Physics of the Cardiovascular System (CVS)

Cardiovascular system (CVS): Blood, Vessels, Heart
1. Supply energy (fuel from food)
2. Supply O_2 from the air we breathe
3. Dispose by-products of combustions (CO_2, H_2O, heat, etc)

Blood: 7% of body mass: 4.5 kg or 4.4 liters in a 64 kg person

Fetal heart
1. Start blood circulation at the eighth week after conception
2. Obtain oxygenated blood from mother via umbilical cord
3. An opening between RA and LA

NOTE:
1. 90% of blood flows from RA to LA through the opening
2. 10% circulates through fetal lungs
3. Within minutes after birth, the opening is closed in effect
4. Complete closure takes several months
5. *Blue baby*: inadequate closure of the opening, requires a surgery

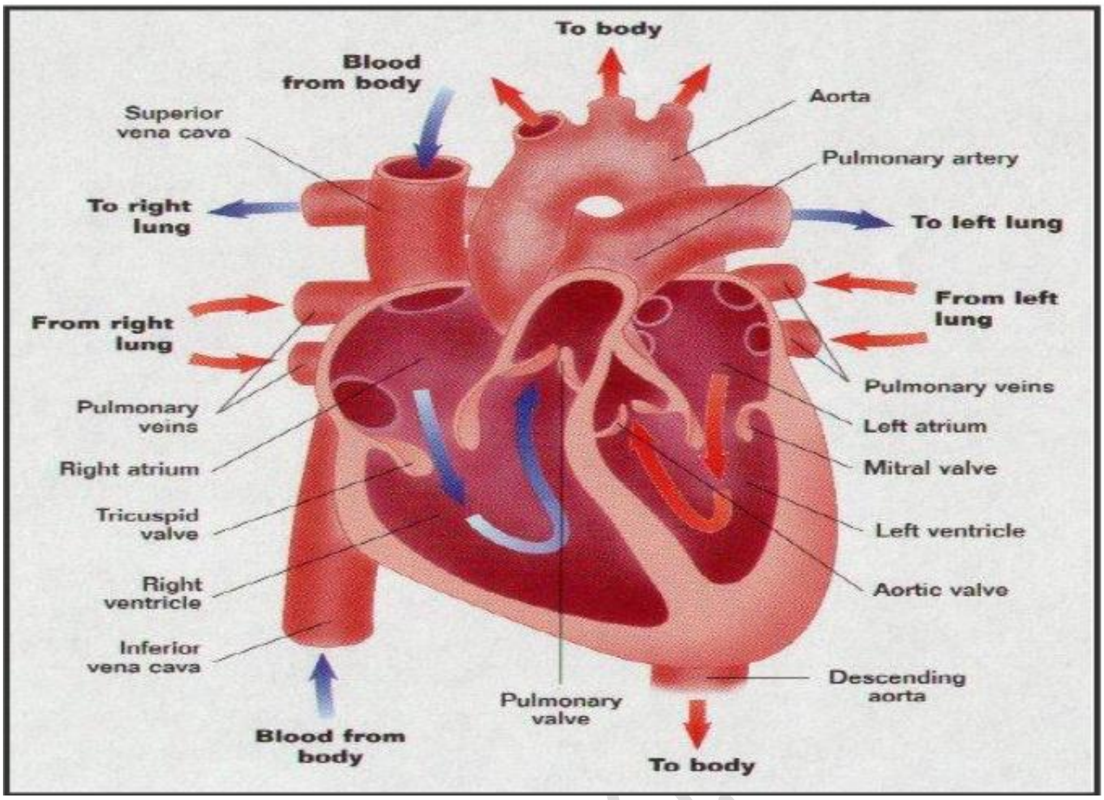
Summary

Notes on fetal heart:
1. Between the atria of the fetal heart is open because the period is incomplete for completion (10%) and after birth closes this hole.
2. The fetus's heart must be completed so that it will not be able to give up its mother's heart and cause its weakness and lack of age because it feeds on the blood through the umbilical cord and is formed in the first 7 weeks of its prenatal formation.

Specialists in (CVS)
1. Hematologist
2. Cardiologist
3. Heart surgeon

1. Heart

The heart is a hollow located in the chest between the lungs behind the sternum and above the diaphragm. It is surrounded by the pericardium. Its size is about that of a fist, and its weight is about 250-300 g. Its center is located about 1.5 cm to the left of the mid sagittal plane. Located above the heart are the great vessels: the superior and inferior vena cava, the pulmonary artery and vein, as well as the aorta. The aortic arch lies behind the heart as shown in Fig. (1).



The normal adult human heart is divided into four distinct muscular chambers, two atria and two ventricles, which are arranged to form functionally separate left and right heart pumps. The left heart, composed of the left atrium and left ventricle, pumps blood from the pulmonary veins to the aorta. The human left ventricle is an axisymmetric, truncated ellipsoid with ~1 cm wall thickness. This structure is constructed from billions of cardiac muscle cells (myocytes) connected end-to-end at their gap junctions to form a network of branching muscle fibers which wrap around the chamber in a highly organized manner . The right heart, composed of right atrium and right ventricle, pumps blood from the vena cavae to the pulmonary arteries. The right ventricle is a roughly crescent shaped structure formed by a 3-5 millimeter thick sheet of myocardial fibers (the right ventricular free wall) which interdigitate at the anterior and posterior insertion points with the muscle fibers of the outer layer of the left ventricle. The right and left ventricular chambers share a common wall, the interventricular septum, which divide the chambers. Both right and left atria are thin walled muscular structures which receive blood from low pressure venous systems . Valves (the tricuspid valve in the right heart and the mitral valve in the left heart) separate each atrium from its associated ventricle and are arranged in a manner to ensure one-way flow through the pump by prohibiting backward flow during the forceful contraction of the ventricles. These valves attach to fibrous rings which encircle each valve annulus; the free ends of these valves attach via chordae tendinae to papillary muscles which emerge from the ventricular

walls. The primary factor that determines valve opening and closure is the pressure gradient between the atrium and the ventricle. However, the papillary muscles contract synchronously with the other heart muscles and help maintain proper valve leaflet position, thus helping prevent regurgitant (backward) flow during contraction.
The semiluner valve, separate each ventricle from its accompanying arterial connection and ensure unidirectional flow by preventing blood from flowing from the artery back into the ventricle. The pressure gradient across the valves is the major determinant of whether they are open or closed .

Notes:

-Enter the blood from the left atrium and hit the left ventricle and then exit from the left ventricle to enter the right atrium and exit from the right ventricle to the lungs and then back to the left atrium.

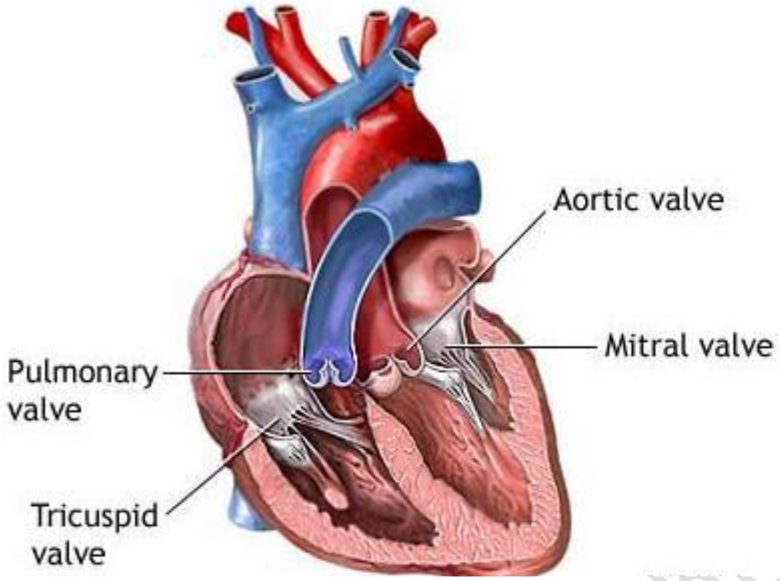
Four valves control the flow of blood from the atria to the ventricles and from the ventricles into the two large arteries connected to the heart as shown in Fig.(2):-

1- The tricuspid valve: - Is in the right side of the heart, between the right atrium and the right ventricle.

