S-A node to K+ by slower the closure of K+ channels . As a result the rate at which spontaneous action potential are initiated is reduced through a two fold effect.

- A. enhanced K+ permeability hyperpolarizes the S-A node membrane because more positive potassium ions leave than normal making the inside even more negative.
- B. the enhanced K+ permeability induced by vagal stimulation also opposes the automatic reduction in K+ permeability responsible for initiating the gradual depolarization of the membrane to threshlod.

- This countering effect decreases the rate of spontaneous depolarization prolonging the time required to drift to threshold. Therefore the S-A node reaches threshold and fire less frequently decreasing the heart rate.

- Para-sympathetic influence on the A-V node decreases the node excitability ,prolonging transmission of impulses to the ventricles even longer than the usual AV nodal delay .
- This effect is brought about by increasing K+ permeability which hyperpolarizes the membrane thereby retarding the initiation of excitation in the A-V node.

- Para-sympathetic stimulation of the atrial contractile cells shorten the action potential reducing the slow inward current carried by Ca+that is the plateau phase is shortened . As a result atrial contraction is weakened.
- The para-sympathetic system has little effect on ventricular contraction because of the sparseness of para-sympathetic innervation to the ventricles.

- Thus when the heart under para-sympathetic influence it beats less rapidly ,the time between atrial and ventricular contraction is stretched out and atrial contraction is weaker these actions are appropriate considering that the para-sympathetic system controls heart action in quiet .released situations when the body is not demanding an enhanced cardiac output.

- Effects of sympathetic stimulation on the heart:
- The sympathetic nervous system control heart action in emergency or exercise situations when there is a need for greater blood flows.
- The main effect of sympathetic stimulation on the S-A node is to speed up depolarization so that threshold is reached more rapidly.

- Nor epinephrine released from the sympathetic nerve endings decreases K+ permeability by accelerating inactivation of the K+ channels with fewer positive potassium ions leaving the inside of the cell becomes less negative creating a depolarizing effect. This swifter drift to threshold under sympathetic influence permits more frequent action potential and a correspondingly faster heart rate.

- Sympathetic stimulation of the A-V node reduces the A-V nodal delay by increasing conduction velocity presumably by enhancing the slow inward Ca+ current.
- Sympathetic stimulation speeds up spread of the action potential throughout the specialized conduction pathway.

- Sympathetic stimulation increases contractile strength so the heart beats more forcefully and squeezes out more blood . This effect is produced by increasing Ca+ permeability which enhances the slow Ca+ influx and intensifies Ca+ participation in excitation – contraction coupling .

- The overall effect of sympathetic stimulation on the heart is to improve its effectiveness as a pump by increasing heart rate ,decreasing the delay between atrial and ventricular contraction , decreasing conduction time throughout the heart and increasing the force of contraction.

- The para-sympathetic and sympathetic effects on heart rate are antagonist [oppose each other]. At any given moment heart rate is determined largely by the balance between inhibition of the S-A node by vagus nerve and stimulation of the cardiac sympathetic nerves .under resting conditions para-sympathetic discharge dominates.

- In fact if all autonomic nerves to the heart were blocked the resting heart rate would increase from its average value of 70 beats per minute to about 100 beats per minute which is inherent rate of the S-A nodes spontaneous discharge when not subjected to any nervous influence .

- heart rate is speeded up by simultaneously increasing sympathetic and decreasing para-sympathetic activity.
- Heart rate is slowed by a concurrent rise in para-sympathetic activity and decline in sympathetic activity . The relative level of activity in these two autonomic branches to the heart in turn is primarily coordinated by the cardiovascular center in the brain stem.

- Stroke-volume: is the volume of blood pumped out by each ventricle during each beat [single beat].
- Two types influence stroke volume:
- 1. intrinsic –control related to the extent of venous return.
- 2. extrinsic-control related to the extent of sympathetic stimulation of the heart.

- both factors increase stroke volume by increasing the strength of heart contraction.
- Intrinsic-control:
- Increased end-diastolic volume results in increased stroke volume. For cardiac muscle the resting cardiac muscle fiber is less than Io[optimal length] therefore the length of cardiac muscle fibers normally varies along the ascending limb of the length tension curve. That is within physiologic limits cardiac muscle does not stretched beyond its optimal length to the point

- That contractile strength diminish with further stretching. The cardiac muscle fibers length which is determined by the extents of venous filling is normally less than the optimal length for developing maximal tension. Therefore an increase in end-diastolic volume that is an increase in venous return by moving the cardiac fiber length closer to optimal length increases the contractile tension of thr fibers on the next systole.

- A stronger contraction squeezes out more blood .thus as more blood is returned to the heart and the end-diastolic volume increases ,the heart automatically pumps out a correspondingly larger stroke volume.
- The main determinant of cardiac muscle fiber length is the degree of diastolic filling.
- The extent of filling is referred to as the preload because it is the work load imposed on the heart before contraction begins.

- Therefore the heart is stretched when more blood is pouring in it.
- The longer the initial cardiac muscle fiber length before contraction [produced by more filing] the greater the force of subsequent cardiac contraction and thus a greater stroke volume.

- Advantage of the cardiac length-tension relationship[starling-law]:
- 1. equalizing output between the right and left sides of the heart so that blood pumped out of the heart is equally distributed between the pulmonary and systemic circulation. if such equalization did not happen too much blood would be dammed up in the venous system before the ventricle with lower output.

- 2. when a larger cardiac output is needed such as during exercise . Venous return is increased through action of the sympathetic nervous system . The resulting increase in end-diastolic volume[EDV] automatically increases stroke volume correspondingly . Also the exercise increase the heart rate these two factors act together to increase the cardiac output so more blood can be delivered to the exercising muscles.

- Contractility: is the strength of contraction at any given end-diastolic volume.
- Sympathetic stimulation to the heart increases the contractility of the heart . On sympathetic stimulation the heart contracts more forcefully and squeezes out a greater percentage of the blood it contains leading to more complete ejection.

- This increased contractility is due to the increased Ca+ influx triggered by nor epinephrine and epinephrine . This extra cytosolic Ca+ lets the myocardial fibers generate more force through greater cross-bridge cycling than they would without sympathetic influence .

- Normally the EDV is 135ml and the end-systolic volume[ESV] is 65ml for a stroke volume of 70ml, under sympathetic influence for the same EDV of 135ml the ESV might be 35ml and the stroke volume 100ml. In effect sympathetic stimulation shifts the frank-starling curve to the left.

- Sympathetic stimulation increases stroke volume not only by strengthening cardiac contractility but also by enhancing venous return. Sympathetic stimulation constricts the veins which squeezes more blood forward from the veins to the heart increasing the EDV and subsequently increasing stroke volume even further.

- High blood pressure increases the work load of the heart. The arterial blood pressure is called the after-load which is work load imposed on the heart after contraction has begun. If arterial blood pressure is chronically elevated or if the exit valve is stenotic the ventricle must generate more pressure to eject blood.

- Heart –failure: is the inability of the cardiac output to keep pace with the body's demand for supplies and removal of wastes. Either one or both ventricles may progressively weaken and fail. When a failing ventricle can not pumped out all the blood returned to it the veins behind the failing ventricle becomes congested with blood.

- The prime defect in heart failure is a decrease in cardiac contractility that is weakened cardiac muscle cells contracts less effectively .
- The intrinsic ability of the heart to develop pressure and eject a stroke volume is reduced so that the heart operates on a lower length – tension curve.

- Compensatory measures for heart failure:
- In the early stages two major compensatory measures help restore stroke volume to normal.
- 1. sympathetic activity to the heart is reflexly increased which increases heart contractility toward normal . But sympathetic stimulation can help compensate only for a limited period of time . However because the heart becomes less responsive to nor epinephrine after prolong exposure and furthermore nor epinephrine store in the hearts sympathetic nerve terminal become depleted.

- 2. when the cardiac output is reduced the kidneys in a compensatory attempt to improve their reduced blood flow retain extra salt and water in the body during urine formation to expand the blood volume . The increase in circulatory blood volume increases the EDV, the resultant stretching of the cardiac muscle fibers enables the weakened heart to pump out a normal stroke volume . The heart is now pumping out the blood returned to it but is operating at a greater cardiac muscle fiber length.

- Forward- failure:
- When the cardiac muscle fibers are stretched to the point that they are operating in the descending limb of the length –tension curve forward failure occurs as the heart fails to pump an adequate amount of blood forward to the tissues because the stroke volume becomes progressively smaller.

- Backward-failure:
- Occurs simultaneously as blood that can not enter and be pumped out by the heart continues to dam up in the venous system and the venous system becomes congested with blood . The congestion in the venous system is the reason why this condition is sometimes termed congestive heart failure.

- Left sided –failure has more serious consequences than right sided- failure . Backward failure of the left side leads to pulmonary oedema because blood dams up in the lungs.
- Systolic –failure is characterize by a decrease in cardiac contractility.
- Diastolic-failure: occurs in which the heart has trouble in filling with blood.

