UNIT 1

General Physiology

HUMAN PHYSIOLOGY

- Study of *function* of human body
- Function closely related to structure

For example, to understand heart function, need to understand heart anatomy

Cells: 75 trillion in human body

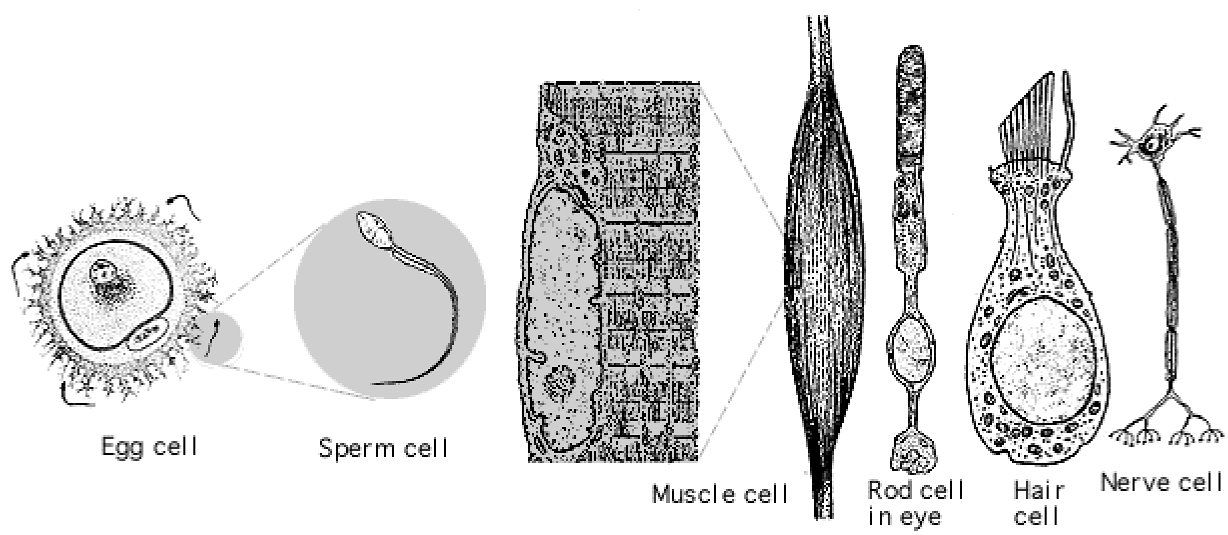
Cells are the basic structural and functional units of the human body & there are many different types of cells (e.g., muscle, nerve, blood, and so on).

Basic cell functions

a) obtain nutrients & oxygen
b) make energy
c) eliminate wastes
d) synthesize proteins & other compounds
e) sense/respond to environment
f) control exchange of material with environment
g) move materials
h) reproduce (only some cells can do this; nerves and muscles cannot)

Specialized cell functions

a) Each cell also performs specialized function, which is usually a modification of basic cell function
b) Examples:
(1) gland cells of digestive system secrete digestive enzymes (d above)
(2) kidney cells selective retain some substances & eliminate others (f)



Primary Tissues: Composed of cells of a single type + extracellular material

1. Nervous tissue

a) Cells specialized for initiation and transmission of electrical impulses
b) Found in:
    (1) brain
    (2) spinal cord
    (3) nerves

2. Muscle tissue

a) Cells specialized for contraction & force generation
b) Three types
    (1) skeletal
    (2) cardiac
    (3) smooth (e.g., used in digestive)

3. Epithelial tissue

a) Cells specialized in exchange of material with environment
b) Two general types of structures

    (1) Sheets (e.g., skin, digestive tract lining) (Fig 1.2c)
    (2) Secretory glands

        (a) Exocrine: secretes through duct to outside of body or into cavity that communicates with outside (e.g., sweat glands, digestive glands)
        (b) Endocrine: lack ducts, release hormones into blood.

4. Connective tissue

a) Cells that connect, support & anchor body parts
b) examples: tendons, bone, blood

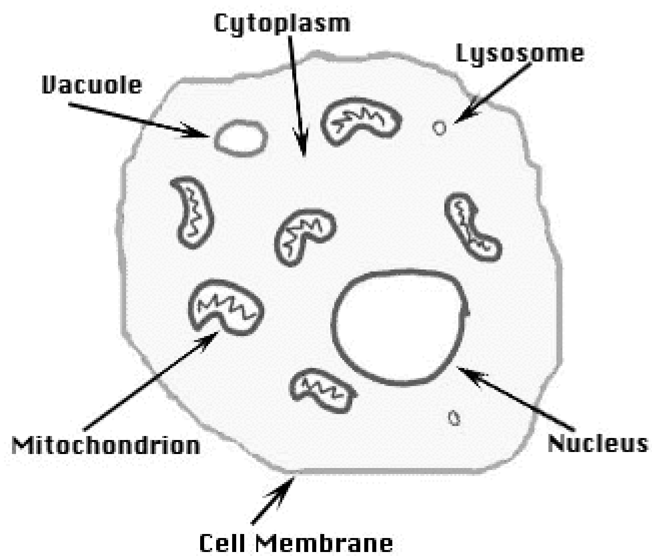
Organs

1. Composed of two or more primary tissues organized to perform a specific function
2. Example: Stomach is composed of
    a) Epithelial tissue (restricts transfer of digestive enzymes to blood; exocrine glands secrete digestive enzymes; endocrine glands that secrete hormones that regulate muscle contraction & exocrine secretion)
    b) Smooth muscles tissue (mixes & propels food)
    c) Nervous tissue (controls contraction & secretion)
    d) Connective tissue (holds all together)

Body Systems

1. Collection of organs that perform related functions and interact to accomplish a common activity essential to survival of body.
2. Example: Digestive system composed of: mouth, pharynx, esophagus, stomach, small & large intestines, salivary glands, pancreas, liver, and gallbladder.

STRUCTURE AND FUNCTION OF CELL AND ITS ORGANALLES



Major parts

1. cell membrane (sometimes called plasma membrane)
2. nucleus
3. cytoplasm

Cell (or plasma) membrane

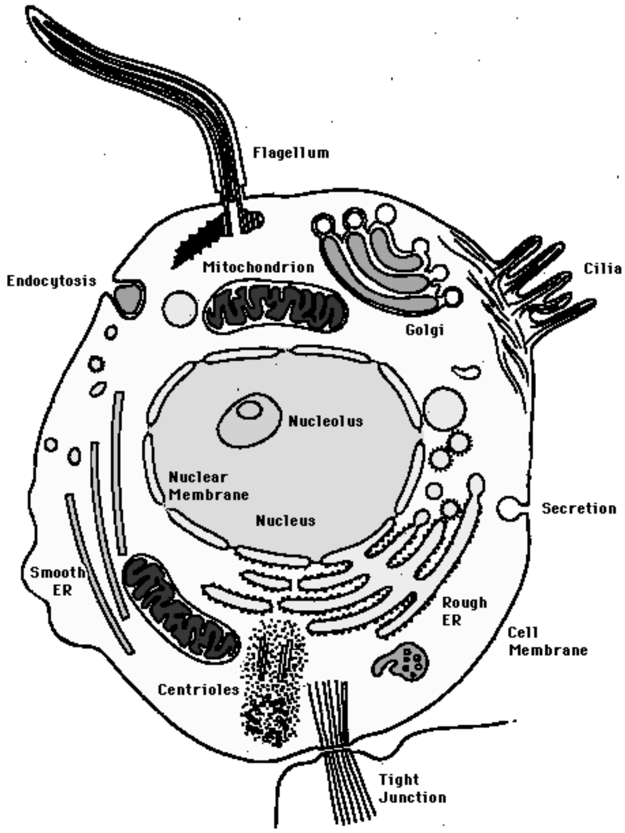
1. Thin structure
2. Encloses each cell
3. Mechanical barrier that is *selectively permeable*
4. Intracellular fluid (ICF) fluid inside cell
5. Extracellular fluid (ECF) fluid outside cells