2- The pulmonary valve: - Is in the right side of the heart, between the right ventricle and the entrance to the pulmonary artery, which carries blood to the lungs.

3- The mitral valve: - Is in the left side of the heart, between the left atrium and the left ventricle.

4- The aortic valve:-Is in the left side of the heart, between the left ventricle and the entrance to the aorta, the artery that carries blood to the body.



Valves are like doors that open and close. They open to allow blood to flow through to the next chamber or to one of the arteries, and then they shut to keep blood from flowing backward .

Arteries of the heart

The arteries are major blood vessels connected to heart.

➢ The pulmonary artery carries blood pumped from the right side of the heart to the lungs to pick up a fresh supply of oxygen.

➢ The aorta is the main artery that carries oxygen-rich blood pumped from the left side of the heart out to the body.

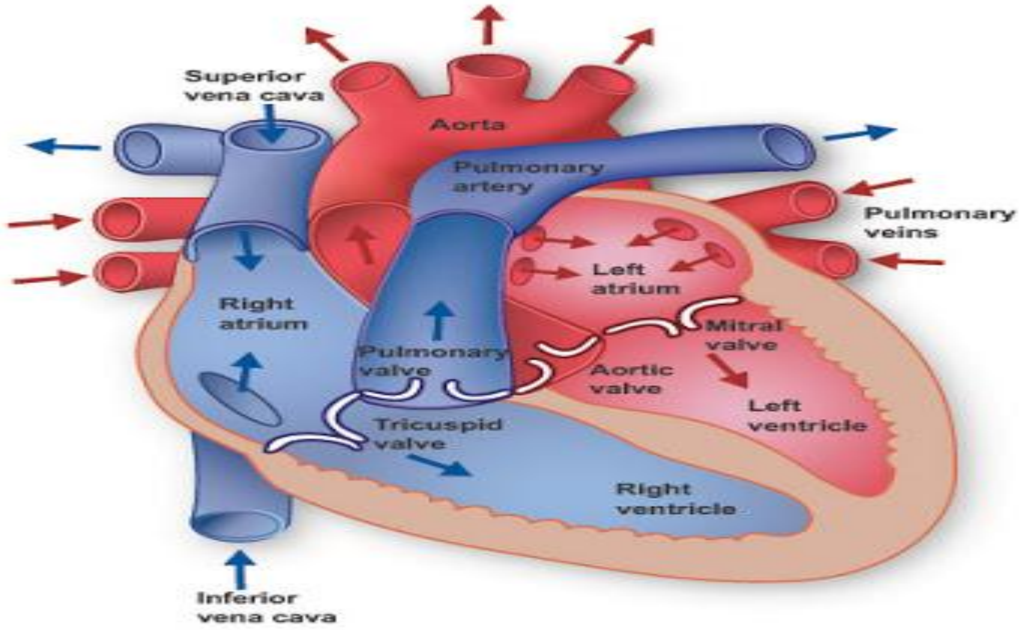
➢ The coronary arteries are the other important arteries attached to the heart. They carry oxygen-rich blood from the aorta to the heart muscle, which must have its own blood supply to function .

Veins of the heart

The veins also are major blood vessels connected to heart.

➢ The pulmonary veins carry oxygen-rich blood from the lungs to the left side of the heart so it can be pumped out to the body.

➢ The superior and inferior vena cava are large veins that carry oxygen-poor blood from the body back to the heart.



. Double pump
. Provides the force needed to circulate the blood
. Two major circulatory system
1. Pulmonary circulation (right side pump): RV (25 mmHg) →pulmonary artery →pulmonary capillary →pulmonary vein →LA (7 ~ 8 mmHg) → LV
2. Systemic circulation (left side pump): LV (125 mmHg) →arteries → arterioles →capillary bed (for a few seconds) →venules →veins → superior vena cava and inferior vena cava →RA (5 ~ 6 mmHg) →RV
. Four chambers
1. Atrium collects returning blood
2. Ventricle generates high pressure

Summary

How does the heart work?

1.The blood is released from the left ventricle to the body to give oxygen to the cells and take the carbon dioxide from the cells. The blood volume is 80 ml. The blood is called the systolic pressure and is 120-130 mm Hg and diastolic pressure. (80 mm Hg).

2. Blood takes the carbon dioxide from the body's cells to the right atrium (5-6 mm Hg) and drops it to the right ventricle.

3. Right ventricle Presses the blood by 20-25 mmHg (systolic pressure). The diastolic pressure is 10 mmHg. It goes to the lung, gives it the carbon dioxide and takes the oxygen, then it returns to the left atrium and with a pressure of (6-7 mm Hg).

4. Right ventricle pumps blood with constriction (80 ml)

Q// What are the components of tubes to pump blood in the heart?
Arteries → small arteries → capillaries→ veins → venous → heart (by Vera cava and superior cava).

(H.W): What causes a "blue baby "?

Cardiac muscle:

. Shares characteristics of skeletal and smooth muscle
1. Strong tension, all-or-none response (like skeletal muscle)
2. Not under direct conscious control, influenced by autonomic nervous system (like smooth muscle)

. Cardiac muscle cells exhibit rhythmic self-excitation
. Long refractory period (~ 250 ms): prevents tetanus (sustained contraction) and limits heart rate

Cardiac output:

. Cardiac output = heart rate ×stroke volume
. Cardiac output is determined by heart rate, contractility (contraction strength), and peripheral flow resistance
. Regulation of heart rate and contractility is very complex and involves CNS and hormonal influences, intrinsic cardiac mechanisms
1. For typical adult, about 5 l/min

. Stroke volume ~ 80 ml
. About 1 min for the average RBC to make one complete cycle of the body
. Maximum cardiac output
1. 25 l/min for young men
2. 40 l/min for trained athletes

Heart valves and artificial heart valves

1. One-way flow
2. Valve closing and turbulent blood flow →heart sound

Blood volume: total volume of about 5 l

1. 80% (4 l) in systemic circulation and 20% (1 l) in pulmonary circulation
2. Systemic circulation: 15% in arteries, 10% in capillaries, 75% in veins
3. Pulmonary circulation: 7% in pulmonary capillaries, 46.5% in pulmonary arteries, 46.5% in pulmonary veins

-We normally think of blood as bright red, most of the blood in the body is dark red .The venous blood is depleted of the O_2 that makes the blood bright red .The blue tint to the veins in your hands is due to pigmentation in the skin, when you cut yourself venous blood usually flows out, but in a fraction of a second it becomes oxygenated.

Blood components :

1. RBC (45%): It transfers oxygen and hemoglobin
2. WBC is large size and contains several types

3. Platelet : be very small
4. Plasma contains ions, electrons, hormones, minerals and other substances
- Blood fluidity varies on water fluidity !!!!
-Each 100 ml of blood is 10 mg of calcium and if this is reduced, it leads to death (4-8 mg) because calcium is important in the work of nerves and muscles.
-When examined by various physical techniques it is found to consist of several different components. The red color is caused by the red blood cells (*erythrocytes*), flat disks about 7µm in diameter, which represent about 45% of the volume of the blood .There are about 5×10^6 red blood cells/mm^3 of blood.
A nearly clear fluid called blood plasma accounts for the other 55%, the combination of red blood cells and plasma causes blood to have flow properties different from those of a fluid like water. Besides red blood cells and plasma, there are some important blood components, such as the white blood cells (*leucocytes*), present in small amounts. White blood cells (~9 to 15 µm in diameter) play an important role in combating disease.
There are about 8000 white blood cells/mm^3 of blood, when there is an infection in the body the number of white blood cells (white count) increases .(In one type of *blood cancer* ,*leukemia* ,there is an excessive production of white blood cells) ,different types of white blood cells respond differently to infection and physicians commonly ask for a differential count ,that is a count of the different types of white blood cells.
The blood also contains platelets (~1 to 4 µm in diameter) are involved in the clotting function of blood ,there are about 3×10^5 platelets /mm^3 of blood.
<u>Ex</u>: If white blood cells have an average diameter of 12 µm, what percentage of the blood volume is white blood cells?
Solu.//
Fraction of cells =No. of cells /mm^3 ×Vol. of a cell in mm^3

$$=8000/\text{mm}^3 \times [(4/3)\pi\,(6\times10^{-3})^3\ \text{mm}^3\,]=7\times10^{-3}$$
$$=0.7\%$$

<u>Hb (Hemoglobin) estimation:</u>
Hb is about 28% of red blood cells ,Hb molecule is spherical with maximum diameter 6.4 µm is composed of hem moiety which contents 1 ferrous iron carried in aporphyrin ring and globin tetramer of polypeptide chains which are bound to the hem moiety and is composed of 2 alpha and 2 beta chains.