- With diastolic failure the ventricles do not fill normally either because the heart muscle do not adequately relax between beats or because the heart muscle stiffens and can not expand as much as usual . Because of impeded filling a diastolic failing heart pumps out less blood than it should with each contraction.

- Nourishing the heart muscle[coronary blood flow]:
- Cardiac muscle cells contain an abundance of mitochondria the O2 –dependent energy organelle. In fact up to 40% of the cell volume of cardiac muscle cells is occupied by mitochondria indicative of how much the heart depends on O2 delivery and aerobic metabolism to generate the energy necessary for contraction. Cardiac muscle also has an abundance of myoglobin which stores limited amounts of O2 within the heart for immediate use.

- Most coronary blood flow occurs during diastole because the coronary vessels are compressed almost completely closed during systole . Although all the blood passes through the heart , the heart muscle can not extract O2 or nutrients from the blood within its chambers for two reasons:
- A. the water tight endocardial lining does not permit blood to pass from the chambers into the myocardium.

- B. the heart walls are thick to permit diffusion of O2 and other supplies from the blood in the chamber to the individual cardiac cells.therefore like other tissues of the body heart muscle must receive blood through blood vessels specifically via the coronary circulation.

- The heart muscle receives most of its blood supply during diastole . Blood flow to the heart muscle cells is substantially reduced during systole for two reasons:
- 1. the contracting myocardium especially in the powerful left ventricle compresses the major branches of the coronary arteries.
- 2. the open aortic valve partially blocks the entrance to the coronary vessels.

- Thus most coronary arterial flow [70%] occurs during diastole driven by the aortic blood pressure with flow declining as aortic pressure drops . Only about 30% of coronary arterial flow occurs during systole. This limited time for coronary blood flow becomes especially important during rapid heart rates when diastolic time is much reduced . Just when increased demands are placed on the heart to pump more rapidly it has less time to provide O2 and nourishment to its own musculature to accomplish the increased work load.

- Extra blood is delivered to the cardiac cells primarily by vasodilatation or enlargement of the coronary vessels which lets more blood flow through them especially during diastole.
- The increased coronary blood flow is necessary to meet the hearts increased O2 requirements because the heart unlike most other tissues is unable to remove much additional O2 from the blood passing through its vessels to support increased metabolic activities.

- Most other tissues under resting conditions extract only about 25% of the O2 available from the blood flowing through them leaving a considerable O2 reserve that can be drwan or when a tissues has increased O2 needs that is the tissue can immediately increase the O2 available to it by removing a greater percentage of O2 from the blood passing through it.

- In contrast the heart even under resting conditions removes up to 65-75% of the O2 available in the coronary vessels far more than is withdrawn by other tissues . This leaves little O2 in reserve in the coronary blood should cardiac O2 demands increase . Therefore the primary means by which more O2 can be made available to the heart muscle is by increasing blood flow.

- Coronary blood flow is adjusted primarily in response to changes in the hearts O2 requirements. Among the proposed links between blood flow and O2 needs is adenosine which is formed from adenosine-triphosphate [ATP] during cardiac metabolic activity . Cardiac cells form and release more adenosine when cardiac increases and the heart accordingly needs more O2 and is using more ATP as an energy source.

- The released adenosine acting as a paracrine factor induces dilatation of the coronary blood vessels allowing more O2 rich blood to flow to the more active cardiac cells to meet their increased O2 demand. Matching O2 delivery to O2 needs is crucial because heart muscle depends on oxidative processes to generate energy . The heart can not get enough ATP through anaerobic metabolism.

- As fuel sources the heart primarily uses free fatty acids and to lesser extent glucose and lactate depending on their availability. Because cardiac muscle is remarkably adaptable and can shift metabolic pathways to use whatever nutrient is available the primary danger of insufficient coronary blood flow is not fuel shortage but O2 deficiency.

- circulation
- The blood pumped by the left side of the heart into the systemic circulation is distributed in various proportions to the systemic organs through a parallel arrangement of vessels that braches from the aorta. This arrangement ensures that all organs receive blood of the same composition that is one organ does not receive left over blood that has passed through another organ .

- Because of this parallel arrangement blood flow through each systemic organ can be independently adjusted as needed.
- Blood is constantly reconditioned so that its composition remain relatively constant despite an ongoing drain of supplies to support metabolic activities and despite the continual addition of wastes from the tissues.

- Organ that recondition the blood normally receive much more blood than is necessary to meet their basic metabolic needs so that can adjust the extra blood to achieve homeostasis for example large percentage of the cardiac output are distributed to .
- 1. the digestive tract to pickup nutrient supplies.

- 2. to the kidneys to eliminate metabolic waste and adjust water and electrolyte composition .
- 3. to the skin to eliminate heat.

Blood flow to the other organs e.g heart . Skeletal muscles , brain and so on is solely for filling these organs metabolic needs and can be adjusted according to their level of activity. For example during exercise additional blood is delivered to the active muscles to meet their increased metabolic needs.

- Because reconditioning organs [digestive organ,kidneys and skin] receive blood flow in excess of their own needs . They can withstand temporary reduction in blood much better than can other organs that do not have this extra margin of blood supply . The brain in particular suffers irreparable damage when transiently deprived of blood supply.

- After only four minutes without O2 permenant brain damage occurs this high priority in the overall operation of the circulatory system is the constant delivery of adeguate blood to the brain which can least tolerate disrupted blood supply.
- In contrast the reconditioning organs can tolerate significant reductions in blood flow for quite a long time and often do for example

- During exercise some of the blood that normally flow through the digestive organs and kidneys is diverted to the skeletal muscles. Like wise to conserve body heat blood flow through the skin is markedly restricted during exposure to cold.

- Blood –flow
- Flow rate of blood through a vessel = is the volume of blood passing through per minute.
- Flow rate is directly proportional to the pressure gradient and inversely proportional to vascular resistance.
- F=P\R
- P is the pressure gradient which is the difference in pressure between the beginning and end of a vessel. Blood flow from area of higher pressure to an area of lower pressure down a pressure gradient.

- Contraction of the heart imparts pressure to the blood which is the main driving force for flow through a vessel. Contraction of the ventricle produce pressure which drive blood to the tissue through circulation . The greater the pressure gradient forcing blood through a vessel the greater is the flow rate through that vessel. It is the difference in pressure between the two ends of a vessel not the absolute pressure within the vessel determines flow rate

- Resistance: is the measure of the hindrance or opposition to blood flow through a vessel caused by friction between the moving fluid and the stationary vascular walls. As resistance to flow increases it is more difficult for blood to pass through the vessel so flow rate decreases [as long as the pressure gradient remains unchanged]. When resistance increases the pressure gradient must increase correspondingly to maintain the

- Same flow rate ,accordingly when the vessels offer more resistance to flow ,the heart must work harder to maintain adequate circulation.
- Resistance to blood flow depends on three factors:
- 1. viscosity of the blood.
- 2.vessel length.
- 3. vessel radius.

- Viscosity refers to the friction developed between the molecules of fluid as they slide over each other during flow of the fluid . The greater the viscosity the greater is the resistance to flow . In general the thicker a liquid the more viscous it is. Blood viscosity is determined primarily by the number of circulating red blood cells when excessive red blood cells are present blood flow is more sluggish than normal. Because blood rubs against the lining of the vessels as it flows past,

- The greater the vessel surface area in contact with the blood the greater the resistance to flow . Surface area is determined by both the length[L] and radius of the vessel.
- The major determinant of resistance to flow is the vessel's radius. Fluid passes more readily through a large vessel than through a smaller vessel . The reason is that a given volume of blood come in contact with much more of the surface area of a small-radius vessel than of a large –radius vessel resulting in greater resistance.

- Resistance is inversely proportional to the fourth power of the radius [multiplying the radius by itself four times]. Thus doubling the radius reduces the resistance to 1\16 its original value and therefore increases flow through the vessel 16 fold [at the same pressure gradient]. The converse is also true only 1\16th as much blood flows through a vessel at the same driving pressure when its radius is halved.

- Importantly the radius of arterioles can be regulated and is the most important factor in controlling resistance to blood flow throughout the vascular circuit.
- The systemic and pulmonary circulations each consist of closed systems of vessels.
- Capillary exchange is the entire purpose of the circulatory system. All other activities of the system are directed toward ensuring an adequate distribution of replenished blood to capillaries for exchange with all cells

- The arterioles, capillaries, and venules are collectively referred to as the micro-circulation because they are visible through a microscope [the micro-circulatory vessels are all located with in the organ].
- If all of the vessels in the body were strung end to end they could circle the circumference of the earth twice.

- Arteries serve as:
- 1. rapid –transit passage ways to the organ.
- 2. pressure- reservoir.
- Arteries are specialized to serve as rapid transit passageways for blood from the heart to the organs because of their large radius. Arteries offer little resistance to blood flow and act as pressure reservoir to provide the driving force for blood when the heart is relaxing.