Nucleus

1. Distinct sphere in center with its own membrane
2. Contains DNA which is packaged into chromosomes

Cytoplasm

1. That part of cell that is not nucleus.
2. Contains organelles dispersed in a gel like mass called cytosol
3. Organelles are separate compartments specialized for particular functions



Organelles

Endoplasmic reticulum

<u>1. Structure</u>

a) One continuous organelle; membrane continuous with cell membrane
b) fluid filled membrane structure
c) two types: rough (RER) & smooth (SER)

<u>2. Function of RER</u>

a) is rough because of attached ribosomes
b) ribosomes synthesize proteins
c) RER involved in synthesis and release of proteins
d) Lots of RER found in cells specialized for protein synthesis

3. Function of SER

a) Most cells: central packaging & discharge site for molecule transport out of ER.
b) Piece of SER pinches off with molecule inside; called a transport vesicle
c) Some cells: SER specializes in lipid synthesis & transport
d) Liver cells, SER detoxifies harmful chemicals & excretes them

Golgi complex

1. Structure

a) Flat, slightly curved membrane enclosed sacs
b) Closely associated with ER
c) one to hundreds of stacks/cell

2. Function

a) Destination point for ER transport vesicle
b) Processes proteins from ER into final form
c) Sort & direct finished products to final destination

Lysosomes

1. Structure

a) Membrane enclosed sacs derived from Golgi complex
b) Contain powerful hydrolytic enzymes

2. Function

a) Digest cellular debris & foreign material
b) Can also digest aged and damaged organelles
c) Injured or dead cell: lysosome ruptures & digests *whole* cell

Mitochondria

1. Structure

a) Bacteria sized rod or oval shaped
b) Outer membrane surrounds mitochondria
c) Inner membrane that forms infoldings called cristae
d) Inner membrane projects into cavity called matrix

2. Function

a) Powerhouse of cell
b) Produce high energy molecules (ATP) in presence of oxygen

Cytosol

1. Structure

1. Semiliquid highly organized gelatinous mass
2. 55% of cell volume

<u>2. Function</u>

1. Intermediary metabolism
   a) metabolism of small organic molecules
   b) glycolysis
2. Protein synthesis
   a) proteins needed in cytosol itself (e.g. glycolytic enzymes)
3. Storage of fat and glycogen

Ribosomes-

<u>1. Structure</u>

- composed of rRNA (ribosomal RNA) & protein
- may be dispersed randomly throughout the cytoplasm or attached to surface of rough endoplasmic reticulum
- often linked together in chains called <u>polyribosomes</u> or polysomes

<u>2. Function</u>

Primary function is to produce proteins

Centrioles

<u>1. Structure</u>

Paired cylindrical structures located near the nucleus

<u>2. Function</u>

Play an important role in cell division

Flagella & cilia

<u>1. Structure</u>

Hair-like projections from some human cells

Cilia are relatively short & numerous (e.g., those lining trachea)

A flagellum is relatively long and there's typically just one (e.g., sperm)

Villi Projections of cell membrane that serve to increase surface area of a cell (which is important, for example, for cells that line the intestine)

COMPARISON OF CELL WITH FACTORY

NO.	CELL	FACTORY
1	CELL MEMBRANE	Fence with gates; Gates open when message is received
2	NUCLEUS	Managers Office
3	ENDOPLASMIC RETICULUM	Conveyer belt of production units
4	GOLGI APPARATUS	Packing units
5	LYSOSOMES	Incenerators
6	VACUOLES	Lorries carrying finished products
7	MITOCHONDRIA	Power generating units

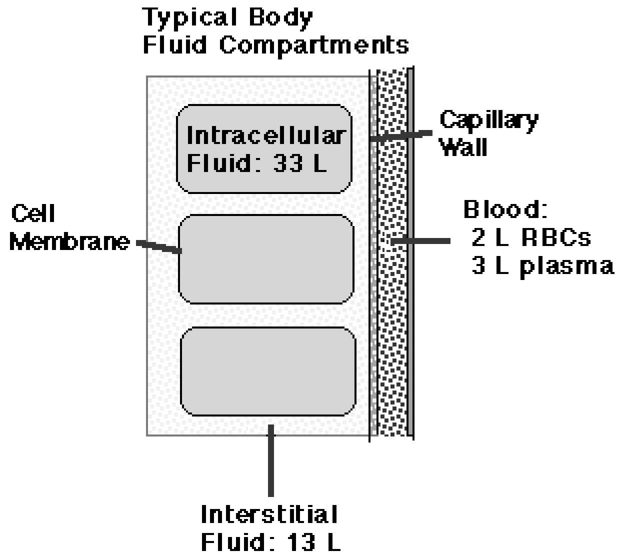
BODY FLUID COMPARTMENTS AND THEIR MEASUREMENTS

BODY FLUID COMPARTMENTS

1. Intracellular Fluid (ICF)
    - a) Within cells
2. Extracellular Fluid (ECF)
    - a) Outside cells
    - b) Further compartmentalized into
        - (1) Plasma
        - (2) Interstitial fluid
        - (3) Boundary is capillary walls
3. Boundary between ECF and ICF are cell membranes

Your Body is Split Into 3 Solution-Filled Compartments

- Body 60-80% water by weight
- 70 kg man has ~ 49 kg water = ~49 liters
- 3 Main compartments:



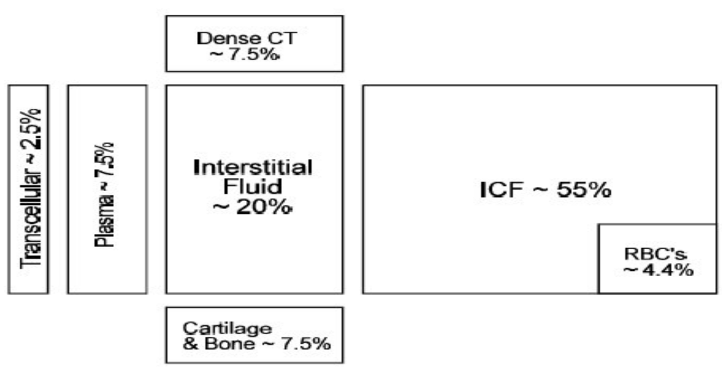
  - Intracellular (inside cells) = ~ 34 liters
  - Interstitial (outside cells) = ~ 13 liters
  - Blood plasma = ~3 liters
    - 40% of blood is red blood cells (RBCs)
    - Note1: plasma is similar to interstitial fluid, but contains plasma proteins
    - Note 2: serum = plasma with clotting proteins removed
    - Note 3: intracellular fluid is very different from interstitial fluid (high K concentration instead of high Na concentration, for example)
  - Boundaries:
    - Capillary walls (1 cell thick) separate blood from interstitial fluid
    - Cell membranes separate intracellular and interstitial fluids
- Loss of about 30% of body water is fatal
  - This can be a problem in the desert
  - Many diseases involving diarrhea can dehydrate the body to this extent (i.e., cholera)