Normal range of Hb :
For male (14-18g/dl)
For female (11.5-16 g/dl)
For children (11.5-14.5 g/dl) for (10-12 year)
For children (11-13 g/dl) for 1 year

PCV estimation :
PCV (packed cell volume)is the volume of RBC expressed as percentage of the volume of the whole blood in the sample
Normal value of PCV:
For male (40-54%)
For female (37-47%)
ESR estimation:
ESR (erythrocyte sedimentation rate) is the rate at which erythrocytes sediment on their native plasma
Normal value of ESR:
For male (0-15mm/hr)
For female (0-20mm/hr)
-How to calculate the number of blood cells, for example red blood cells ?
-It is calculated by microscopy by taking a blood sample either by cell ,cell and this method is old, inaccurate and illogical (approximately 10%).
- Another method is capillary where the rate of the diameter is taken. For example, (4-20 micrometers), the rate is approximately 7 micrometers, as much as a cell of RBC, a cell enters the capillary. A magnetic or electric field is placed on the tube causing attenuation (1), only in red blood cells and platelets, while in white blood cells, this device is not used because WBC contains several types that can not be distinguished and are calculated by microscopy.
General Notes:
-(4.4 liters) of blood is not found only in the heart, but in all arteries, veins and capillaries
- Each cell needs 1 min. , In order to cut a full cycle in the body to pump blood
- The capillary function gives O_2 and takes CO_2
-The blood value as a percentage in the vein (75%) is more than the artery and capillary because the blood is stagnant(static) and the pressure is greater , the diameter is larger in addition to containing the valves while the artery does not have valves and keeps the blood from returning , thus does not cause varicose veins ….etc.
- The blood is a bright red while in fact it is a dark red. Because most blood in the vein (75%) and this does not contain O_2 is dark red so when

we are injured bright red to contain O_2 and blood comes out of the vein , not from artery.

2. Physics of Blood Flow

Conservation of flow rate:

. Flow rate = blood volume/time, l/min

. Blood flow rate is continuous under three assumptions

1. Blood is incompressible
2. Vessels are rigid
3. There are no sinks (leakage or hemorrhage) or sources (transfusion) of blood flow

. Continuous flow $\rightarrow F_{total}$ = cardiac output = $F_{arteries} = F_{arterioles} = F_{caps} = F_{venules} = F_{veins}$

Flow velocity

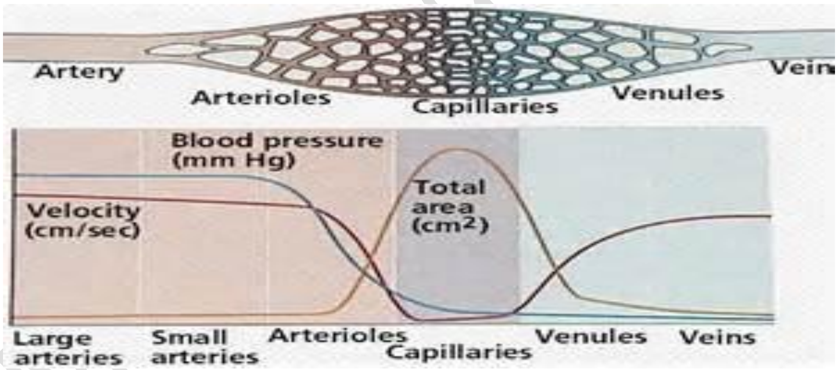
1. Flow rate = cross-sectional area ×velocity ($F = A\,v$)
2. For a group of n parallel blood vessels,

+ $A_{total} = n\,A_{average}$

+ $F = A_{total} \times v_{average}$

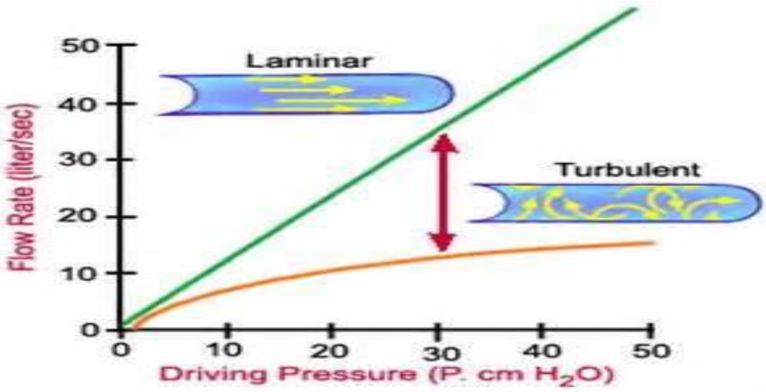
+ $F = A_{arteries} \times v_{arteries} = A_{arterioles} \times v_{arterioles} = A_{caps} \times v_{caps} = .A_{venules} \times v_{venules} = A_{veins} \times v_{veins}$ = constant

3. Flow velocity is inversely related to total cross-sectional area:



4. $v_{arteries} > v_{arterioles} > v_{caps} < v_{venules} < v_{veins}$

Flow resistance



1. Laminar flow (v < critical velocity)

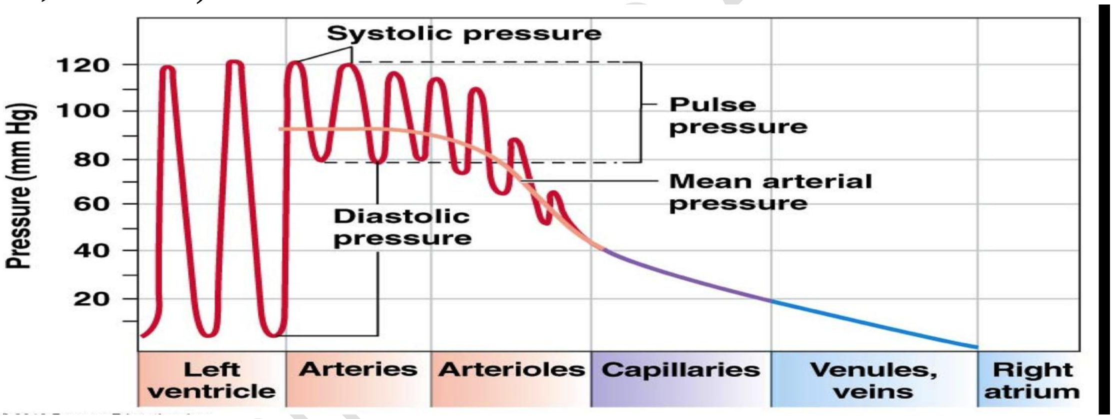
- Silent
- Maximum velocity at the center
- Zero velocity at the wall
- Pouiseuilles law:

$$F = \Delta P \frac{\pi}{8} \frac{1}{\eta} \frac{r^4}{L}$$

r is dominant factor for controlling flow through vessel
- Smooth muscle in vessel walls (except capillaries) controls *r*
2. Turbulent flow (*v* > critical flow)
- Audible →heart sound (*phonocardiogram*)
- Higher flow resistance than laminar flow
- Most likely to occur at constrictions, further reducing flow

3. Blood Vessels and Flow Regulation

1. Different vessels have distinct anatomy and physiology. This is due in part to large changes in blood pressure throughout the circulation
2. Combined length of all blood vessels > earth's circumference (~ 25,000 miles)



3. **Arteries**
. Thick, compliant walls
1. Must withstand high BP
2. Puncture can be fatal
3. High BP damages arterial walls, leading to vessel disease
. Large diameter
1. Low flow resistance
2. Transmits entire heart pressure to arterioles

4. **Arterioles**
. Large pressure drop →controls flow distribution
. Local control
1. Meet local metabolic rate
2. Increase flow to muscles during exertion
. Reflex (global) control

1. Regulate arterial BP
2. Maintain flow to vital organs (brain)

. Role of arterioles in hypertension

1. Autonomic nervous system innervates smooth muscle surrounding blood vessels.
3. Excessive constriction of arterioles is primary mechanism responsible to high BP.
4. Constriction of arterioles →high peripheral resistance →BP increases to maintain flow