- All vessels are lined with a thin layer of smooth flat endothelial cells that are continuous with the endothelial lining of the heart [endocardium].
- A thick wall made up of smooth muscle and connective tissue surrounds the arteries endothelial lining. Arterial connective contains an abundance of two types of connective tissue fibers.

- 1. collagen –fibers :which provide tensile strength against the high driving pressure of blood ejected from the heart .
- 2. elastin –fibers which give the arterial walls elasticity so that they behave much like a balloon.

As the heart pumps blood into arteries during ventricular systole a greater volume of blood enters the arteries from the heart than leaves them to flow into smaller vessels have a greater resistance to flow . The arteries elasticity enable

- Them to expand to temporarily hold this excess volume of ejected blood , storing some of the pressure energy imparted by cardiac contraction in their stretched walls just as a balloon expands to accommodate the extra volume of air you blow into .
- When the ventricle relaxes and ceases pumping blood into the arteries ,the stretched arterial walls passively recoil like an inflated balloon that is released . This recoil pushes the excess blood

- Contained in the arteries into the vessels downstream ensuring continued blood flow to the organs when the heart is relaxing and not pumping blood into the system. the heart alternately contract to pump blood into the arteries and then relaxes to refill from the veins . When the heart is relaxing and refilling no blood is pumped out. However capillary flow does not fluctuate between cardiac systole and diastole that is blood flow is continuous through the capillaries supplying the organs.

- The driving force for the continued flow of blood to the organs during cardiac relaxation is provided by the elastic properties of the arterial walls.
- Blood –pressure: is the force exerted by the blood against a vessel wall. It depends on:
- 1. volume of blood contained within the vessel.
- 2. compliance or dispensability of the vessel walls[how easily they can be stretched].

- If the volume of blood entering the arteries were equal to the volume of blood leaving the arteries during the same period , arterial blood pressure would remain constant this is not the case however.
- During ventricular systole a stroke volume of blood enters the arteries from the ventricle while only about one third as much blood leaves the arteries to enter the arterioles. During diastole no blood enters the arteries while blood continues to leave driven by elastic recoil.

- The maximum pressure exerted in the arteries when blood is ejected into them during systole is the systolic arterial blood pressure averages 120mmHg..
- The minimum pressure within the arteries when blood is draining off into the rest of the vessels during diastole is the diastolic arterial pressure averages 8ommHg.although ventricular pressure falls to 0mmHg during diastole arterial pressure does not fall to 0mmHg because the next cardiac contraction occurs and refill the arteries before all the blood drains off.

- Blood pressure can be measured indirectly by using sphygmomanometer.
- The technique involves balancing the pressure in the cuff against the pressure in the artery . When cuff pressure is greater than the pressure in the vessel ,the vessel is pinched closed so that no blood flows through it . When blood pressure is greater than cuff pressure the vessel is open and blood flows through .

- Pulse-pressure: the pulse that can be felt in an artery lying close to the surface of the skin is due the difference between systolic and diastolic pressures. This pressure difference is known as the pulse pressure when blood pressure is 120\80mmHg pulse pressure is 40mmHg.

- Mean arterial blood pressure: is the main driving force for blood flow. It is the average pressure driving blood forward into the tissues throughout the cardiac cycle.
- At resting heart rate about two thirds of the cardiac cycle is spent in diastole and only one third in systole.
- Mean arterial blood pressure= diastolic pressure+ 1\3 pulse pressure.

- The mean arterial blood pressure not the systolic or diastolic pressure is maintained and regulated by blood pressure reflexes.
- Because arteries offer little resistance to flow only a negligible amount of pressure energy is lost in them because of friction , therefore arterial pressures ,systolic,diastolic pulse or mean is essentially the same through the arterial tree.

- Arterioles: arterioles are the major resistance vessels in the vascular –tree because their radius is small enough to offer considerable resistance to flow. In contrast to the low resistance of the arteries the high degree of arteriolar resistance causes a marked drops in mean pressure as blood flows through these small vessels . On average the pressure falls from 93mmHg [the mean arterial blood pressure entering the arterioles] to 37mmHg the pressure of blood leaving the arterioles and entering the capillaries . This decline in pressure helps establish the pressure differential that encourage the flow of blood from the heart to the various organs downstream.

- Arteriolar resistance also converts the pulsatile systolic to diastolic pressure swings in the arteries into the non fluctuating pressure present in the capillaries.
- The radius and accordingly the resistance of arterioles supplying individual organ can be adjusted independently to accomplish two features:

- 1. to variably distribute the cardiac output among the systemic organs depending on the body's momentary needs.
- 2. to help regulate arterial blood pressure.
- Arteriolar walls contain very little elastic connective tissue . However they do have a thicker layer of smooth muscle that is richly innervated by sympathetic nerve fibers , the smooth muscle is also sensitive to many local chemical changes and to a few circulating hormones .

- Vascular-tone : arteriolar smooth muscle normally displays a state of partial contraction known as vascular tone which establish a baseline of arteriolar resistance. Two factors are responsible for vascular tone:
- 1. arteriolar smooth muscle has considerable myogenic activity that is its membrane potential fluctuate independent of any neural or hormonal influences leading to self-induced contractile activity.

- 2. the sympathetic fibers supplying most arterioles continually release Nor epinephrine which further enhances vascular tone.

This ongoing activity makes it possible to either increase or decrease the level of contractile activity to accomplish vasoconstriction or vasodilatation respectively. Were it not for tone it would be impossible to reduce the tension in an arteriolar wall to accomplish vasodilatation . Only varying degree of vasoconstriction would be possible.

- The fraction of the total cardiac output delivered to each organ is not always constant . It varies depending on the demands for blood at the time. The amount of the cardiac output received by each organ is determined by the number and caliber of arterioles supplying that area.

- The driving force [pressure] for flow is identical for each organ . Therefore differences in flow to various organs are completely determined by differences in the vascularization and by differences in resistance offered by the arterioles supplying each organ . On a moment to moment basis the distribution of cardiac output can be varied by differentially adjusting arteriolar resistance ih the vascular beds.

- Active- hyperemia: it is an abnormal need for blood. When muscle cells are more active metabolically they need more blood to bring in 02 and nutrients and to remove metabolic wastes. The increased blood flow meets these increased local needs. Conversely when muscle is in relaxed state the muscle cells need less blood and therefore there will local arteriolar vasoconstriction and a subsequent reduction in blood flow to the area.

- Local metabolic changes can thus adjust blood flow as needed without involving nerves or hormones.
- Local chemical factors which produce relaxation of arterioles: 1.decrease local 02 concentration.2.increase local CO2 concentration.3. increase local H+concentration.4. increased local K+ concentration.5. increased osmolarity.6.increased adenosine release.7. increased prostaglandin release.

- function of endothelial –cells
- 1. line the blood vessels and heart chambers ,serve as a physical barrier between the blood and the remainder of the vessel wall.
- 2.secrete vaso-active substances in response to local chemical and physical changes these substances cause relaxation[vasodilatation]or contraction[vasoconstriction]of the underlying muscle.

- 3. secrete substances that stimulate new vessel growth and proliferation of smooth muscle cells in vessel walls.
- 4. participate in the exchange of materials between the blood and surrounding tissue cells across capillaries through vesicular transport.
- 5. influence formation of platelet plugs ,clotting and clot dissolution.
- 6. participate in the determination of capillary permeability by contracting to vary the size of the pores between adjacent endothelial cells.

- Nitric-oxide NO
- Is small highly reactive short –lived gas molecule that once was known primarily as a toxic air pollutant. Nitric –oxide cause relaxation of arteriolar smooth muscle by inhibiting the entry of contraction –inducing Ca+ into these smooth muscle cells.
- Function of Nitric –oxide:
- 1. Causes relaxation of arteriolar smooth muscle , by means of this action nitric –oxide plays an important role in controlling blood flow through the tissue and in maintaining mean arterial blood pressure.

- 2. dilate the arterioles of the penis and clitoris thus serving as the direct mediator of erection of these reproductive organs . Erection is accomplished by rapid engorgement of these organs with blood.
- 3. used as a chemical warfare against bacteria and cancer cells by macrophages.
- 4. interfere with platelet function and blood clotting at sites of vessel damage.

- 5. serve as novel neurotransmitter in the brain and elsewhere.
- 6. play a role in the changes underlying memory.
- 7. by promoting relaxation of digestive tract smooth muscle , help regulate peristalsis [a type of contraction that pushes digestive tract contents forward].
- 8. relaxes the smooth muscle cells in the airways of the lungs,helping keep these passage open to facilitate movement of air in and out of the lungs.

- 9. modulate the filtering process involved in urine formation.
- 10. direct blood flow to 02-starved tissue.
- 11. may play a role in relaxation of skeletal muscle.