Water is Very Special in Biology

- Most abundant chemical of life
- Special water properties of importance in physiology:

Property	Biological Applications
Liquid over wide temperature range	**Chemical reactions take place readily in liquids. Useful for circulatory systems. Many microorganisms find body fluids an attractive place to live.**
Excellent solvent	**Good for chemical reactions, waste removal, delivery of food materials.**
Ionizing solvent (high dielectric constant)	**Ionizes salts, makes conductive solutions. Important for nerves and other excitable tissues.**
Low viscosity (flows readily)	**Important for circulatory systems. Less work for the heart.**
High surface tension (surface acts as though coated with tough film)	**Tends to make the lung alveoli collapse. Causes serious medical problems when lung surfactant is low.**
High heat capacity (large amount of heat required to raise water temperature)	**Useful for moving large amounts of heat in the circulatory system.**
High heat of vaporization (large amount of heat removed when water evaporates)	**Used by mammals for sweating (the only way the body can lose heat if the ambient temperature is above body temperature).**
High heat conduction	**Useful for removing the heat produced by biological reactions. Prevents overheating of the body.**

Distribution of TBW



FLUID COMPARTMENTS IN DETAIL

The major division is into Intracellular Fluid (ICF: about 23 liters) and Extra cellular Fluid (ECF: about 19 liters) based on which side of the cell membrane the fluid lies. Typical values for the size of the fluid compartments are listed in the table.

Body Fluid Compartments (70 kg male)

	% of Body Weight	% of Total Body Water	Volume (Litres)
ECF	27	45	19
Plasma	**4.5**	**7.5**	**3.2**
ISF	**12.0**	**20.0**	**8.4**
Dense CT water	*4.5*	**7.5**	**3.2**
Bone water	*4.5*	*7.5*	**3.2**
Transcellular	**1.5**	**2.5**	**1.0**
ICF	33	55	23
TBW	60%	100%	42 liters

Intracellular Fluid

The Intracellular Fluid is composed of at least 10^{14} separate tiny cellular packages. The concept of a single united "compartment" called intracellular fluid is clearly artificial. The ICF compartment is really a "virtual compartment" considered as the sum of this huge number of discontinuous small collections.

Location: The distinction between ICF and ECF is clear and is easy to understand: they are separated by the cell membranes

Composition: Intracellular fluids are high in potassium and magnesium and low in sodium and chloride ions

Behaviour: Intracellular fluids behave similarly to tonicity changes in the ECF

Extracellular Fluid

A similar argument applies to the Extracellular Fluid. The ECF is divided into several smaller compartments (eg plasma, Interstitial fluid, fluid of bone and dense connective tissue and transcellular fluid). These compartments are distinguished by different locations and different kinetic characteristics. The ECF compositional similarity is in some ways, the opposite of that for the ICF (ie low in potassium & magnesium and high in sodium and chloride).

Interstitial fluid (ISF) consists of all the bits of fluid which lie in the interstices of all body tissues. This is also a ‘virtual’ fluid (ie it exists in many separate small bits but is spoken about as though it was a pool of fluid of uniform composition in the one location).

The ISF bathes all the cells in the body and is the link between the ICF and the intravascular compartment. Oxygen, nutrients, wastes and chemical messengers all pass through the ISF. ISF has the compositional characteristics of ECF (as mentioned above) but in addition it is distinguished by its usually low protein concentration (in comparison to plasma). Lymph is considered as a part of the ISF. The lymphatic system returns protein and excess ISF to the circulation. Lymph is more easily obtained for analysis than other parts of the ISF.

Plasma is the only major fluid compartment that exists as a real fluid collection all in one location. It differs from ISF in its much higher protein content and its high bulk flow (transport function). Blood contains suspended red and white cells so plasma has been called the 'interstitial fluid of the blood'. The fluid compartment called the blood volume is interesting in that it is a composite compartment containing ECF (plasma) and ICF (red cell water).

The fluid of bone & dense connective tissue is significant because it contains about 15% of the total body water. This fluid is mobilised only very slowly and this lessens its importance when considering the effects of acute fluid interventions.

Transcellular fluid is a small compartment that represents all those body fluids which are formed from the transport activities of cells

Typical Electrolyte concentrations in some Transcellular fluids (in mmol/l)

	[Na^+]	**[K^+]**	**[Cl^-]**	**[HCO_3^-]**
Saliva	20-80	10-20	20-40	20-60
Gastric juice	20-100	5-10	120-160	0
Pancreatic juice	120	5-10	10-60	80-120
Bile	150	5-10	40-80	20-40
Ileal fluid	140	5	105	40
Colonic fluid	140	5	85	60
Sweat	65	8	39	16
CSF	147	3	113	25

MEASUREMENT OF COMPARTMENT VOLUMES

The Dilution Principle

Compartment volumes are measured by determining the volume of distribution of a tracer substance. A known amount of a tracer is added to a compartment. The tracer concentration in that compartment is measured after allowing sufficient time for uniform distribution throughout the compartment. The compartment volume is calculated as:

Volume = Amount of tracer / Concentration of tracer

Ideally, the tracer should have certain properties (see box)

> ***Properties of an Ideal Tracer***
> The tracer should:
>
> - be nontoxic
> - be rapidly and evenly distribute throughout the nominated compartment not enter any other compartment.
> - not be metabolised
> - not be excreted (or excretion is able to be corrected for) during the equilibration period
> - be easy to measure
> - not interfere with body fluid distribution

If the tracer is excreted in the urine, then the loss can be determined and corrections made in the calculation. If the tracer is metabolised, a series of measurements can be made and assuming exponential decline (first order kinetics), the volume of distribution can be determined by extrapolation back to zero time.

Total Body Water

This is estimated by measuring the volume of distribution of isotopes of water. Tritium oxide (THO) is used because it is a weak beta emitter making it easy to measure in a liquid scintillation counter. Rapid mixing of tritiated water throughout all compartments occurs during a 3 to 4 hour equilibration period. Results are accurate and reproducible to within 2 percent.

Extracellular Fluid

Tracers used fall into 2 groups:

- Ionics (eg 82Br, $^{35}SO_4$, chloride isotopes)
- Crystalloids (eg Inulin, mannitol)

The ionic tracers are small and distribute throughout the ECF but there is some entry into cells. ECF will be over-estimated with these tracers

The crystalloids are larger and less diffusable throughout the ECF. They do not enter cells but the lack of full ECF distribution results in a low estimate of ECF.