5. **Capillaries**

. Maximize exchange

1. Huge surface area (~ football field)
2. Thin walls (no smooth muscle) to facilitate diffusion
3. Low blood velocity (~ 1 mm/s) gives more time for exchange

. Flow is regulated by precapillary sphincter (on-off)

. Only 1 of 30 capillaries is open in resting muscle

6**. Veins and venules**

. Veins: very large radius and thin wall

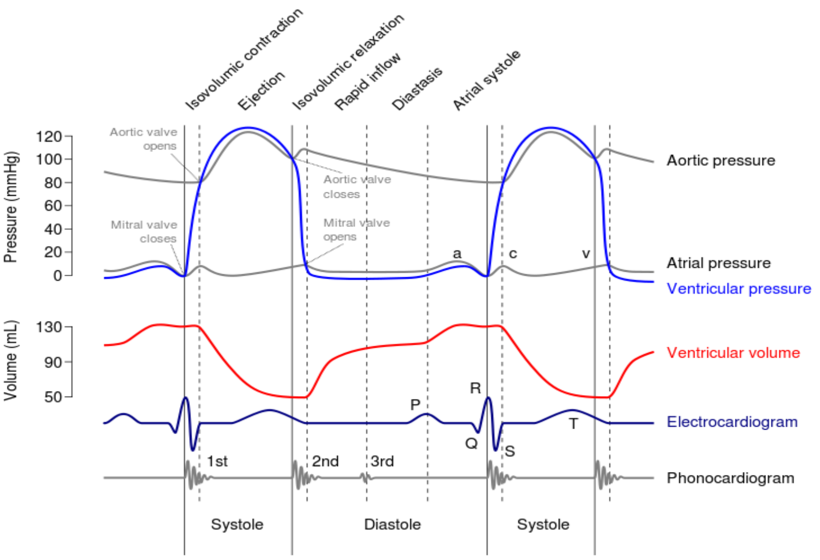
1. Largest cross-sectional area
2. Negligible flow resistance
3. Large volume: holds 75% of blood and acts as blood reservoir

. Pressure in veins governs ventricular filling (i.e. volume of blood filling heart), an important determinant of cardiac output. If ventricular filling increases, the stretched heart responds with increased contractive force (*Starling's law*), which increases stroke volume and cardiac output.

. Veins have one-way valve. Constriction of the veins drives blood toward heart, increasing cardiac output via Starling mechanism.

4. Arterial Blood Pressure

- BP during cardiac cycle:



1. Systole: ventricles contract, arteries expand, hold 2/3 of stroke volume
2. Diastole: ventricles relax, arteries recoil, squeezing blood to arterioles
- Effect of gravity on arterial blood pressure:
- Arterial BP affected by gravity ($P = \rho gh$)
1. Resistive losses are small
2. No blood to head for upward acceleration of $a > 3g$
3. Adaptation to counteract gravity: one-way valve in veins, skeletal muscles squeeze veins, forcing blood back to heart
- Measurement of arterial BP:
- *Sphygmomanometer*: inflatable cuff and pressure gauge
1. Inflate cuff at heart level until $P > P_{systole}$ →no blood flow
2. Slowly deflate. Listen for *Korotkoff sounds* (K sounds, due to turbulent blood flow)
3. First sound $\rightarrow P = P_{systole}$
4. Last sound $\rightarrow P = P_{diastole}$
- Work of heart
1. Work = area under $P(V)$ curve
2. Heart works harder for higher BP
-a typical adult has about 4.5 liters of blood and each section of the heart pumps about 80 ml on each contraction ,about 1 min is needed for the average red blood cell to make one complete cycle of the body.

<u>The Starling's law :</u>

The blood flows between the artery , the capillary and the vein. When it enters the capillary, it is exchanged between the cells, where the cells contain a fluid, the material is exchanged between it and the capillary. (In the fluid area, there is a constant osmosis pressure of 20 mmHg, while the artery is 30 mmHg and the vein is 15 mm Hg) so the blood presses on the walls of artery, vein and capillary.

- The walls of the capillary are window , made up of a single layer and the material enter from the walls of the capillary as oxygen and other substances and enters the CO_2 and other substances (Craps, neutral substances, ...)

The pressure in the artery is greater than the pressure in the capillary (30 greater than 20). The substances go out, such as oxygen and other substances. However, the pressure in the vein is less than the pressure in the capillary (15 less than 20). The substances such as CO_2 and other substances to come out of the vein. Any difference in these values or pressure will cause swelling or dizziness.

<u>EX</u>: **Estimate the volume of blood your heart pumps to your systemic circulation each day?**

Solu.//

$(80\ cm^3/beat)\times(72 beats/min)\times(1440 min/day)=8.3\times10^6\ cm^3/day$

EX: If the average power consumed by the heart is (10W) ..what percentage of a (2500kcal daily) is used to operate the heart?[4.2J=1Cal]

Solu.//

E(for day) =2500 kcal×4.2×10^3 J/kcal≈1×10^7 J/day

The average power consumed by the heart is l0 W =10J/sec

10J/sec×3600 sec/hr ×24 hr/day =8.6×10^5 J/day

Percentage →

$$\frac{8.6\times10^5}{10^7} = 8.6\times10^{-2} \cong 8.6\%$$

Summary

Work done by the heart:

-The left and right ventricles differ by pressure, the blood in both is 80 milliliters, but the pressure in the left ventricle is (120-130 mmHg) while in the right ventricle (20-25 mmHg).

-- The left ventricle presses (3) times from the right ventricle because the cycle to the lungs less (few arteries and veins) and be short while in the other are far and the arteries are large and need greater pressure.

-The left ventricle muscles are also thicker. The heart shape of the left side is larger and the gap in the left ventricle is in the form of a circle while in the right ventricle is oval.

-If we assume that the average pressure in the left ventricle is 100 mmHg because of the pressure relationship with the volume change of blood, the work done in the heart is (1.1 J / sec) where the pressure is 1.4 $\times 10^5$ dyne / cm^2 after converting (mm Hg to dyne/cm^2) , the volume of blood (80 ml) , also the work represents (1/3) heart cycle, but each contraction completes (2/3) which ($\times$ 3) so that every contraction (3.3) inside the heart where the relax does not occur any work .

- Heart efficiency 10% So this value is not complete (30 watts) and possible change this value when doing any stress or exercise..

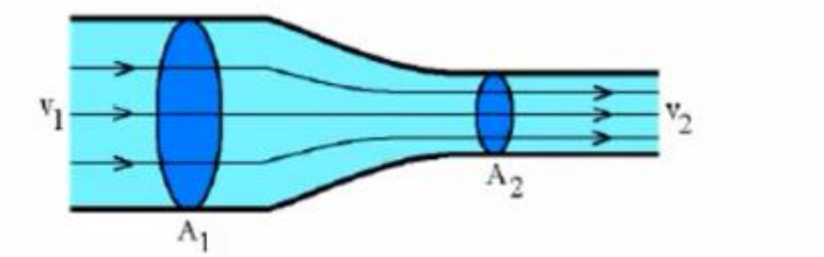
Fluid flow and the continuity equation:

-Fluids are playing a very important role in many fields of sciences and medical sciences.

-Fluid movement for Solute transport in soft connective tissue is a fundamental process, involving many physiological phenomena such as nutrient supply removal of metabolic waste product and movement of newly-synthesized molecules.

A gas is a fluid that is easily compressed; it fills any vessel in which it is contained. A liquid is a fluid which is hard to compress .A given mass of liquid will occupy a fixed volume, irrespective of the size of the container.

….Consider a hose with a decreasing diameter along its length as shown in the figure



Continuity equation is a direct consequence of the fact that what goes into the hose must come out

$$Q_{in}=Q_{out}$$

The volume of water flowing through the hose per unit time or the flow rate (Q) at the left must be equal to the flow rate at the right or in fact anywhere along the hose.

$$Q = \frac{\Delta V}{\Delta t} = Const.$$

The flow rate is measured in the units of volume per unit time, m^3/s.
The flow rate at any point in the hose is equal to the area of the hose at that point times the speed with which the fluid is moving .consider a fluid is flowing in a tube as shown in figure, where the radius of the tube is decreasing, thus at a certain point at tube the fluid flow rate is:

$$Q = \frac{\Delta V}{\Delta t} = \frac{A\Delta x}{\Delta t} = A\bar{v} = Const.$$

$$A_1\overline{v_1} = A_2\overline{v_2}$$

Take $A=\pi r^2$, so the continuity equation can be written as:

$$.r_1^{\,2}\overline{v_1} = r_2^{\,2}\overline{v_2}$$

This means that speed of flow increases by decrease of the diameter of the tube.