- Shear –stress:
- Due to friction blood flowing over the surface of the vessel lining creates a longitudinal force known as shear stress on the endothelial cells. An increase in shear stress causes the endothelial cells to release NO which diffuses to the underlying smooth muscle and promotes vasodilatation ,the resultant increase in arteriolar diameter reduces shear stress in the vessel . In response to shear stress on a long term basis endothelial cells orient themselves parallel to the direction of blood flow.

- Myogenic response to stretch:
- Arteriolar smooth muscle responds to being passively stretched by myogenically increasing its tone via vasoconstriction thereby acting to resist the initial passive stretch. Conversely a decrease in arteriolar stretching induces a reduction in myogenic vessel tone by promoting vasodilatation.

- The extent of passive stretch varies with the volume of blood delivered to the arterioles from the arteries. An increase in mean arterial pressure drives more blood forward into the arterioles and stretch them furtherwhere as occlusion blocks blood flow into the arterioles and reduces arteriolar stretch.

- Active –hyperaemia:
- When there is an increase in the activity of a tissue by any means there will an increase in blood flow and supply to the tissue by vasodilatation of the arterioles and opening of more collateral blood vessels and if these two process are not enough a new blood vessels will be formed by the process called angiogenesis.

- Reactive-hyperaemia:
- When the blood supply to a region is completely occluded arterioles in the region dilate because:
- 1. myogenic relaxation which occurs in response to the diminished stretch accompanying no blood flow.
- 2.. Changes in local chemical composition.

- After the occlusion is removed blood flow to the previously deprived tissue is transiently much higher than normal because the arteriolar are widely dilated . The post occlusion increase in blood flow is called reactive hyperaemia. It can take place in any tissue . Such a response is beneficial for rapidly restoring the local chemical composition to normal. Of course prolonged blockage of blood flow leads to irreversible change.

- Auto-regulation of blood flow:
- When mean arterial pressure falls [for example because of hemorrhage or weakened heart] the driving force is reduced so blood flow to organs decreases . The resultant changes in local metabolites and the reduced stretch in the arterioles collectively bring about arteriolar dilation to help restore tissue blood flow to normal despite the reduced driving pressure .

- On the negative side wide spread arteriolar dilatation reduces the mean arterial pressure still further which aggravate the problem.
- Conversely in the presence of sustained elevation in mean arterial pressure local chemical and myogenic influences triggered by the initial increased blood flow to tissues bring about an increase in arteriolar tone and resistance. This greater degree of vasoconstriction subsequently reduces tissue blood flow toward normal despite the elevated blood pressure.

- Auto-regulation or self –regulation is the term for these local arteriolar mechanisms that keep tissue blood flow fairly constant despite rather wide deviations in mean arterial driving pressure . Not all organs auto-regulate equally for example.
- 1. the heart and brain auto-regulate best.
- 2. the kidneys are good at auto-regulation.
- 3. skeletal muscle has poor auto-regulatory abilities.

- Therefore auto-regulation is a means by which each tissue resist alterations in its own blood flow secondary to changes in mean arterial pressure by making appropriate adjustments in arteriolar radius.

- Sympathetic nerve fibers supply arteriolar smooth muscle every where in the systemic circulation except in the brain. Increased sympathetic activity produces generalized arteriolar vasoconstriction where as decreased sympathetic activity leads to generalized arteriolar vasodilatation. These wide changes in arteriolar resistance bring about changes in mean arterial pressure because of their influence on total peripheral resistance=P\R applies to the entire circulation as well as to a single vessel.

- Flow [F] through all the vessels in either the systemic or pulmonary circulation is equal to the cardiac output.
- P is the pressure gradient equals the difference in pressure between the beginning and the end of the systemic circulatory system. the beginning pressure is the mean arterial pressure as the blood leaves the left ventricle at an average of 93mmHg. The end pressure in the right atrium is 0mmHg therefore 93-0=93mmHg which is equivalent to the mean arterial pressure.

- R is the resistance offered by all the systemic peripheral vessels . By far the greatest percentage of the total peripheral resistance is due to arteriolar resistance because arterioles are the primary resistance vessels. The extent of total resistance offered collectively by all the systemic arterioles influences the mean arterial pressure immensely.

- Adam provides an analogy to this relationship . At the same Adam restricts the flow of water down stream it increases the pressure up stream by elevating the water level in the reservoir behind the dam. Similarly generalized sympathetically induced vasoconstriction reflexly reduces blood flow downstream to the organ while elevating the up stream mean arterial pressure thereby increasing the main driving force for blood flow to all the organs.

- These effects seem counter productive? Why increase the driving force for flow to the organs by increasing arterial blood pressure. While reducing flow to the organs by narrowing the vessels supplying them?
- In effect the sympathetically induces arteriolar responses help maintain the appropriate driving pressure head [that is the mean arterial pressure] to all organs.

- The extent to which each organ actually receives blood flow is determined by local arteriolar adjustments that override the sympathetic constrictor effect. If all arterioles were dilated. Blood pressure would fall substantially s there would not be an adequate driving force for blood flow.
- Tonic sympathetic activity thus constricts most vessels [with the exception of those in the brain] to help maintain a pressure head on which organs can draw as needed through local mechanism that control arteriolar radius.

- The nor epinephrine released from sympathetic nerve endings combine with alpha adrenergic receptors on arteriolar smooth muscle to bring about vasoconstriction . Cerebral[brain] arterioles are the only ones that do not have alph receptors so no vasoconstriction occurs in the brain. Cerebral vessels are almost entirely controlled by local mechanism that maintain a constant blood flow to support a constant level of brain metabolic activity .

- In fact reflex vasoconstrictor activity in the remainder of the cardiovascular system is aimed at maintaining an adequate pressure head for blood flow to the vital organ[like the brain]. it is important that cerebral arterioles are not reflexly constricted by neural influence because brain blood flow most remain constant to meet the brains continual need for 02 no matter what is going on elsewhere in the body.

- Thus sympathetic activity contributes in an important way to maintaining mean arterial pressure assuring an adequate driving force for blood flow to the brain at the expense of organs that can better withstand reduced blood flow .other organs that really need additional blood such as active muscles [including active heart muscle] obtain it through local controls that override the sympathetic effect.

- Skeletal and cardiac muscle have the most powerful local control mechanism with which to override generalized sympathetic vasoconstriction . For example if you are peddling a bicycle the increased activity in the skeletal muscle of your legs bring about an overriding local vasodilatation in those particular muscles despite the generalized sympathetic vasoconstriction that accompanies exercise . As a result more blood flows through your leg muscles but not through your inactive arm muscles.

- There is no significant parasympathetic innervations to arterioles with the exception of the abundant parasympathetic vasodilator supply to the arterioles of the penis and clitoris . The rapid profuse vasodilatation induced by parasympathetic stimulation in these organs [by means of promoting release of NO] is largely responsible for accomplishing erection.
- Vasodilatation elsewhere is produced by decreasing sympathetic vasoconstrictor activity below its tonic level.

- Nor epinephrine combines with alpha receptor to cause vasoconstriction. Epinephrine combine with both beta2 and alpha 1 receptors. Activation of beta 2 cause vasodilatation but not all tissues have beta 2 receptors they are most abundant in the arterioles of the heart and skeletal muscles.
- During sympathetic discharge the released epinephrine combines with beta 2 receptors in the heart and skeletal muscle to reinforce vasodilatory mechanism in these tissues.

- Arterioles in digestive organs and kidneys in contrast are equipped only with alph1 receptors . Therefore the arterioles of these organs undergo more profound vasoconstriction during generalized sympathetic discharge than those in the heart and skeletal muscle do.

- Both vasopressin and angiotensin 11 are potent vasoconstrictors . their role in this regard is especially crucial during haemorrhage . A sudden loss of blood reduces the blood volume which triggers increased secretion of both these hormones to help restore blood volume.

- Capillaries: the sites for exchange of materials between blood and tissue cells ,branch extensively to bring blood with in the reach of every cell. There are no carrier-mediated transport systems across capillaries with the exception of these in the brain that play a role in the blood-brain barrier . Materials are exchanged across capillary walls mainly by diffusion.

- Diffusion molecules have only a short distance to travel between blood and surrounding cells because of the thin capillary wall and small capillary diameter coupled with the close proximity of every cell to a capillary . This short distance is important because the rate of diffusion slows down as the diffusion distance increases.
- Capillary walls are very thin 1 micron in thickness in contrast ,the diameter of human hair is 100 micron.

- Each capillary is so narrowed 7 micron average diameter that red blood cells 8 micron diameter have to squeeze through single file. Consequently plasma contents are either in direct contact with inside of the capillary wall or are only a short diffusing distance from it.
- Because of extensive capillary branching no cell is farther than 0.01 cm from a capillary.

- Total number of capillaries 10-40 billion capillaries and a surface area of 600meter square . Capillaries contain 5% of cardiac output [250 ml of blood]. Blood flows more slowly in the capillaries than elsewhere in the circulatory system . The extensive capillary branching is responsible for this slow velocity of blood flow through capillaries.