What is measured is not the 'true' ECF so it is conventional to refer to the compartment measured not as ECF but as a space defined by the tracer used and the equilibration time (eg '20 hour bromide space').

Measurements indicate that the ECF can be modelled as consisting of:

- a rapidly equilibrating pool ("functional ECF") which makes up about 27 to 30% of total body water (This rapid pool represents plasma and most of the ISF)
- a slowly equilibrating pool (24 hours) which makes up 15% of total body water. (This slow pool mostly represents the water of dense connective tissue and bone and some of the transcellular fluid)

Plasma Volume

Measurement of plasma volume requires a tracer which is mostly limited to this compartment and this is achieved by using a tracer which binds to albumin. The tracers used are the azo dye known as **Evan's blue** (or T1824) which binds avidly to albumin, or **radio-iodine labelled serum albumin (RISA)**. Distribution is rapid but no equilibrium is reached because of continuous disappearance of albumin from the vascular space. This problem is overcome by using serial measurements and plotting the disappearance curve of the label. This is a first order process (ie exponential decline) which gives a straight line when plotted on a logarithmic scale. Extrapolation back to zero time allows estimation of the virtual concentration at this time. The volume is determined via the dilution principle using this concentration at zero time. As the concentration of the tracer is determined in a plasma sample, the measured volume of distribution is the plasma volume.

Blood Volume

The tracer is the patient's own red cells which are tagged with **radio-chromium (51Cr-red cells)**. The labelled red cells are centrifuged, resuspended in saline and reinfused. The volume of distribution (VD) is determined after about 10 minutes. As the radioactive label distributes throughout the whole intravascular compartment, the measured VD is the blood volume (rather than the red cell volume). However, the distribution of the label is not uniform because the haematocrit is different in different parts of the circulation. Accounting for these effects, the whole body haematocrit can be estimated as about 91% of large vein haematocrit and this value should be substituted in the equations.

It is usual therefore to measure the amount of the label in a red cell sample and therefore to directly measure the red cell volume.
Plasma volume or red cell volume can be determined indirectly if the blood volume and haematocrit (Hct) are known.

Formulae for Blood Volume

- Blood Volume = Plasma volume x (100/100-Hct)
- Blood Volume = Red cell vol x (100/Hct)

(where Hct = Haematocrit)

The remaining volumes cannot be calculated directly and are therefore ***derived*** from the above volumes

1. Intracellular Volume = TBW - ECF
2. Interstitial Volume = ECF - Plasma Volume

FLUID AND ELECTROLYTE BALANCE

Fluid regulation is essential to homeostasis. If water or electrolyte levels rise or fall beyond normal limits, many bodily functions fail to proceed at their normal rates. Maintaining normal pH levels is also important for normal body functioning because small changes in pH can produce major changes in metabolism.

Water is a constituent of all living things. It is often referred to as the *universal biological solvent*. Only liquid ammonia is able to dissolve more substances than water.

Water acts to minimise temperature changes throughout the body because of its high specific heat.

A considerable amount of energy is needed to break the hydrogen bonds between water molecules in order to make the water molecules move faster (that is, increase the temperature of water). Therefore, water can absorb much heat without rapidly changing its own temperature.

The adult human body consists of about 60% water by weight, depending upon age and the amount of body fat. The water content of the tissues of the body varies. Adipose tissue (fat) has the lowest percent of water; the skeleton has the second lowest water content. Skeletal muscle, skin, and the blood are among the tissues that have the highest content of water in the body.

Infants have a higher percent of water than adults do as much as 77%. The total water content of the body decreases most dramatically during the first 10 years and continues to decline through old age, at which time it may be only 45% of the total body weight. Men tend to have higher percentages of water (about 65%) than women (about 55%) mainly because of their increased muscle mass and lower amount of subcutaneous fat. Fat has less water content than any other body tissue. This also accounts for a lower than normal water percentage in obese people.

The water in the body has many important functions, which are listed in table below.

	Water has many important functions in the body
1	All chemical reactions occur in the medium.
2	It is crucial in regulating chemical and bioelectrical distributions within cells.
3	Transports substances such as hormones and nutrients.
4	O_2 transport from lungs to body cells.
5	CO_2 transport in the opposite direction.
6	Dilutes toxic substances and waste products and transports them to the kidneys and the liver.
7	Distributes heat around the body

Water in the body is in a constant state of motion. Shifting between the three major fluid compartments of the body and in addition being continuously lost from, and taken into, the person.

In a normal, healthy human being WATER INPUT = WATER OUTPUT.

Maintaining this ratio is of prime importance in maintaining health.

Approximately 90% of the body's water intake comes via the gastro-intestinal tract. The remaining 10% is called metabolic water and is produced as the result of various chemical reactions in the cells of the body's tissues.

The normal healthy adult loses water via the route shown in table below.

GASTRO-INTESTINAL TRACT	(FAECES)	6%
LUNGS	(WATER VAPOUR)	13%
SKIN	(DIFFUSION & SWEAT)	19%
KIDNEYS	(URINE)	62%

The amount of water lost via the kidneys is under hormonal control. The average amount of water lost and consumed per day is around 2.5 litres (approx. $4^1/_4$ pints) in a healthy adult.

Body fluid is found in three different fluid compartments within the body. These are:

1. Blood plasma

2. Interstitial fluid

3. Intracellular fluid

Number 1 and 2 above make up the portion of body fluid known as extracellular fluid.

In terms of body weight and total percentage of body water, these can be summarised as in table below.

	% Body weight	*% total body water*
Extracellular fluid	20	37.5
(Comprising		
Blood plasma	(5)	(7.5)
Interstitial fluid)	(15)	(30.0)
Intracellular fluid	40	62.5

From the table it can be seen that most of the body's water is locked up within tissue cells

The walls of the blood vessels form a barrier to the free passage of fluid between interstitial fluid and blood plasma. At the capillaries, these walls are only one cell thick. These capillary walls are generally permeable to water and small solutes but impermeable to large organic molecules such as proteins. Thus, the blood plasma tends to have a higher concentration of such molecules when compared to the interstitial fluid. Much of this interstitial fluid is taken up by the lymphatic system and eventually finds its way back into the blood stream. This process is discussed in the pages on the lymphatic system.