1. Bernoulli's equation:

Daniel Bernoulli Swiss physicist (1700-1782) made important discoveries in fluid dynamics .Born into a family of mathematicians; he was the only member of the family to make a mark in physics.
Bernoulli derived an important equation to describe the flow of fluids; this equation is stated that the work done on a fluid as it flows from one place to another is equal to the change in its mechanical energy. This equation is applicable for incompressible fluids , nonviscous fluids

(where no energy loss), laminar flow ,and for steady state flow (when the flow speed at any point is constant with time).
This can be generalized for any two points through the flow of the fluid, so Bernoulli's equation can be written as:

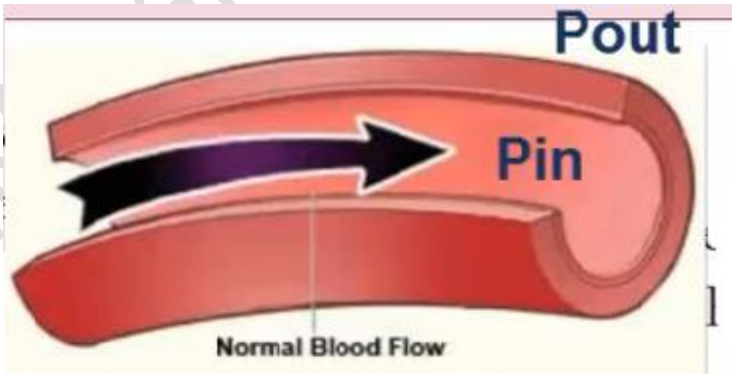
$$.P + \frac{1}{2}\rho\overline{v^2} + \rho g y = Const.$$

Thus Bernoulli's equation can be stated as the pressure of the fluid plus its mechanical energy density (kinetic energy density+ potential energy density) is the same everywhere in the flow.
Rearrange the equation leads to the following:

$$.P_{out} - P_{in} = \frac{1}{2}\rho(\bar{v}^2_{in} - \bar{v}^2_{out}).$$

Bernoulli's principle can explain the clogging of arteries when the blood flows through an artery section of cross sectional area .According to Bernoulli the pressure of blood within this section will drop inside the arterial wall and on the other hand the pressure on the outside arterial wall will be larger than inside causing the clogging of the blood vessel.

<u>Ex</u>: the diameter of a horizontal blood vessel is reduced from 12 to 4 mm ,what is the flow rate of blood in the vessel ,if the pressure at the wide part is 8 KPa and 4 KPa at the narrow one .(Hint: the density of blood to be 1060kg.m^{-3}) .
Solution//



By applying Bernoulli's equation for horizontal flow and by taking one point in the wider section and the other at the narrower one , we get:

$$.P_{out} - P_{in} = \frac{1}{2}\rho(\bar{v}^2_{in} - \bar{v}^2_{out}).$$

Using the continuity equation,

$$v_{wid} = \frac{r^2_{narr}}{r^2_{wid}} v_{narr} = (\frac{4}{12})^2 v_{narr} = \frac{1}{9} v_{narr}.$$

Then sub statute and solve for v_{narr} to get:

$$4\times10^3 = \frac{1}{2}(1060)\overline{v^2{}_{narr}}(1-\frac{1}{81})$$

$$v^2{}_{narr} = \frac{81\times2\times4\times10^3}{80\times1060} = 7.64(m/s)^2$$

The flow rate is constant everywhere and can be calculated relation
$Q=\pi r^2_{narr}\, v_{narr} = 3.14\times(4\times10^{-3})^2\times2.76$
$=1.387\times10^{-4}\, m^3 s^{-1} = 138.7$

2. The role of gravity on blood circulation:

From Bernoulli's ,the pressure of the fluid change according to its kinetic energy density and as well as it potential energy density, because of that ,the blood pressure in human organs is affected by its location from earth.
During the blood circulation, the venous system is used to return the blood from the lower extremities to the heart .It is expected to have a problem of lifting blood long distances to the heart against the force of gravity.
If we have a person in the reclining (laying down) position, the measurement of blood pressure in the large arteries are almost the same everywhere.
The small drop in pressure between the heart and the feet or the brain is due to the viscous force , according to Bernoulli's equation.

$$.P + \frac{1}{2}\rho\overline{v^2} + \rho g y = Const.$$

We can analyze the situation in the reclining position.
-The velocities in the three main arteries (Brain,Heart ,and Feet) are small so that the term $.\frac{1}{2}\rho\overline{v^2}$ can be ignored.

Furthermore in this position also the height of the brain , heart and feet are almost equal so that the term ρgy can be ignored from the formula.
This results in equal blood pressure in the three parts

$$P_B = P_H = P_F$$

Note that B,H and F refer to the brain ,heart and feet.
-In the *standing position* , the situation is different ,where only the term $.\frac{1}{2}\rho\overline{v^2}$ can be ignored and the term ρgy has a significant effect.

Hence the gauge pressure at the brain P_B at the heart P_H and the foot P_F are related by:

$$P_F = P_H + \rho g h_H = P_B + \rho g h_B$$

Note that $h_F=0$ in the standing position.
-Typical values for adults standing upward $h_H=1.3\ m$ and $h_B=1.7m$
- Typical value of the blood pressure at heart is $P_H=13.3KPA$ and take the blood density to be 1060 $kg.m^{-3}$,we find:

$$P_F = P_H + \rho g h_H$$
$$= 13.3\times10^3+(1060)(10)(1.3) \approx 27.1kpa$$

-In a similar way , we find that:

$$P_F = P_H + \rho g h_H = P_B + \rho g h_B$$
$$P_B = P_H + \rho g(h_H-h_B)=1.33\times10^3+(1060)(10)(-0.4)=9.06KPa$$

-This explains why the pressures in the lower and upper parts of the body are very different when the person is standing , although hey are about equal in the reclining .
-The high blood pressure at the foot explain the possibility of lifting blood uphill to the heart and in addition the muscles surrounding the veins contract and cause constriction.

<u>Ex</u>: When a 1.7 m tall man stands, his brain is 0.5 m above his heart .If he bends so that his brain is 0.4 m below his heart by how much does the blood pressure in his brain changes?
Solution//
We know that the blood pressure f the organ change by changing its position from the earth .The blood pressure at the brain in the standing case is given by:

$$P_F = P_H + \rho g h_H = P_B + \rho g h_B$$
$$P_{B\ stand.} = P_H + \rho g(h_H-h_B)_{stand.}$$

Where $(h_H-h_B)_{stand.} = -0.5\ m$

So $P_{B\ stand} =13.3\times10^3+1060 \times10\times(-0.5)= 8kpa$
The blood pressure at brain in the bending position is given by :

$$P_{B\ stand.} = P_H + \rho g(h_H-h_B)_{bending.}$$

Where $(h_H-h_B)_{bending} =0.4\ m$,this results in
$P_{B\ bending} =13.3\times10^3+1060\times10\times(0.4)=17.54kpa$
So the blood pressure at the brain will increase by bending , so the change in blood pressure is :
$\Delta P=P_{B\ bending} - P_{B\ stand.}=17.54-8=9.54kpa$

3. Effect of acceleration on blood pressure :

It is a common system for some people having hypotension to fell dizziness when they exist in an elevator of upward acceleration.

<u>Question</u> //Is the blood pressure at organs affected when man under upward or downward acceleration?

Answer //

When a person experiences an upward or downward acceleration his weight will be different.

Upward acceleration :If a man experience upward acceleration ***a*** ,then his effective weight becomes ***m(g+a)***.

Applying Bernoulli's equation to the foot ,brain and heart with ***g*** replaced by ***g+a*** ,so we have :

$$P_B = P_H + \rho(g+a)(h_H-h_B)$$

$$\text{Or} \quad P_B = P_H - \rho(g+a)(h_B - h_H)$$

For stand person the term *($h_B - h_H$)* is positive and also the same for *(g+a)* The blood pressure at the brain will be reduced even farther by increasing the upward acceleration ***a*** .