- Flow rate refer to the volume of blood per unit of time flowing through a given segment of the circulatory system .
- The velocity of flow is the linear speed or distance per unit of time with which blood flows forward through a given segment of the circulatory system.

- Because the circulatory system is a closed system the volume of blood flowing through any level of the system must equal the cardiac output.for example if the heart pumps out 5 liters of blood per minute and 5 liters per minute of blood return to the heart then 5 liters per minute must flow through the arteries, arterioles, capillaries and veins. Therefore the flow rate is the same at all levels of the circulatory system .

- How ever the velocity with which blood flows through the different segments of the vascular tree varies because velocity of flow is inversely proportional to the total cross sectional area of all the vessels at any given level of the circulatory system. The cross –sectional area of all the capillaries added together is about 1300 times greater than the cross –sectional area of the aorta because there are so many capillaries accordingly blood slows considerably as it passes through the capillaries.

- This slow velocity allows adequate time for exchange of nutrients and adequate time for exchange of nutrients and metabolic end products between blood and tissue cells which is the sole purpose of the entire circulatory systems . As the capillaries rejoin to form veins the total cross- sectional area is once again reduced and the velocity of blood flow increases as blood returns to the heart.

- Also because of the capillaries tremendous total cross- sectional area the resistance offered by all the capillaries is much lower than that offered by all the arterioles even though each capillary has a smaller radius than each arteriole. Furthermore arteriolar caliber and accordingly resistance is subject to control where as capillary caliber can not be adjusted.

- Water –filled capillary pores permit passage of small water –soluble substances. In most capillaries narrow water –filled gaps or pores lie at the junctions between the cells these pores permit passage of water –soluble substances. Lipid soluble substances such as 02 and CO2 can readily pass through the endothelial cells themselves by dissolving in the lipid bilayer barrier.

- The size of the capillary pores varies from organ to organ . At one extreme the endothelial cells in brain capillaries are joined by tight junctions so that pores are nonexistent these junctions prevent trans-capillary passage of materials between the cells and thus constitute part of the protective blood –brain barrier. In most tissues small water –soluble substances such as ions. Glucose and amino acids can readily pass through the water –filled pores but large non lipid –soluble material that can not fit through the pores such as plasma proteins are kept from passing.

- Liver capillaries have such large pores that even proteins pass through readily. The leakiness of various capillary beds is therefore a function of how tightly the endothelial cells are joined which varies according to the different organ cells.
- Recent studies however suggest that endothelial cells can actively change to regulate capillary permeability that is in response to appropriate signals. Thus the degree of leakiness does not necessarily remain constant for given capillary bed.

- For example histamine increases capillary permeability by triggering contractile responses in endothelial to widen the intercellular gaps . This is not a muscular contraction because no smooth muscle cells are present in capillaries .
- Because of these enlarged pores the affected capillary wall is leakier as a result normally retained plasma proteins escape into the surrounding tissue where they exert an osmotic effect. A long with histamine induced vasodilatation the resulting additional local fluid retention contribute to inflammatory swelling

- Vesicular transport also plays a limited role in the passage of materials a cross the capillary wall .large non-lipid soluble molecule such as protein hormones that must be exchanged between blood and surrounding tissues are transported from one side of the capillary wall to the other in endocytotic –exocytotic vesicle.

- Pre-capillary sphincters are not innervated but have a high degree of myogenic tone and sensitive to local metabolic changes .they act stopcocks to control blood flow through the particular capillary that each one guards.
- Arterioles perform a similar function for a small groups of capillaries.
- Capillaries themselves have no smooth muscle so they can not actively participate in regulating their own blood flow.

- Generally tissues that are more metabolically active have a greater density of capillaries . Muscles for example have relatively more capillaries than their tendinous attachments.
- Only about 10% of the pre-capillary sphincters in a resting muscle are open at any moment however so blood is flowing through only about 10% of the muscles capillaries.

- As chemical concentrations strat to change in a region of the muscle tissue supplied by closed down capillaries , the pre-capillary sphincters and arterioles in the region relax. Restoration of the chemical concentrations to normal as a result of increased blood flow to that region removes the impetus for vasodilatation so the pre –capillary sphincters close once again and the arterioles return to normal tone. In this way blood flow through any given capillary is often intermittent as a result of arteriolar and arteriolar and pre-capillary sphincter action working in concert .

- When the muscle as a whole becomes more active a greater percentage of the pre-capillary sphincters relax simultaneously opening up more capillary beds while concurrent arteriolar vasodilatation increases total blood flow to the organ . As a result of more blood flowing through more open capillaries , the total volume and surface area a available for exchange increase and the diffusion distance between the cells and an open capillaries decreases.

- Thus local blood flow through a particular tissue [assuming a constant blood pressure]is regulated by:
- 1.the degree of resistance offered by the arteriole in the organ controlled by sympathetic activity and local factors.
- 2. the number of open capillaries controlled by action of the same local metabolic factors on pre-capillary sphincters.

- Exchange between blood and tissue cells are not made directly. Interstitial fluid the true internal environment is in immediate contacts with cells act as go-between . Only 20% of the ECF circulate as plasma , the remaining 80% consists of interstitial fluid which bath all the cells in the body. Cells exchange materials directly with interstitial fluid with the type and extent of exchange being governed by the properties of cellular plasma membrane.

- Movement across the plasma membrane may be either 1. passive [that is by diffusion down electro-chemical gradient or by facilitated diffusion] 2. or active [that is by active carrier-mediated transport or by vesicular transport].
- Exchange across the capillary wall between plasma and interstitial fluid are largely passive. The only transport across this barrier that require energy is the limited vesicular transport .

- Because capillary wall are highly permeable exchange is so through that the interstitial fluid takes on essentially the same components as incoming arterial blood with the exception of the large plasma proteins that usually do not escape from the blood . Therefore when we speak of exchanges between blood and tissue cells we tactily include interstitial fluid as a passive intermediary.

- Because there are no carrier – mediated transport system in most capillary walls , solutes cross primarily by diffusion down concentration gradients . The chemical composition of arterial blood is carefully regulated to maintain the concentration of individual movement in the appropriate direction across the capillary walls.

- Bulk-flow: is a volume of protein free plasma actually filters out of the capillary. Mixes with surrounding interstitial fluid and the reabsorbed. They called bulk because the various constituents of the fluid are moving together in bulk or as a unit.
- The capillary wall acts like a sieve with fluid moving through its water –filled pores .

- When a pressure inside the capillary exceeds pressure on the outside fluid is pushed out through the pores in a process known as ultra filtration[filtration]. The fluid which move out of the capillary is protein free. The filtration process always needs pressure.

- Reabsorption: it is a process which move fluid toward the lumen of capillary . When inward – driving pressures exceed outward pressures across the capillary wall net inward movement of fluid from the interstitial fluid into the capillaries takes-place through the pores.
- Bulk –flow occurs because of differences in the hydrostatic and colloid osmotic pressures between plasma and interstitial fluid.

- Capillary-blood pressure: on average the hydrostatic pressure is 37mmHg at the arteriolar end of a tissue capillary[compared to a mean arterial of 93mmHg]. It decline even further to 17mmHg at the capillary venular end.
- Plasma-colloid osmotic also known as oncotic pressure: is a force caused by colloidal dispersion of plasma proteins . It encourages fluid movement into the capillaries. Plasma – colloid osmotic pressure averages 25mmHg.

- Interstitial fluid hydrostatic pressure; is the fluid pressure exerted on the outside of the capillary wall by interstitial fluid. This pressure tends to force fluid into the capillaries. it is either at or slightly below atmospheric pressure we can say 1mmHg above atmospheric pressure.
- interstitial fluid colloid osmotic pressure: is very close to zero tend to move fluid outside the capillary into interstitium.

- Therefore the two pressures that tend to force fluid out of the capillaries are capillary blood pressure and interstitial fluid colloid osmotic pressure. The two opposing pressure that tend to force fluid into the capillary are plasma –colloid osmotic pressure and interstitial fluid hydrostatic pressure.
- A positive net exchange pressure[when the outward pressure exceeds the inward pressure] represents an ultra-filtration pressure.

- A negative net exchange pressure [when the inward pressure exceeds the outward pressure] represents a reabsorptive pressure.
- Ultra-filtration takes-place at the beginning of the capillary as this outward pressure gradient forces a protein –free filtrate through the capillary pores.
- Reabsorption of fluid take place as this inward pressure gradient forces fluid back into the capillary at its venular end.
- No active forces or local energy expenditure are involved in the bulk exchange of fluid between the plasma and the surrounding interstitial fluid.