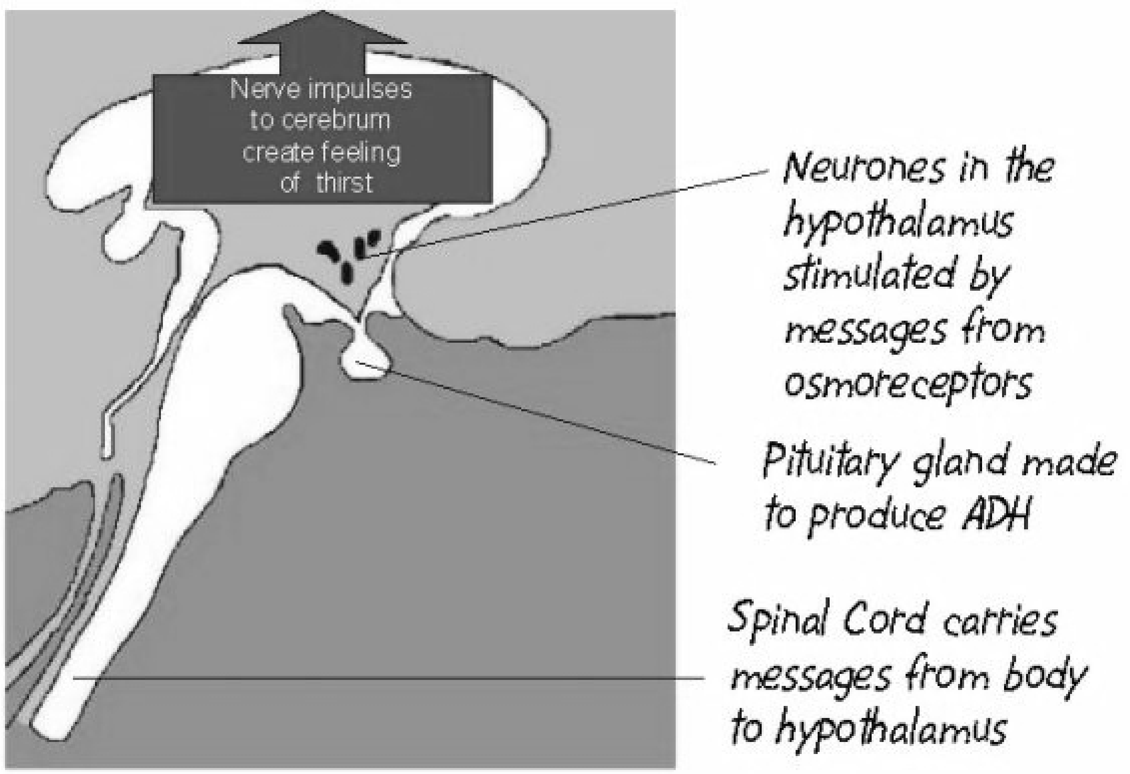
Because water and small solutes such as sodium ($Na^{+)}$, potassium ($K^{+)}$, calcium (Ca^{++}), etc. can be freely exchanged between the blood plasma and the interstitial fluid, regulation of these electrolytes can be controlled by the action of the kidneys on the blood. This exchange depends mainly upon the hydrostatic and osmotic forces of both of these fluid compartments.

The mechanisms for the regulation of body fluids are centred in the *hypothalamus*. The hypothalamus also receives input from the digestive tract that helps in the control of thirst.

The regulation of body fluid volume and extracellular osmolarity is under the control of Anti Diuretic Hormone (ADH)

ADH has many areas of influence in the body. One of the major functions of ADH is to increase the permeability of the distal convoluted tubules and the collecting tubules in the kidneys. This allows more water to be reabsorbed in the kidneys. This is manifest in times of drought or if the body is short of fluid intake (such as during sleep) and results in a concentrated, darker coloured urine of reduced volume. Absence of ADH occurs when the individual is over-hydrated such as at a party if a lot of beer, cider, alcopops etc. are being drunk Here the urine is dilute, pale or colourless and of high volume.

Primary factors involved in the triggering of ADH production are osmoreceptors and baroreceptors (pressure receptors). Secondary factors include, stress, pain, hypoxia, severe exercise, surgery (especially anaesthetics such as cyclopropane and nitrous oxide).



Osmoreceptors

These trigger ADH production in response to the following:

Dehydration produced by either water loss or lack of fluid intake. This increases the osmolarity of the plasma.

Relative dehydration in which there is no overall loss of the body's water content but the gain of sodium ions. The effect is again to raise the osmolarity of the plasma.

The precise location of the osmoreceptors is as yet unclear but it seems likely that they are to be found in the hypothalamus or the third ventricle of the brain

Baroreceptors

ADH secretion is also stimulated by changes in the circulating volume of body fluid that results in an increase or decrease of internal pressure.

A reduction of around 8-10% from the normal body volume of water due to haemorrhage or excess perspiration in desert conditions will result in ADH secretion.

Pressure receptors are located in the atria of the heart and the pulmonary artery and vein and relay their messages to the hypothalamus via the vagus nerve.

Thirst response

This is connected to the response of the osmoreceptors. How in fact it actually works is not yet completely understood. We know that it takes up to one hour for ingested fluid to be completely absorbed and distributed in the body. So how is it that a person seems to know instinctively how much to drink? Why is thirst satisfied so quickly after taking in a fluid? Why are some fluids more thirst quenching than others are?

It would appear that the moistening of the mucosal linings of the mouth and pharynx initiates some sort of neurological response, which sends a message to the thirst centre of the hypothalamus. Perhaps more importantly stretch receptors in the gastro-intestinal tract also appear to transmit nerve messages to the thirst centre of the hypothalamus, which inhibit the thirst response.

Clinical problems with fluid balance

There are many ways in which the body's fluid balance can be upset resulting in severe problems and even death.

Dehydration will obviously occur in conditions of drought where the individual is unable to obtain water. However, conditions such as diarrhoea, severe vomiting, excessive sweating, bleeding, and surgical removal of body fluids can also result in dehydration. Three types of dehydration may occur as a result of the above. Hypertonic dehydration occurs when the fluid loss results in an increase in the electrolyte levels. This causes the blood pressure to fall and the blood to become thicker and can result in heart failure. Isotonic dehydration results in no perceptible difference from the normal electrolyte balance. This may lead to hypotonic dehydration where the fluid and electrolyte losses keep pace with each other. Any intake of pure water will alter the fluid electrolyte balance (too much water not enough electrolyte). This is why it is important in cases of severe diarrhoea to replace the body fluid with a balanced preparation of salts and water.

Problems with the production of urine can also lead to dehydration. Impaired ability to concentrate urine can be caused by:

Damage to the medulla of the kidneys. This can occur in chronic renal disorders such as pyelonephritis. The problem here results in damage to the Loop of Henle. Consequently inadequate water re-absorption in the loop occurs and the urine is too dilute resulting in fluid loss.

Inadequate ADH production. This can occur in the condition of diabetes insipidus. Individuals suffering from this may eliminate as much as 5 to 20 litres ($8^1/_2$pints to 34 pints) of urine per day. A psychological disorder known as polydipsia may occur where the sufferer is obsessed with drinking (usually water). This results in dilution of the plasma causing artificial lowering of the osmolarity and decreasing ADH secretion.

Solute diaresis occurs in individuals suffering from diabetes mellitus. Here elevated blood sugar levels brings about an inability of the kidney to re-absorb water resulting in excess fluid loss.

In any of the above conditions, fluid balance must be maintained otherwise dehydration or even hypovolaemic shock (due to insufficient volume of body fluid) may occur.

Oedema is a condition in which there is an excess of fluid within the interstitial compartment. This often results in tissue swelling (see fig. 4) it is common whenever there is a lymphatic blockage as in elephantiasis where a parasitic worm blocks the lymph vessels. Other causes result from an impaired ability of the body to dilute the urine.

Renal failure can lead to this problem especially the early stages of acute renal failure and the later stages of chronic renal failure.