At certain value of ***a*** , the human will losses consciousness because the collapse of the arteries in the brain when the blood pressure at the brain equal zero.

Put P_B =0 in the above equation ,we get:

$$0= P_H - \rho(g+a)(h_B - h_H)$$

This can results in

$$(g+a) = \frac{P_H}{\rho(h_B - h_H)}$$

Take ($h_B - h_H$) =0.4 m , P_H=13.3 kpa and ρ =1060kg.m^{-3} ,we get:

$$(g+a) = \frac{13.3\times10^3}{1060(0.4)} = 31.4 m.s^{-2} = 3.2g$$

So the value of the upward acceleration causing consciousness is 2.2 g This factor should limit the speed with a pilot can pull out of dive. A related experience is the feeling of light headache that sometimes occurs when one suddenly stands up.

<u>Note</u> :

We can also show the change of the blood pressure at the foot by the upward acceleration situation , by putting ***g+a*** instead of

$$P_F=P_H+\rho(g+a)h_H$$

This relation shows that the blood pressure at the foot will increase by increasing the upward acceleration.

Downward acceleration: If a man in an upright position experience downward acceleration then his effective weight becomes ***m(g-a)*** .

Applying Bernoulli's equation to the foot, brain and heart with ***g*** replaced by ***g-a*** , so we have:

$$P_B=P_H+\rho(g-a)(h_H-h_B) \quad \text{or} \quad P_B=P_H-\rho(g-a)(h_B-h_H)$$

Thus the blood pressure at the brain will increase even farther by increasing the downward acceleration ***a*** ,which opposite to what occurs by the upward acceleration.

This increase should be controlled and observed, where at certain value of ***a*** the blood pressure at the brain may cause an explosion of the arteries in the brain, which is so dangerous.

The same calculation for the blood pressure at the foot results in a decrease of the blood pressure by increasing the downward acceleration.

Viscosity (η):

The quantity that describes a fluid's resistance to flow. The cgs unit used to measure viscosity is the poise, the SI unit for viscosity is the Pascal second (Pas) ,which equals (10 poises).

The viscosity of water is about (10^{-3}pas) at 20^0C ,the viscosity of blood typically (3×10^{-3}-4×10^{-3}pas) ,but depends on the percentage of red blood cells in the blood (the *hematocrit*).

The percentage of the blood that is cells is called the hematocrit. thus if a person has hematocrit of 40,40 percent of the blood volume is cells and the remainder is plasma. The *hematocrit* of men averages about 42 where as that of women averages about 38.

These values vary tremendously ,depending on:-

1-whether or not the person has anemia.

2-The degree of bodily activity.

3-The altitude(h) at which the person resides .

When the hematocrit rises to 60 or 70 , which it often does in *polycythemia*

Another factor that affects blood viscosity is the concentration and types of proteins in the plasma, but these effects are so much less important than the effect of hematocrit that they are not significant considerations in most homodynamic studies; the viscosity of blood plasma is about 1.5 times that of water.

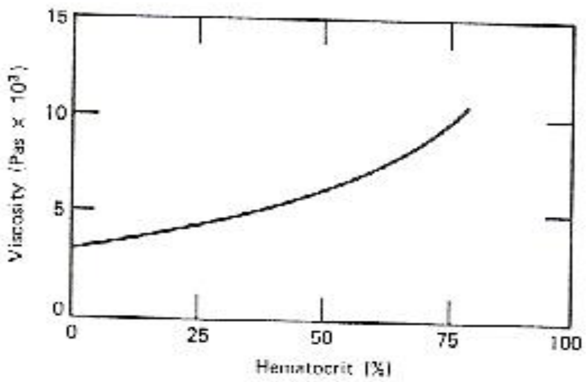


Figure As the percent of red blood cells in the blood increases (higher hematocrit) the viscosity increases, decreasing the flow rate.

Reynolds Number (N_R):

We remember that Poiseulle's is applicable for laminar flow ,so it is necessary to determine whether the flow is laminar or turbulent .There is a dimensionless quantity called Reynolds Number (N_R) used to distinguish the type of the flow.

-consider a fluid of density ρ and viscosity coefficient η flows with an average velocity ῡ through a tube of radius R ,hence the Reynolds number is defined by :

$$N_R = \frac{2\rho\bar{v}R}{\eta}$$

It is found experimentally that if :

$N_R<2000$ ………flow is laminar

$N_R>3000$ ………flow is turbulent

$2000< N_R<3000$……flow is unstable

Ex: The flow rate of blood in a blood vessel of 2 cm in diameter is 1 liter per minute, Determine whether the flow is laminar or turbulent, if the density of blood is 1060kg.m^{-3} and the coefficient of viscosity of the blood is 2.1×10^{-3}pas.s?

Solu.//

The flow rate of the blood $Q == \pi R^2 \bar{\upsilon} = \frac{1\times10^{-3}}{60} = 1.66\times10^{-5}\, m^3 ls$

So that $\bar{\upsilon} == \frac{Q}{\pi R^2} = \frac{1.66\times10^{-5}}{3.14(1\times10^{-2})^2} = 0.053\times10^{-5}\, mls$

$$N_R = \frac{2\rho\bar{\upsilon}R}{\eta} = \frac{2(1060)\times0.053x10^{-5}(1\times10^{-2})}{2.1\times10^{-3}} = 535$$

$N_R<2000$, so the flow is laminar.

5. Cardiovascular Disease

1. Congestive heart failure (CHF)

. Normally heart increases contractility in two ways
1. By increasing nervous stimulation of the heart
2. By increasing ventricular filling (*Starling mechanism*)

. CHF is characterized by a heart that is weak and enlarged due to greatly increased ventricular filling. But for a very high ventricular filling, cardiac output falls.

. Backward failure of the heart: the heart cannot pump out all the blood returning from veins. Blood, therefore, backs up in the veins, which increases pressure in the veins and capillaries, causing fluid to accumulate in the tissues (*edema*)
1. Right ventricle failure: back-up in systemic circulation (*swollen legs*)
2. Left ventricle failure: back-up in pulmonary circulation (*pulmonary congestion*, *very serious*)

. Treatment
1. Rest
2. Drugs to increase contractility, excretion
3. Heart transplant

2. Risk factors, promoters of vessel disease

. Sex, age, weight, family history, general health, …

. *Hypertension*: 60 million in US, 50% are aware, silent killer
1. Systolic BP > 140 mmHg
2. Diastolic BP > 90 mmHg
3. Leading cause of stroke and heart disease
4. Arterioles constricted, regulation goes awry
5. 10% (50% in US) are sodium sensitive (salt elevates BP)
6. No obvious symptoms →silent killer
7. Damages arteries →hardening of arteries→ narrowing (*atherosclerosis*)

. *Cholesterol*
1. Found only in animal tissue
2. Synthesized by liver from saturated fat
3. Important for metabolism, precursor to hormones
4. Two types: LDL (low density lipoprotein) and HDL
5. LDL_s deposit on vessel walls →bad cholesterol
6. HDL_s reduce the amount of LDLs →good cholesterol

. *Smoking*
1. Increases BP
2. Smoke contains CO →stresses heart
3. Increases platelet clumping →promotes *atherosclerosis*
4. Effects are reversible

. Other factors

1. Salt: not certain except effect on hypertension
2. Caffeine: no strong link to heart disease
3. Chronic stress: may increase risk in some individuals

Vessel disease

. Arteries surrounded by tough connective tissue. However, high blood pressure can damage the tissue, leading to vessel disease.

. *Arteriosclerosis*: hardening of arteries

. *Atherosclerosis*: plaque (fat, calcium) deposits on and within lining of damaged vessel

. Vessel wall damage →blood clots →clog arteries

3. Heart attack

. 0.5 million deaths annually in US

. Infarction: death of heart muscle due to blockage of coronary arteries

1. Heart uses 5/6 of blood oxygen
2. Often little or no collateral circulation
3. Coronary arteries are first to suffer complete blockage (SaO_2 ~ 0% in venous return from heart)

. Partial blockage

1. Angina pectoris: pain during exertion
2. Develop collateral circulation in a few days

. Sudden (acute) blockage

1. Blood clot forms rapidly on rough surface
2. Clot or deposit breaks off, blocks vessel downstream

. Symptoms of heart attack

1. The most common symptom (> 80%) is a heavy, persistent pressure in the center of the chest, lasting 10 min or more.
2. The pain often radiates upward to the neck, jaw, or left arm and shoulder.