- Role of bulk flow: bulk flow that is ultra filtration and reabsorption are not important in the exchange of nutrients and waste.
- Bulk flow is extremely important however in regulating the distribution of ECF between the plasma and interstitial fluid. If the plasma volume is reduced for example by hemorrhage blood pressure falls .the resulting lowering of capillary blood pressure alters the balance of forces across the capillary walls. Because the net outward pressure is decreased while the net inward pressure remains unchanged ultrafluid is shifted from the interstitial compartment into the plasma as a result of reduced filtration and increased reabsorption.

- The extra fluid soaked up from the interstitial fluid provide additional fluid for the plasma temporarily compensating for the loss of blood. Conversely if the plasma volume becomes over expanded as with excessive fluid intake the resulting rise in capillary blood pressure forces extra fluid from the capillaries into the interstitial fluid temporarily relieving the expanded plasma volume until the excess fluid can be eliminated from the body by long –term measure such a increased urinary output.

- These internal fluid shifts between the two ECF compartments occur automatically and immediately when ever the balance of forces acting across the capillary walls is changed . They provide a temporary mechanism to help keep plasma volume fairly constant.

- Lymphatics:
- The lymphatic system is an accessory route by which interstitial fluid can be returned to the blood . Even under normal circumstances slightly more fluid is filtered out the capillaries into the interstitial fluid than is reabsorbed from the interstitial fluid back into the plasma.
- On average the net ultra-filtration pressure starts at 11mmHg at the beginning of the capillary whereas the net reabsorption pressure only reaches 9mmHg by the vessel end.

- Because of this pressure differential on average more fluid is filtered out of the first half of the capillary than is reabsorbed in its last half. The exta fluid filtered out as a result of this filtration-reabsorption imbalance is picked up by the lymphatic –system.
- The lymphatic system is an extensive network of one –way vessels provided an accessory route by which fluid can be returned from the interstitial fluid to the blood

- Pick and flow of lymph:
- Small blinded terminal lymph vessels known as initial lymphatics permeate almost every tissue of the body . The endothelial cells forming the walls of initial lymphatics slightly overlap like shingles on a roof with their overlapping edges being free instead of attached to the surrounding cells. This arrangement creates one-way valve like openings in the vessel.

- Fluid pressure on the outside of the vessel pushes the innermost edge of a pair of overlapping edges inward creating a gap between the edges [that is opening the valve]this opening permits interstitial fluid to enter. Once interstitial fluid enters a lymphatic vessel it is called lymph. Fluid pressure on the inside forces the overlapping edges together closing the valves so that lymph does not escape.

- These lymphatics valve like opening are much larger than the pores in blood capillaries . Consequently large particles in the interstitial fluid such as escaped plasma proteins and bacteria can gain access to initial lymphatics but are excluded from blood capillaries.
- Initial lymphatics converge to form larger and larger lymph vessels which eventually empty into the venous system near where blood enters the right atrium. there is no heart to push lymph toward the venous system.

- Lymph flow is accomplished by two mechanisms:
- 1. lymph vessels beyond the initial lymphatics are surrounded by smooth muscle which contract rhythmically as a result of myogenic activity . When this muscle is stretched because the vessel is distended with lymph the muscle inherently contracts more forcefully pushing the lymph through the vessel . This intrinsic lymph pump is the major force for propelling lymph . Stimulation of lymphatic smooth muscle by the sympathetic nervous system further increases the pumping activity of the lymph vessels

- 2. because lymph vessels lie between skeletal muscles , contraction of these muscles squeezes the lymph out of the vessels . One way valves spaced at intervals within the lymph vessels direct the flow of lymph toward its venous outlet in the chest. The average rate of flow through the lymph vessels is 3 liters per day compared with 7200 liters per day through the circulatory system.

- Functions of the lymphatic system
- 1. return of excess filtered fluid
- Normally capillary filtration exceeds reabsorption by about 3 liters per day [20liters filtered 17 liters reabsorbed] the cumulative effects of this process being repeated with every heart beats results in the equivalent of more than the entire plasma volume being left behind in the interstitial fluid each day.

- 2. defense against disease
- The lymph percholate through lymph nodes located en-route with in the lymphatic system, passage of this fluid through the lymph nodes is an appropriate aspects of the body's defense mechanism against disease for example bacteria picked up from the interstitial fluid are destroyed by special phagocytes within the lymph nodes.

- 3. transport of absorbed fat.
- The lymphatic system is important in the absorption of fat from the digestive tract. The end products of the digestion of dietary fat are packed by cells lining the digestive tract into fatty particles that are too large to gain access to the blood capillaries but can easily enter the initial lymphatic.

- Return of filtered protein
- Most capillaries permit leakage of some plasma proteins during filtration these proteins can not readily be absorbed back into the blood capillaries but can easily gain access to the initial lymphatic. if the proteins were allowed to accumulate in the interstitial fluid rather than being returned to the circulation via the lymphatic the interstitial fluid –colloid osmotic pressure [an outward pressure] would progressively increase while the plasma –colloid osmotic pressure [an inward pressure] would progressively falls.

- As a result filtration forces would gradually increase and reabsorption forces would gradually decrease , resulting in progressive accumulation of fluid in the interstitial spaces at the expense of loss of plasma volume . Edema occurs when too much interstitial fluid accumulates.

- Veins:
- Blood leaving the capillary beds enters the venous system for transport back to the heart , the venous system complete the circulatory system. Capillaries drain into venules which progressively converge to form veins that exit the organ. In contrast to arterioles venules have little tone and resistance, excessive communication take place via chemical signals between venules and nearby arterioles this venulo-arteriolar signaling is vital to matching capillary inflow and outflow within an organ.

- Veins serve as a blood reservoir as well as passage ways back to the heart . Veins have a large radius so they offer little resistance to flow . Furthermore because the total cross-sectional area of the venous system gradually decreases as smaller veins converge into progressively fewer but larger vessels , blood flow speeds up as blood approaches the heart. Because of their storage capacity veins are often called capacitance – vessels . Veins have much thinner walls with less smooth muscle than arterioles.

- Veins in contrasts to arterioles have very little elasticity because venous connective tissue contains considerably more collagen fibers than elastic fibers. Unlike arteriolar smooth muscle venous smooth muscle has little inherent myogenic tone. Because of these features veins are highly distensible to accommodate additional volumes of blood with only a small increase in venous pressure

- Arteries stretched by an excess volume of blood will recoil because of the elastic fibers in their walls driving the blood forward.
- Veins containing an extra volume of blood simply stretch to accommodate the additional blood without tending to recoil. In this way veins serve as a blood reservoir that is when demand for blood are low the veins can store extra blood in reserve because of their passive distensibility. Under resting conditions the veins contain more than 60% of the total blood volume.

- Contrary to a common miss conception blood stored in the veins is not being held in a stagnant holding tank . Normally all the blood is circulating all the time. When blood is at rest and many of the capillary beds are closed the capacity of the venous reservoir is increased as extra blood bypass the capillaries and enters the veins . When this extra volume of blood stretches the veins the blood moves forward through the veins more slowly because the total cross-sectional area of the veins has been increased as a result of the stretching ,therefore the blood spends more time in the veins.

- As result of this slower transit time through the veins the veins are essentially storing the extra-volume of blood because it is not moving forward as quickly to the heart to be pumped out again. When the stored blood is needed such as during exercise extrinsic factors reduce the capacity of the venous reservoir and drive the extra-blood from the veins to the heart so it can be pumped to the tissues.

- Venous-capacity: is the volume that the veins can accommodate . It depends on
- A. distensibility of the vein walls[how much they can stretch to hold blood].
- B. the influence of any externally applied pressure squeezing inwardly on the veins.
- At a constant blood volume as venous capacity increases more blood remains in the veins instead of being returned to the heart .such venous storage decreases the effective circulating blood volume.[the volume of blood returned to and pumped out of the heart]. Conversely when venous capacity decreases more blood is returned to the heart and subsequently pumped out. these changes in venous capacity directlly influence the magnitude of venous return.

- Venous- return : is the volume of blood entering each atrium per minute from the veins.
- By the time the blood enters the venous system blood pressure averages only 17mmHg . However because atrial pressure is near 0mmHg a small but adequate driving pressure still exist to promote the flow of blood through the large radius low resistance veins. if atrial pressure becomes pathologically elevated as in the presence of a leaky AV valve the venous to atrial pressure gradient is decreased reducing venous return and causing blood to dam up in the venous system . Elevated atrial pressure is thus one cause of congestive heart failure.

- In addition to the driving pressure imparted by cardiac contraction five other factors enhance venous return:
- 1. sympathetically induced venous vasoconstriction.
- 2.effect of venous valves.
- 3. skeletal muscle activity.
- 4. respiratory activity.
- 5. the effect of cardiac suction.
- Most of these secondary factors affect venous return by influencing the pressure gradient between the veins and the heart.

- Effect of sympathetic activity on venous return:
- Veins are not very muscular and have little inherent tone but venous smooth muscle is abundantly supplied with sympathetic nerve fibers. Sympathetic stimulation produces venous vasoconstriction which modestly elevates venous pressure this in turn increases the pressure gradient to drive more of the stored blood from the veins into the right atrium thus enhancing venous return.