Liver failure can result in inefficient metabolism of aldosterone a hormone that controls sodium (Na^+) levels. Because the aldosterone is not properly broken down by the body the levels of this hormone will rise resulting in increased Na^+ reabsorption and consequently ware reabsorption as water will be attracted to the sodium ions. This results in a concentrated dark coloured urine and fluid retention.

Heart failure means that the production of aldosterone is enhanced due to the lowering of the BP. The result is the same as in liver failure.

Excessive ADH secretion is a rare condition which may occur as a result of tumours in the lung, brain or pancreas resulting in increased reabsorption of water.

Steady pressure of thumb onto lower leg for 10-20 seconds. If depression remains after removal of pressure fluid retention is indicated.

In any condition where there is fluid retention as in kidney failure, heart failure or liver failure as described above or as at rave parties where excess amounts of water are consumed a condition known as water intoxication may occur. This can lead to severe vomiting and diarrhoea. In more severe cases this can result in neurological dysfunction, circulatory shock and even death.

Electrolyte Balance

An electrolyte is actually any chemical that dissociates into ions when dissolved in a solution. Ions can be positively charged (cations) or negatively charged (anions).

The major electrolytes found in the human body are:

Sodium (Na^+)

Potassium (K^+)

Calcium ($Ca^{==}$)

Magnesium (Mg^{++})

Chloride (Cl^-)

Phosphate (HPO_4^{--})

Sulphate (SO_4^{--})

Bicarbonate (HCO_3^-)

Interstitial fluid and blood plasma are similar in their electrolyte make up. Na^+ and Cl^- being the major electrolytes. In the intracellular fluid, K^+ and HPO_4^- are the major electrolytes.

ELECTROLYTE DISTRIBUTION			
Electrolyte	Extracellular meq/liter	Intracellular meq/liter	Function
Sodium	142	10	fluid balance, osmotic pressure
Potassium	5	100	Neuromuscular excitability acid-base balance
Calcium	5	-	bones, blood clotting
Magnesium	2	123	enzymes
Total Positive ions	154	205	

Electrolyte Distribution			
Electrolyte	Extracellular meq/liter	Intracellular meq/liter	Function
Chloride	105	2	fluid balance, osmotic pressure
Bicarbonate	24	8	acid-base balance
Proteins	16	55	osmotic pressure
Phosphate	2	149	energy storage
Sulfate	1	-	protein metabolism
Total Negative ions	154	205	

Sodium Balance

This plays a crucial role in the excitability of muscles and neurones. It is also of crucial importance in regulating fluid balance in the body. Sodium levels are extremely closely regulated by kidney function. Sodium is easily filtered in the glomerular portion of the kidneys and most of it is reabsorbed in the kidney tubules. (see lecture notes for the session on the kidneys for a fuller explanation of this process.) The rate of excretion is directly affected by the rate of filtration of sodium in the glomerulus. (GFR). Major factors that control the GFR include the blood pressure at the glomerulus and the stimulation of renal arteriole by the sympathetic nervous system.

The hormone aldosterone (as has already been mentioned) controls the rate of reabsorption of sodium in the distal convoluted tubules and the collecting ducts of the kidneys.

The amount of sodium reabsorbed in the proximal convoluted tubule remains almost constantly at around 67%.

Release of aldosterone occurs as a result of a complex process known as the renin-angiotensin-aldosterone pathway.

If the arterial BP falls, renin is released. This readily converts angiotensinogen into it's active form angiotensin I. This then travels to the capillary beds where it becomes angiotensin II which is one of the most powerful vasoconstrictors in the body. It is also a stimulator for aldosterone release from the adrenal glands. Because water has a close chemical affinity for sodium, it will follow that more water is reabsorbed in the kidney as well and this will put up the BP to a normal level.

An increase in the arterial BP will result in the release of atrial natriuretic factor (ANF) from the l. and r. atria of the heart. This hormone actually inhibits renin and aldosterone release. By so doing the loss of sodium by the kidneys is enhanced by the decrease of aldosterone stimulated reabsorption. As we have already seen that water will follow sodium, it follows that water is lost from the body allowing the BP to drop to a normal level.

Potassium Balance

Potassium is the major cation of intracellular fluid. Concentration within the cells is 28x that of the extra cellular fluids. As with sodium it is extremely important in the correct functioning of excitable cells such as muscles, neurones, sensory receptors etc. It is also importantly involved in the regulation of fluid levels within the cell and in maintaining the correct pH balance within the body.

Potassium output is usually equal to potassium input. Sodium reabsorption by aldosterone is usually in exchange for either hydrogen ions or potassium ions. Therefore if sodium ions are reabsorbed more potassium is lost and vice versa. Thus, high levels of potassium in the interstitial fluid stimulate aldosterone response. Diseases such as Cushing's disease (over production of ACTH) and hyperaldosteronism (overproduction of aldosterone) can lead to a condition known as hypokalaemia (symptoms caused by low potassium levels) which manifests in muscle weakness, flaccid paralysis, cardiac arrhythmias and alkalosis.

The pH balance of the body also affects potassium levels. In acidosis potassium excretion is decreased (leads to hyperkalaemia higher than normal levels of potassium) whereas the opposite occurs in alkalosis.

Calcium and Phosphorous Balance

Calcium is found mainly in the extracellular fluids whilst phosphorous is found mostly in the intracellular fluids.

Both are important in the maintenance of healthy bone and teeth.

Calcium is also important in the transmission of nerve impulses across synapses, the clotting of blood and the contraction of muscles. If the levels of calcium fall below normal level both muscles and nerves become more excitable.

Phosphorous is required in the synthesis of nucleic acids and high-energy compounds such as ATP. It is also important in the maintenance of pH balance.

If the levels of calcium in the body fall the parathyroid gland is stimulated to secrete parathyroid hormone (PH). This causes an increase in both the calcium and the phosphate levels of the interstitial fluids by releasing them from the reservoirs of these minerals lodged in the bones and the teeth. PH also decreases calcium excretion by the kidneys.

If the levels of calcium in the body become too high the thyroid gland releases a hormone called calcitonin. This inhibits the release of calcium and potassium from the bones. It also inhibits the absorption of calcium from the gastro-intestinal tract and increases calcium excretion by the kidneys.

Magnesium Balance

Most magnesium is found in the intracellular fluid and in bone. Within cells magnesium functions in the sodium-potassium pump and as an aid to the action of enzymes. It plays a role in muscle contraction, action potential conduction, and bone and teeth production. Aldosterone controls magnesium concentrations in the extracellular fluid. Low Mg^{++} levels result in an increased aldosterone secretion, and the aldosterone increases Mg^{++} reabsorption by the kidneys.

Chloride Balance

Chloride (Cl^-) is the most plentiful extracellular anion with an extracellular concentration 26 times that of its intracellular concentration. Chloride ions are able to diffuse easily across plasma membranes and their transport is closely linked to sodium movement, which also explains the indirect role of aldosterone in chlorine regulation. When sodium is reabsorbed, chlorine follows passively. It helps to regulate osmotic pressure differences between fluid compartments and is essential in pH balance. The chloride shift within the blood helps to move bicarbonate ions out of the red blood cells and into the plasma for transport. In the gastric mucosa, chlorine and hydrogen combine to form hydrochloric acid.

pH Balance

pH is a measurement of the hydrogen concentration of a solution. Lower pH values indicate a

higher hydrogen concentration, or a higher acidity. Higher pH values indicate a lower hydrogen concentration, or higher alkalinity.