Weakness and profuse sweating are also common.

3. Sometimes the pain is a burning sensation, similar to heartburn.
4. Rarely associated symptoms: brief and sharp pain, pain on breathing

. Precautions for high-risk persons

1. Sensible diet, life style
2. Avoid overexertion, especially after eating

. Treatments

1. Angina: nitroglyerin (vasodilator) can relieve symptoms
2. Drugs →dissolve clot
3. Angioplasty →clean out vessel
4. By-pass surgery

4. **Stroke**, **cerebrovascular accident** (200,000 deaths annually in US)

. Blockage or rupture of brain blood vessel

. Stroke symptoms (varied, often lateralized)

. One-sided numbness or weakness

. Blurred or decreased vision
. Sudden severe headache
. Problems speaking or understanding
. Dizziness, loss of balance

Note :

A fast heart rate (*tachycardia*) increases the work load since the amount of time the heart muscles spend contracting increases.

Normocardia : is a normal heart rate that range between 60 and 100 beat /min**.**

***Tachycardia** :is a heart rate in excess of 100 beats/min.

***Bradycardia**: is a heart rate that is less than 60 beats/min.

An *aneurysm* is a weakening in the wall of an artery resulting in an increase in its diameter. The increased diameter increases the tension in the wall proportionately .If it were not for the supporting action of the surrounding tissue the wall would blow out the way a bicycle inner tube does under similar conditions .If an aneurysm does rupture it is often fatal-especially if the rupture is in the brain ,a type of *cerebrovascular accident* (CVA).

Hypertension:

It is increased blood pressure. Two measurements indicate what the blood pressure is. The systolic pressure results from contraction of the left ventricle of the heart, forcing blood into the aorta and out into its branches that form the systemic arterial circulation. The pressure wave of this contraction is measured peripherally. The diastolic pressure results from relaxation of the left ventricle of the heart, and the pressure diminishes to a level sustained by the residual pressure retained by the elasticity of the arteial system .

There can be considerable variation in blood pressure between persons. The average adult blood pressure is around 120/80 mmHg, as measured by a sphygmomanometer with blood pressure cuff around the upper arm while sitting. In general, a sustained diastolic pressure >90 mmHg and a sustained systolic pressure >140 mmHg define hypertension. However, lower is better. Young persons may have a blood pressure of 90/60 mm Hg, and as long as that can be maintained, the better one's overall health will be. However, sustained increases in blood pressure above 115/75 mm Hg can increase morbidity .

Hypertension is a silent disease. It is *insidious* and *relentless*. The only reliable way to detect hypertension is to regularly check blood pressure. This should be done as part of a physical exam on every adult .

If hypertension is <u>not</u> treated, there will be organ damage to *kidneys*, *heart*, and *brain* which is generally <u>not</u> reversible. Death in persons with hypertension most often occurs from *heart failure*, *chronic renal failure*, and *stroke*

Causes for Hypertension

Over 90% of the time, an identifiable cause for hypertension cannot be found. This is known as "primary" or "essential" hypertension. The term "essential" arose from a belief long ago that an increased pressure was essential to maintain blood perfusion through an abnormal arterial system. Auto regulation of blood pressure is based upon vascular changes, and dietary sodium may play a major role in this process. Increased *sodium* intake leads to increased intravascular fluid volume with resultant *increased cardiac output* and an *increase* in blood pressure. This increased blood pressure then *increases renal perfusion pressure* that should trigger increased *excretion* of *sodium* with water. In essential hypertension the process of sodium excretion is impaired, probably due to *multigenic influences*.

The onset of hypertension is typically in middle age. Some factors that may contribute to primary hypertension include:

1. *Genetics*: persons whose parents had hypertension are more likely to be hypertensive themselves.

2. *Diet*: more salt (sodium chloride) in the diet promotes increasing blood pressure.

3. *Stress*: native peoples of the world are far less likely to develop hypertension than persons living in cities of developed nations.

4. *Vascular alteration*: over time, hypertension results in thickening of small muscular arteries and arterioles, which makes them less responsive to vasodilators.

Less than 10% of the time, hypertension has an identfiable underlying cause, though this does not necessarily mean that recognition will provide a cure for hypertension. Causes for hypertension may include:

1. *Renal Diseases*: just about any renal disease leading potentially to renal failure can result in hypertension.

2. *Endocrine Diseases*.

3. *Neurogenic Causes*: such as increased intracranial pressure (tends to be of sudden onset).

4. *Vascular Diseases* .

Consequences of Hypertension

Heart Disease: the pressure load placed on the left ventricle results in left ventricular *hypertrophy*. The heart enlarges and dilates, with hypertrophy more marked than dilation, until the left heart begins to fail, particularly when the heart reaches 500 gm in weight. Congestive heart failure and cardiac arrhythmias may result from the failing heart .

Hypertension's effects on other organs

➢ **Brain:** The brain depends on a nourishing blood supply to work properly and survive. But high blood pressure can cause several problems, including: (**Transient ischemic attack, Stroke, Dementia, Mild cognitive impairment)**.

➢ **Kidneys:** Kidneys filter excess fluid and waste from your blood — a process that depends on healthy blood vessels. High blood pressure can injure both the blood vessels in and leading to kidneys, causing several types of kidney disease (nephropathy). Having diabetes in addition to high blood pressure can worsen the damage: (**Kidney failure, Kidney scarring, Kidney artery aneurysm)** .

➢ **Eyes**: Tiny, delicate blood vessels supply blood to eyes. Like other vessels can be damaged by high blood pressure **:(Eye blood vessel damage, Fluid buildup under the retina, Nerve damage)** .

*** **Harmful effects of smoking**

Cigarette:

Refers to a tobacco cigarette but can apply to similar devices containing other *herbs* ,such as *cloves* or *cannabis* ,also device to smoke *nargile*.
Approximately 5.5 trillion cigarettes produced globally each year and smoked by over 1.5 billion people.
Smoking cigarettes kills *more people* in the U.S. *than* alcohol, car accidents, suicide, AIDS, homicide, and illegal drugs combined.

What's in a Cigarette?

There are approximately
1)4000 redients in cigarettes.

2) When *burned*, they create more than 7,000 chemicals.
3) At least 69 of these chemicals are known to cause cancer, and many are poisonous.

Here are a few of the chemicals in tobacco smoke, and other places they are found:

- Acetone – found in nail polish remover
- Acetic Acid – an ingredient in hair dye
- Ammonia – a common household cleaner
- Arsenic – used in rat poison
- Benzene – found in rubber cement
- Butane – used in lighter fluid

- Cadmium – active component in battery acid
- Carbon Monoxide – released in car exhaust fumes
- Formaldehyde – embalming fluid
- Hexamine – found in barbecue lighter fluid
- Lead – used in batteries
- Naphthalene – an ingredient in moth balls
- Methanol – a main component in rocket fuel
- Nicotine – used as insecticide
- Tar – material for paving roads
- Toluene - used to manufacture paint
- Benzo[a]pyrene.

Nicotine

1.Volatile alkaloid ,sever toxic. 2. Fatal neurotoxin. 3.One drop cause death. 4.It is 8.2% of dried leaves of tobacco . 5.Chronic use causes physical dependence while sudden cease lead to withdrawal effects.

- **Why is smoking addictive**:

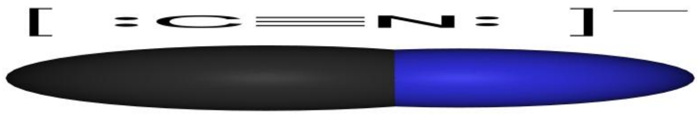
Nicotine *alters the balance of chemicals* in **brain**. It mainly affects **dopamine** and **noradrenalin**. When nicotine changes the levels of these chemicals, mood and concentration levels change. The changes happen very quickly. When one *inhale* the nicotine, it immediately rushes to brain where it takes effect to produce *feeling* of *pleasure* and *reduces stress* and *anxiety*. This is why many smokers enjoy the nicotine *rush* and become dependent on it.