- Veins normally have such a large radius that the moderate vasoconstriction from sympathetic stimulation has little effect on resistance to flow , even when constricted veins still have a relatively large radius and are still low –resistance vessels. in addition to mobilizing the stored blood venous vasoconstriction enhance venous return by decreasing venous capacity ,with the filling capacity of the veins reduced less blood draining from the capillaries remains in the veins but continues to flow instead toward the heart.

- It is important to recognize the different outcomes of vasoconstriction in arterioles and veins . Arteriolar vasoconstriction immediately reduces flow through these vessels because of their increased resistance [less blood can enter and flow through a narrowed arterioles]. Where as venous vasoconstriction immediately increases flow through these vessels because of their decreased capacity [narrowing of veins squeeze out more of the blood already in the veins ,increasing blood flow through these vessels].

- Effect of skeletal muscle activity on venous return:
- Many of the large veins in the extremities lie between skeletal muscles so muscle contraction compresses the veins. This external venous compression decreases venous capacity and increases venous pressure in effect squeezing blood in the veins forward toward the heart. this pumping action known as the skeletal muscle pump in one way extra-blood stored in the veins is returned to the heart during exercise . Increased sympathetic activity and the resultant venous vasoconstriction also accompany exercise further enhancing venous return . The skeletal muscle pump also counters the effect of gravity on the venous system.

- Effect of gravity on venous pressure:
- In an up right adult the blood in the vessels extending between the heart and the foot is equivalent to 1.5meter column of blood the pressure exerted by this column of blood as a result of the effect of gravity is 90mmHg. The pressure imparted to the blood by the heart has declined to about 10mmHg in the lower leg veins because of frictional losses in preceding vessels.

- Together these pressures produce a venous pressure of 100mmHg in the ankle and foot veins.similary the capillaries in the region are subjected to these gravitational effects. When a person is lying down the force of gravity is uniformly applied so it need not be considered. When a person stands up however gravitational effects are not uniform . In addition to the usual pressure from cardiac contraction ,vessels below heart level are subject to pressure from the weight of the column of blood extending from the heart to the level of the vessels.

- There are two important consequences of this increased pressure :
- 1. the distensible veins yield under the increased hydrostatic pressure further expanding so their capacity is increased , even though the arteries are subject to the same gravitational effects they are not nearly as distensible and do not expand like veins. Much of the blood entering from the capillaries tends to pool in the expanded lower leg veins instead of returning to the heart . Because venous return is reduced cardiac out put decreases and the effective circulating volume shrinks.

- 2. the marked increase in capillary blood pressure resulting from the effect of gravity causes exceesive fluid to filter out of capillary beds in the lower extremities producing localized edema [that is swollen feet and ankles].
- Two compensatory measures normally counteract these gravitational effects:

- 1. the fall in mean pressure that occurs when a person moves from a lying –down to an upright position triggers sympathetically induced venous vasoconstriction which drives some of the poled blood forward.
- 2. the skeletal muscle pump interrupt the column of blood by completely emptying given vein segments intermittently so that a particular portion of a vein is not subjected to the weight of the entire venous column from the heart to that portion level. Reflex venous vasoconstriction can not completely compensate for the gravitational effects without skeletal muscle activity.

- When a person stands still for long time ,therefore blood flow to the brain is reduced because of the decline in effective circulatory volume. Despite reflexes aimed at maintaining mean arterial pressure ,reduced flow of blood to the brain inturn leads to fainting which returns the person to a horizontal position eliminating the gravitational effects on the vascular system and restoring effective circulation [fainting is a remedy to the problem not to the problem it self].

- Because the skeletal muscle pump facilitates venous return and helps counteract the detrimental effects of gravity on the circulatory system , when you are working at a desk it is a good idea to get up periodically and when you are on your feet to move around the mild muscular activity gets the blood moving . It is further recommended that people who must be on their feet for long periods of time use elastic stockings that apply continuous gentle external compression similar to the effect of skeletal muscle contraction to further counter the effect of gravitational pooling of blood in the leg veins.

- Venous –valves:
- Large veins are equipped with one way valves spaced at 2-4cm intervals, these valves let blood move forward toward the heart but keep it from moving back toward the tissues.
- These venous valves also play a role in counter acting the gravitational effects of upright posture by helping minimize the backflow of blood that tends to occur when a person stands up and by temporarily supporting portions of the column of blood when skeletal muscle are relaxed.

- Varicose- veins occurs when the venous valves become incompetent and can no longer support the column of blood above them.
- Effect of respiratory –activity on venous return:
- As a result of respiratory activity the pressure within the chest averages 5mmHg less than atmospheric pressure. As the venous system returns blood to the heart from the lower regions of the body it travels through the chest cavity where it is exposed to this sub-atmospheric pressure because the venous system in the limbs and abdomen is subject to normal atmospheric pressure , an externally applied pressure gradient exists between the lower veins

- [at atmospheric pressure]and the chest veins [at 5mmHg less than atmospheric pressure]. This pressure difference squeezes blood from the lower veins to the chest veins promoting increased venous return this is called respiratory pump.

- During exercise there will be :
- 1. increase respiratory activity.
- 2. increase in skeletal muscle activity.
- 3. venous vasoconstriction.

All the above enhance venous return during exercise.

- The heart function as a suction pump to facilitate cardiac filling:
- During ventricular contraction the AV valves are drawn downward enlarging the atrial cavities .as a result the atrial pressure transiently drop below 0mmHg thus increasing the vein to atria pressure gradient so that venous return is enhanced . In addition the rapid expansion of the ventricular chambers during ventricular relaxation creates a transient negative pressure in the ventricles so that blood is sucked in from the atria and veins that is the negative ventricular pressure increases the vein to atria to ventricular pressure gradient , further enhancing venous return.

- Regulation of blood pressure
- Mean arterial pressure is the blood pressure that is monitored and regulated in the body , not the arterial systolic and diastolic or pulse pressure nor the pressure in any other part of the vascular tree. Blood pressure is regulated by controlling:
- 1. cardiac –output.
- 2. total peripheral –resistance.
- 3.blood –volume.

- Mean arterial pressure : is the main driving force for propelling blood to the tissues. This pressure must be closely regulated for two reasons:
- 1. it must be high enough to ensure sufficient driving pressure without this pressure the brain and other organs will not receive adequate flow no matter what local adjustment are made in the resistance of the arteriole supplying them.
- 2. the pressure must not be so high that it create extra work for the heart and increases the risk of vascular damage and possible rupture of small blood vessrls.

- Because mean arterial pressure depends on the cardiac output and the degree of arteriolar vasoconstriction if the arterioles in one organ dilate the arterioles in other organs must constrict to maintain an adequate arterial blood pressure . An adequate pressure is needed to provide a driving force to push blood not only to the vasodilated organ but also to the brain which depends on a constant blood supply.

- When a person moves from lying down to standing up position ,pooling of blood in the leg veins from the gravity effect reduces venous return ,decreasing stroke volume and thus lowering cardiac output and blood pressure. This fall in blood pressure is normally detected by the baro-receptors which initiate immediate compensatory responses to restore blood pressure to its proper level.

- Mean arterial pressure is constantly monitored by baro-receptors [pressure –sensors] within the circulatory system . When deviation from normal are detected multiple reflex responses are initiated to return mean arterial pressure to its normal value [short –term within seconds] . Short term adjustment are made by alterations in cardiac output and total peripheral resistance mediated by means of autonomic nervous system influences on the heart ,veins and arterioles.

- Like any reflex the baro-receptors reflex include a receptors ,an afferent pathway, integrating center, an efferent pathway and effecter organ.
- The most important receptors involved in the moment to moment regulation of blood pressure ,the carotid sinus and aortic arch baro-receptors are mechano-receptors sensitive to changes in both mean arterial pressure and pulse pressure. Their responsiveness to fluctuations in pulse pressure enhances their sensitivity as pressure sensors. Because small changes in systolic or diastolic pressure may alter the pulse pressure without changing the mean pressure.

- These baro-receptors are strategically located to provide critical information about arterial blood pressure in the vessels leading to the brain. The baro-receptors constantly provide information about mean arterial pressure. In other words they continuously generate action potential in response to the ongoing pressure within arteries. when arterial pressure [either mean or pulse pressure] increases the receptor potential of these baro-receptors increases ,thus increasing the rate of firing in the corresponding afferent nerouns.

- Conversely a decrease in mean arterial pressure slow the rate of firing generated in the afferent neurons by the baro-receptors.
- The integrating center that receives the afferent impulses about the state of mean arterial pressure is the cardio-vascular center located in the medullae oblongata with in the brain stem. The efferent pathway is the autonomic nervous system. The cardiovascular control center alters the ratio between sympathetic and para-sympathetic activity to the effecter organs [the heart and the blood vessels] .