Therefore, hydrogen ion balance is often referred to as pH balance or acid-base balance. Hydrogen ion regulation in the fluid compartments of the body is of critical importance to health. Even a slight change in hydrogen ion concentration can result in a marked alteration in the rate of chemical reactions. Changes in hydrogen ion concentration can also affect the distribution of ions such as sodium, potassium, and calcium. It also can affect the structure and function of proteins.

The normal pH of the arterial blood is 7.4, whereas that of the venous blood is 7.35. The lower pH of the venous blood is due to the higher concentration of carbon dioxide in the venous blood, which dissolves in water to make a weak acid, called carbonic acid. When the pH changes in the arterial blood, two conditions may result: acidosis or alkalosis. Acidosis is a condition occurring when the hydrogen ion concentration of the arterial blood increases and, therefore, the pH decreases. Alkalosis is the condition occurring when the hydrogen ion concentrations in the arterial blood decreases and the pH increases.

Sources of hydrogen ions in the body include: carbonic acid formed as mentioned above, sulphuric acid (a by-product in the breakdown of proteins), phosphoric acid (a by-product of protein and phospholipid metabolism), ketone bodies from fat metabolism, and lactic acid (a product formed in skeletal muscle during exercise).

About half of all the acid formed or introduced into the body is neutralised by the ingestion of alkaline foods. The remaining acid is neutralised by three major systems of the body. Namely chemical buffers, the respiratory system and the kidneys.

Chemical buffers have an instantaneous effect on pH changes. They are very effective in minimising pH changes but do not entirely eliminate the change. Within cells chemical buffer generally take about 2 to 4 hours to minimise changes in pH. The respiratory system also helps to minimise pH changes; the effects occur within minutes. Renal regulation of pH is able to completely return the pH to normal and requires from hours to several days.

COMPOSITIONS AND FUNCTIONS OF BLOOD

BLOOD

Properties of Blood:

Our bodies consist of metabolically active cells that need a continuous supply of nutrients and oxygen. Metabolic waste products need to be removed from the cells to maintain a stable cellular environment. Blood is the primary transport medium that is responsible for meeting these cellular demands.

Materials transported by the blood include nutrients, waste products, gases, and hormones. The blood helps to regulate the fluid and electrolyte balance, acid base balance, and the body temperature. Protection against pathogens is provided by white blood cells, and the clotting mechanism prevents excessive loss of blood after injuries.

Functions of Blood:

1 - Transportation:

- oxygen & carbon dioxide
- nutrients
- waste products (metabolic wastes, excessive water, & ions)

2 - Regulation - hormones & heat (to regulate body temperature)

3 - Protection - clotting mechanism protects against blood loss & leucocytes provide immunity against many disease-causing agents

BLOOD IS A LIQUID CONNECTIVE TISSUE THAT MEASURES ABOUT 5 LITERS IN THE ADULT HUMAN AND ACCOUNTS FOR 8 PERCENT OF THE BODY WEIGHT. ITS NORMAL pH RANGE IS 7.35-7.45.

The following activities are under the transportation function:

Carries O_2 and nutrients to the cells
Transports CO_2 and wastes from the tissues to the lungs and the kidneys where wastes can be removed from the body
Carries hormones to the endocrine glands to the target tissues

The following activities are under the regulation function:

Helps to regulate body temperature by removing heat from active areas, such as skeletal muscles and transporting it to other areas of the skin so the heat can be dissipated
Plays a significant role in fluid and electrolyte balance because salt and plasma proteins contribute to the osmotic pressure by providing weight and bulk to our blood
Functions in pH regulation through the action of buffers in the blood

Functions of the blood that are in the protection category:

Clotting mechanisms prevent fluid loss through hemorrhage when blood vessels become damaged
Certain cells in the blood, phagocytic white blood cells help to protect the body against diseases by engulfing and destroying the agent
Antibodies in the plasma help protect against disease by their reactions with offending agents

BLOOD FUNCTIONS AS A TRANSPORT MEDIUM. IT ALSO HAS ROLES IN TEMPERATURE REGULATION, FLUID AND ELECTROLYTE BALANCE, pH REGULATION, PREVENTION OF FLUID LOSS, AND DISEASE PREVENTION.

CHARACTERISTICS OF BLOOD

Blood has distinctive physical characteristics:

Amount- a person has 4-6 liters of blood, depending on the body size. Of the total blood volume in the human body, 38% to 48% is composed of the various blood cells also called ?formed elements?. The remaining 52% to 62% of the blood volume is the plasma or the liquid portion of the blood.

Color- yeah? of course it's red. Arterial blood is bright red because it contains high levels of oxygen. Venous blood has given up much of its oxygen in tissues and has a darker, dull red color. This may be important in the assessment of the source of bleeding.

PH- the normal pH range of blood is 7.35-7.45, which is slightly alkaline.

Viscosity- this means the thickness or the resistance to flow. Blood is about 3 to 5 times thicker than water. Viscosity is increased by the presence of blood cells and the plasma proteins, and this thickness contributes to normal blood pressure.

COMPOSITION OF BLOOD

When a sample of blood is spun in a centrifuge, the cells and cell fragments are separated from the liquid. Because the formed elements are heavier than the liquid matrix, they are packed in the bottom of the tube by the centrifugal force. The straw colored liquid on the top is the plasma.

A GIVEN VOLUME OF BLOOD IS 55 PERCENT PLASMA AND 45 PERCENT FORMED CELLS.

Plasma is the liquid portion of blood and it is about 90% water. The remaining portion consists of more than 100 different organic and inorganic solutes that are dissolved in water. Because plasma is a transport medium, its solutes are continuously changing as substances are added or removed by the cells.

Plasma proteins are the most abundant solutes in the plasma. These proteins remain in the blood and interstitial fluid and are not used for energy. The three major classes of plasma proteins are: albumins, globulins, and fibrinogen. Many of the plasma proteins are synthesized in the liver, and each one has a different function.

Albumins- is the most abundant plasma proteins. It is synthesized by the liver. Because they are so abundant, they contribute to the osmotic pressure of the blood and play an important role in maintaining fluid balance between blood and interstitial fluid. If the osmotic pressure of the blood decreases, fluid moves from the blood into the interstitial spaces, which results in edema. This also decreases blood volume and, in severe cases, may reduce blood pressure. When blood osmotic pressure increases, fluid moves from the interstitial spaces into the blood and increases the blood volume. This increases blood pressure and decreases the amount of water available to the cells.

Globulins- there are three types of globulins; alpha, beta, and gamma. Alpha and beta globulins are produced in the liver and function in transporting lipids and fat soluble vitamins in the blood. Gamma globulins are the antibodies that function in immunity.

Fibrinogen- makes up the smallest fraction of plasma proteins. It is produced in the liver and functions in blood clotting. These types of plasma proteins are the largest of the molecules.