The more you smoke, the more your brain becomes used to the nicotine. This means that you have to smoke more to get the same effect. When you stop smoking, the *loss* of nicotine changes the levels of dopamine and noradrenalin. This can make you feel *anxious*, *depressed* and *irritable*.

Q// why is smoking a addictive ?(H.W)

Cyanide

- Present as HCN in tobacco smoke 1600 ppm.
- The indoor allowed level must not exceed 10pmm.



Carbon monoxide (CO)

- Very toxic gas in tobacco smoke is 1000 time exceed the allow level in breathing air.
- Taken up more readily by lung than oxygen.
- Bind to hemoglobin and form stable Carboxyhemoglobin resulted in histotoxic anoxia.
- Together with nicotine increases the risk of heart disease and hardening of the arteries .

<u>Tar</u>

- Releasing after cigarette burns.
- Main cause of lung and throat cancer in smokers.
- Together with nicotine causes airway cellular damages ,impair the defense mechanism and lead to bronchitis and pneumonia .

Health Effects:

- **Nicotine is primary psychoactive ,highly addictive agent causes**

1. Heart attack (MI) . 2. Stroke (Brain attack). 3. Arteriosclerosis :- .death due to cardiovascular diseases is due to :

- Hypoxia due to formation carboxyhemoglobine (COHb).
- exhaust cardiac muscle due to nicotine . (impair peripheral blood vessels .e.g. **Buerger's disease**)

4) COPD including emphysema and chronic bronchitis 5) Cancer

- Is proportional increase with the period and frequency of smoking and decline with dropping off smoking .
- The risk of developing lung cancer in smoking addict persons is 20 time more than in nonsmokers.

- **Filter** *don't* adjust formaldehyde ,acrolein and ammonium salts which are considered mutagenic and carcinogenic substances in cigarette smoke .

Risks and developing cancer :

A. pulmonary carcinoma

B. Bladder

C. Blood (acute myeloid leukemia)

D. Cervix

E. Colon and rectum (colorectal)

F. Esophagus

G. Kidney and ureter

H. Larynx

I. Liver

J. Oropharynx (includes parts of the throat, tongue, soft palate, and the tonsils)

K. Pancreas

L. Stomach

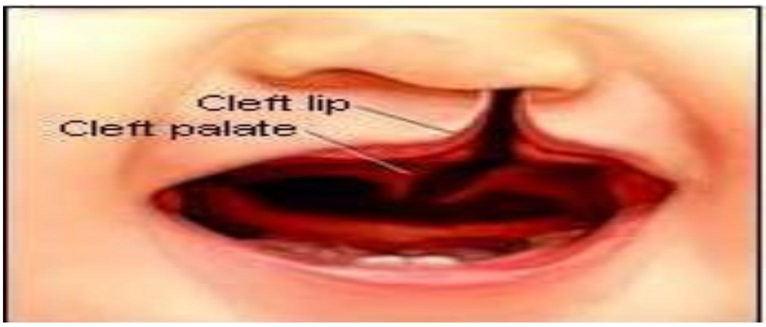
M. Trachea, bronchus, and lung

Reproductive effects:

1.Preterm (early) delivery 2.Stillbirth (death of the baby before birth) 3.Low birth weight 4.Sudden infant death syndrome (known as **SIDS** or crib death) 5.Ectopic pregnancy 6.Smoking can also affect *men's sperm*, reduce *fertility* , increase risks for birth defects and *miscarriage* .

7.Spermatogenesis *decreases* due to HCN effect on somniferous tubules. 8.Vasoconstriction of ovarian artery ,decrease LH that lead to delay the *ovulation* so affect *fertility* . 9. Hypoxia ,CO intoxication of *placenta* due to vasoconstriction .

Orofacial clefts in infant :



Effect in bone:

- 1. Women past childbearing, years who smoke have lower bone density (weaker bones) are at greater risk for broken bones. 2. Smoking affects the health of your teeth and gums and can cause tooth loss.

Effect on eye:

1. cataracts 2.macular degeneration (damage to a small spot near the center of the retina, the part of the eye needed for central vision).

3.Conjunctivitis and inflammation of *optic nerve* due to *vit* **A** deficiency (CN in smoke *destructs* vit A).

Effect in hormones:

- Smoking is a cause of type 2 *diabetes mellitus* . The risk of developing diabetes is 30–40% higher for active smokers than nonsmokers.

Nervous Effects:

1.Nicotine induce releasing of adrenaline stimulating *glycogenolysis* in liver and muscles. 2. *Increase* blood glucose level so the smoker is feeling active. 3. Excessive smoking leads to exhaustion the activity substances and *dropping* of blood glucose level so feeling exhausting. 4. Smoking causes general adverse effects on the body.

5. It can cause inflammation and adverse effects on *immune function*. 6. Smoking is a cause of rheumatoid arthritis

Health Effect in secondhand smokers:

Secondhand smoke is the combination of smoke from the burning end of a cigarette and the smoke breathed out by smokers

- . Secondhand Smoke Causes Cardiovascular Disease increasing risk by 25-30%

- Even brief exposure to second hand smoke can damage the lining of blood vessels and cause your platelets to become sticker ,can cause deadly heart attack

- Secondhand smoke causes Lung cancer in adult who have never smoked and increasing by 20-30% for second hand smoke at home and work place.

- Secondhand smoke causes SIDS in the first year of the life.

I. Smoking by pregnant woman increase risk of SIDS ,while infants who exposed to second hand smoke after birth also at greater risk for SIDS because chemicals of secondhand smoke appear to affect the brain in ways that interfere with its regulation of infants breathing.

II. Infants who die from SIDS have higher concentrations of nicotine in their lungs and higher levels of cotinine (a biological marker for secondhand smoke exposure) than infants who die from other causes.

Secondhand Smoke Harms Children:

- Children whose parents smoke get sick more often. Their lungs grow less than children who do not breathe secondhand smoke, and they get more bronchitis , pneumonia and asthma attack .
- Children whose parents smoke around them get more ear infections.

Facts about Smoking:

1.Women who use birth control pills and smoke have a greater risk of heart attack.2.Smoking is the main cause of chronic lung disease.

3.Low tar and nicotine cigarettes do not reduce the risk of heart attack. People who use these cigarettes often smoke more.

4.Smoking shortens a two pack a day smoker's life by eight years.

5.Persons smoking 1 to 9 cigarettes a day shorten their lives by four years.

6.Children who live in homes where people smoke have more lung infections than children who live in homes where no one smokes.

7. Exhaled smoke has more poisonous chemicals than the smoke inhaled by the smoker. Smoke coming off the end of the cigarette (second hand smoke) has twice the tar and nicotine and five times the carbon monoxide of inhaled smoke.

Quitting and Reduced Risks:

1.cuts cardiovascular risks. Just 1 year after quitting smoking, your risk for a heart attack drops sharply, and stroke drop2-5 years after quitting. 2.If you quit smoking, your risks for *cancers* of the *mouth*, *throat*, *esophagus*, and *bladder* drop by half within 5 years. 3.Ten years after you quit smoking, your risk for *lung cancer* drops by half

drugs to help you quit smoking:

- Nicotine Replacement Therapy (NRT) is a way of getting nicotine into the bloodstream without smoking. There are nicotine gums, patches, inhalers, tablets, lozenges, and sprays.

- **Bupropion (Zyban)** anti-depressant that reduces symptoms of nicotine withdrawal. works best if it's started 1 or 2 weeks before quit smoking. The usual dosage is one or two 150 mg tablets per day.

- **Combining bupropion and NRT .**

Some doctors may recommend combination therapy for heavily addicted smokers, such as using bupropion along with a nicotine patch and/or a short-acting form of NRT (such as gum or lozenges).

- **Varenicline (Chantix)** It works by interfering with nicotine receptors in the brain. This means it has 2 effects: it lessens the pleasure a person gets from smoking, and it reduces the symptoms of nicotine withdrawal. taken after meals, with a full glass of water. The daily dose increases over the first 8 days it's taken. The dose starts at one 0.5 mg pill a day for the first 3 days, then the 0.5 mg pill twice a day for the next 4 days. At the start of the second week, the dose is raised to 1 mg in the morning and evening.

- **Clonidine** given as a pill twice a day or as a once-a-week skin patch.