- If for any reason mean arterial pressure rises above normal ,the carotid sinus and aortic arch baro-receptors increase the rate of firing in their respective afferent neurons. On being informed by increased afferent firing that the blood pressure has become too high, the cardiovascular control center responds by decreasing sympathetic and increasing para-sympathetic activity to the cardiovascular system.

- The efferent signals decrease heart rate , decrease stroke volume and produce arteriolar and venous vasodilatation which in turn lead to a decrease in cardiac output and a decrease in total peripheral resistance with subsequent fall in blood pressure back toward normal.

- Conversely when blood pressure falls below normal baro-receptors activity decreases inducing the cardiovascular center to increase sympathetic cardiac and vasoconstrictor nerve activity while decreasing its para-sympathetic out put. this pattern of activity leads to an increase in heart rate and stroke volume coupled with arteriolar and venous vasoconstriction . These changes increase both cardiac out put and total peripheral resistance raising blood pressure back toward normal.

- Long –term regulation of blood pressure :

They require minutes to days to bring blood pressure to normal . They involve adjusting total blood volume by restoring normal salt and water balance through mechanisms that regulate urine output and thirst. The size of total blood volume in turn has a profound effect on cardiac output and mean arterial blood pressure. The principle of this control is water follow salt intake for example if ingest salt you will drink water so the plasma volume and blood volume will increase this will increase venous return and cardiac out put which lead to increase in blood pressure. But if you drink water a lone you can not increase blood pressure because this will inhibit ADH hormone release and will excreted in the urine .

- Shock: is a decrease in cardiac output which lead to inadequate blood flow to the tissues it can divide in to
- 1. hypovolaemic- shock
- 2. cardiogenic –shock.[weakened heart].
- 3. vasogenic –shock[wide spread vasodilatation triggered by the presence of vasodilator substances as in septic and anaphylactic shock.
- 4. neurogenic –shock [nerve- produced] due to loss of sympathetic vascular tone leads to generalized vasodilatation.

- Consequences and compensation of shock
- Loss of blood ----decrease in venous return ----fall in cardiac output----fall in blood pressure.
- Compensatory measure immediately attempt to maintain adequate flow to the brain. The baro-receptor reflex response to the fall in blood pressure brings about increased sympathetic and decreased para-sympathetic activity to the heart. The result is an increase in heart rate to offset the reduced stroke volume brought about by the loss of blood volume.

- With sever fluid loss the pulse is weak because of the reduced stroke volume but rapid because of the increased heart rate. Increased sympathetic activity to the veins produces generalized venous vasoconstriction which leads to increase in venous return. Simultaneously sympathetic stimulation of the heart increases the heart contractility so that it beats more forcefully and ejects a greater volume of blood likewise increasing the stroke volume. the increase in heart rate and in stroke volume collectively increase cardiac output.

- Sympathetically induced generalized arteriolar vasoconstriction leads to an increase in total peripheral resistance. Together the increase in cardiac output and total peripheral resistance bring about a compensatory increase in arterial blood pressure.
- The original fall in arterial blood pressure is also accompanied by a fall in capillary blood pressure which results in fluid shifts from the interstitial fluid into the capillaries to expand the plasma volume . This response is some times termed auto-transfusion. This ECF fluid shift is enhanced by plasma protein synthesis by the liver during the next few days following haemorrhage. The plasma proteins exerts a colloid osmotic pressure that helps retain fluid in the plasma.

- Urinary output is reduced thereby conserving water that normally would have been lost from the body . Reduction in urinary output results from decreased renal blood flow caused by compensatory renal arteriolar vasoconstriction. Increased thirst is also stimulated by a fall in plasma volume . Over a longer course of time [a weak or more] lost red blood cells are replaced through increased red blood cell production triggered by a reduction in 02 delivery to the kidneys.

- Venous pulsation:
- The pulsation observed in the jugular veins reflects the pressure changes in the right atrium provided no obstruction of the vein exists . As the atrium contracts so the pressure in the atrium rises to force blood into the right ventricle at the end of ventricular diastole. This rise in atrial pressure shows in the jugular veins as the a-wave which begins at the peak of the P-wave of the ECG and immediately before the onset of the first heart sounds.

- As the atrium relaxes, the intra-atrial pressure falls represented by the down stroke from the peak of the a- wave. But at the same ventricular systole begins and the intraventricular pressure rises above that in the atrium resulting in closure of the tricuspid valve . As the valve cusps balloon into the atrial cavity there is a temporary halt in the falling intra-atrial pressure and transient rise shown as the c- wave. The onset of the a-wave corresponds with the incidence of the tricuspid component of the first heart sound.

- As atrial relaxation continues after the c-wave the pressure also continues to fall until at the X-trough it reaches its lowest point. With inflow of blood from the great veins into the atrium atrial pressure begins to rise again to the second peak of the venous pulse which is the V-wave . At this point ventricular diastole has proceeded far enough for the intra-atrial to exceed that in the ventricle and the tricuspid valve opens.

- The intra-ventricular pressure is still falling and blood flows through the valve into the ventricle with resultant fall in the intra-atrial pressure also until at the Y-trough. The ventricle is filled and the pressure in ventricle and atrium begins to rise again to even out until the onset of the next a-wave. Any rise in right atrial pressure will cause an increase in the height of the a-wave thus if tricuspid stenosis is present very large a-waves are seen in the neck.

- Summary of JVP:
- A- wave is due to atrial contraction.
- C-wave is due to transmitted carotid impulse at the onset of systole[not usually visible].
- V-wave is due to passive atrial filling against closed tricuspid valve in systole.
- X- descent is due to right atrial relaxation and descent of tricuspid valve in systole.
- Y-descent is due to passive filling of right ventricle at the start of diastole.
- The two peaks of the a-and v-waves are the most easily seen

- The hemodynamic effect of respiration on CVS:
- There is a fall in intra-thoracic pressure during inspiration which tends to suck blood into the chest producing an increase in the flow of blood through the right heart. However a substantial volume of blood is sequestered in the chest as the lungs expand , the increase in the capacities of the pulmonary vascular bed usually exceeds any increase in the output of the right heart and there is therefore a reduction in the flow of blood into the left heart during inspiration.

- Therefore during inspiration there will be:
- 1. a fall in jugular venous pressure.
- 2. a fall in arterial blood pressure up 10mmHg.
- 3. acceleration of heart –rate [rapid heart –rate].
- 4. splitting of second heart sound.

Inspiration prolongs right ventricle ejection delaying P2 and shorten left ventricle ejection advancing A2.

- In contrast expiration is accompanied by a fall in venous return to the right heart, a reduction in the out put of the right heart, a rise in the venous return to the left heart[as blood is squeezed out of the lungs] and increase in the out put of the left heart.
- Therefore during expiration there will be:
- 1. increase in jugular venous pressure.

- 2. rise in arterial blood pressure.
- 3. slowing of heart rate.
- 4. fuses of the second heart sound.

Pulses –paradoxus : this term is used to describe the dramatic fall in blood pressure during inspiration that is characteristic of tamponade ,pericardial constriction and sever air-- way obstruction . The phenomenon is an exaggeration of the normal state of affairs.

- In airway obstruction it is due to accentuation of the changes in intra-thoracic pressure with respiration. In pericardial disease however compression of the heart prevents the normal increase in flow through the right heart on inspiration which exaggerates the usual drop in venous return to the left heart and produces a marked fall in blood pressure.

- Pressure values in cardiac cycle:
- 1.Left side of the heart;
- A. left atrium 4-12mmHg
- B. left ventricle systole 90-140mmHg.
- end-diastole 4-12mmHg.
- C. aorta systolic 90-140mmHg.
- diastolic 60-90mmHg.
- mean 70—105mmHg

- 2. right side of the heart:
- A. Pulmonary artery.
- Systolic 15-30mmHg.
- Diastolic 5-15mmHg.
- Mean 10-20mmHg.
- B. right atrium 0-8mmHg.
- C. right ventricle

Systolic 15-30mmHg.

End-diastolic 0-5mmHg.

- Examination of the arterial pulse :
- The character of the pulse is determined by both stroke volume and arterial compliance and should be assessed by palpating the carotid arteries. large stroke volume typically produce a bounding pulse with wide amplitude as in anaemia ,aortic regurgitation and other causes of large stroke volume.
- Low stroke volume as in poor left ventricular function ,mitral stenosis and other causes produce thin ,thready weak pulse. In aortic stenosis there will impedance of left ventricular emptying and may cause slow rising weak and delayed pulse.

- Arteries are elastic and absorb or dampen the pulse wave. If they become non-compliant [stiff and rigid] due to the effects of ageing ,hypertension or atherosclerosis they may amplify the pulse wave. A prominent pulse can therefore be a feature of widespread arterial disease , moreover the relatively common combination of poor left ventricular function and wide spread arterial disease can produce a seemingly normal pulse.