Nutrients, oxygen, and carbon dioxide are transported as solutes in the plasma.

FORMED ELEMENTS

- Red blood cells (or erythrocytes)
- White blood cells (or leucocytes)
- Platelets (or thrombocytes)

The production of these formed elements or blood cells is called hemopoeisis!

Red Blood Cells (or erythrocytes):

1 - Biconcave discs

2 - Lack a nucleus & cannot reproduce (average lifespan = about 120 days)

3 - Transport hemoglobin (each RBC has about 280 million hemoglobin molecules)

4 - Typical concentration is 4-6 million per cubic mm (or hematocrit [packed cell volume] of about 42% for females & 45% for males)

5 - Contain carbonic anhydrase (critical for transport of carbon dioxide)

Hemoglobin

- composed of globin (made up of 4 highly folded polypeptide chains) + 4 heme groups (with iron)
- each molecule can carry 4 molecules of oxygen
- called oxyhemoglobin when carrying oxygen & called reduced hemoglobin when not carrying oxygen
- can also combine with carbon dioxide & helps transport carbon dioxide from the tissues to the lungs

White blood cells (or leucocytes or leukocytes):

- have nuclei & do not contain hemoglobin
- typical concentration is 5,000 - 9,000 per cubic millimeter
- types of WBCs:
  - granular white blood cells include:
    - neutrophils (50 - 70% of WBCs)
    - eosinophils (1 - 4%)
    - basophils (less than 1%)
  - agranular (or non-granular) white blood cells include:
    - lymphocytes (25 - 40%)
    - monocytes (2 - 8%)

Granular white blood cells contain numerous granules in the cytoplasm, & their nuclei are lobed. Agranular white blood cells have few or no granules in the cytoplasm & have a large spherical nucleus. Granular white blood cells are produced in the bone marrow, while agranular white blood cells are produced in lymph tissue, e.g., Lymph nodes (specialized dilations of lymphatic tissue which are supported within by a meshwork of connective tissue called reticulin fibers and are populated by dense aggregates of lymphocytes and macrophages).

The primary functions of the various white blood cells are:

- Neutrophils - phagocytosis (bacteria & cellular debris); very important in inflammation
- Eosinophils - help break down blood clots & kill parasites
- Basophils - synthesize & store histamine (a substance released during inflammation) & heparin (an anticoagulant); functions(s) remain unclear
- Monocytes - phagocytosis (typically as macrophages in tissues of the liver, spleen, lungs, & lymph nodes)
- Lymphocytes - immune response (including production of antibodies)

Some important characteristics of White Blood Cells (particularly neutrophils):

1 - phagocytic
2 - capable of diapedesis (also called extravasation)

3 - capable of ameboid movement (check out Ameboid Movement - Amoeba)

4 - exhibit chemotaxis (attracted to certain chemicals, such as those released by damaged cells)

Platelets (or thrombocytes)

1 - Formed in the bone marrow from cells called megakaryocytes

2 - Have no nucleus, but can secrete a variety of substances & can also contract (because they contain actin & myosin)

3 - Normal concentration in the blood is about 250,000 per cubic millimeter

4 - remain functional for about 7 - 10 days (after which they are removed from the blood by macrophages in the spleen & liver)

5- Play an important role in hemostasis (preventing blood loss)

Plasma:

1 - Water - serves as transport medium; carries heat

2 - Proteins

- Albumins
    - 60-80% of plasma proteins

    - most important in maintenance of osmotic balance
    - produced by liver
- Globulins
    - alpha & beta
        - some are important for transport of materials through the blood (e.g., thyroid hormone & iron)
        - some are clotting factors
        - produced by liver
    - gamma globulins are immunoglobulins (antibodies) produced by lymphocytes
- Fibrinogen
    - important in clotting
    - produced by liver

3 - Inorganic constituents (1% of plasma) - e.g., sodium, chloride, potassium, & calcium

4 - Nutrients - glucose, amino acids, lipids & vitamins

5 - Waste products - e.g., nitrogenous wastes like urea

6 - Dissolved gases - oxygen & carbon dioxide

7 - Hormones

BLOOD TYPING

Everybody has a blood type. The most common blood type classification system is the ABO (say "A-B-O") system discovered by Karl Landsteiner in the early 1900s. There are four types of blood in the ABO system: A, B, AB, and O. Your blood type is established before you are born, by specific genes inherited from your parents. You receive one gene from your mother and one from your father; these two combine to establish your blood type. These two genes determine your blood type by causing proteins called agglutinogens (a-GLOO-tin-a-gins) to exist on the surface of all of your red blood cells.

There are three alleles or versions of the blood type gene: A, B, and O. Since everybody has two copies of these genes, there are six possible combinations; AA, BB, OO, AB, AO, and BO. In genetic terms, these combinations are called genotypes, and they describe the genes you got from your parents.

In addition to the proteins (agglutinogens) existing on your red blood cells, other genes make proteins called agglutinins (a-GLOO-tin-ins) that circulate in your blood plasma. Agglutinins are responsible for ensuring that only the blood cells of your blood type exist in your body.

Your genotype determines your blood type.

The agglutinogen produced by the O allele has no special enzymatic activities. However, the agglutinogens produced by the A and B alleles do have enzymatic activities, which are different from each other. Therefore people whose genotype is OO are said to have type O blood, meaning the agglutinogen on their red blood cells doesn't have any enzymatic activity. People with Type O blood have agglutinins A and B in their blood plasma. Agglutinin A helps the body destroy any type A blood cells that might enter the circulation system. Agglutinin B helps the body destroy any type B blood cells that might enter the circulation system.

People who have an AA genotype are said to have type A blood because the agglutinogen on their red blood cells has the enzyme activity associated with the A allele. It is important to recognize that people with the AO genotype also have the enzyme activity associated with the A allele, so they are also said to have type A blood. (Remember the O allele doesn't have any enzyme activity associated with it!) People with Type A blood have agglutinin b in their blood plasma. Agglutinin b helps the body destroy any type B blood cells that might enter the circulation system.

Likewise, people with the BB and the BO genotypes are said to have type B blood. These people have agglutinin a in their blood plasma. Agglutinin a helps the body destroy any type A blood cells that might enter the circulation system.

People who have the AB genotype have the enzyme activity associated with both the A and B alleles. These people have no agglutinins in their blood plasma.

The concepts of genotype and phenotype can be easily understood in the case of blood type. Genotype refers the actual genes an individual possesses that determine a particular trait. Phenotype refers to the characteristics of that trait an individual displays. In the case of blood type, both the AA and AO genotypes cause individuals to display the A blood type phenotype. Similarly, both the BB and BO genotypes cause individuals to display the B blood type phenotype. Individuals who are phenotypically type O or type AB have only one possible genotype, OO and AB, respectively.

In different parts of the world, the fraction of individuals with blood type A, B, O, or AB differs. The frequency with which blood types are observed is determined by the frequency with which the three alleles of the ABO gene are found in different parts of the world (allele frequency). Variation in the allele frequency at the ABO gene reflects the social tendency of populations to marry and reproduce within a national, regional, or ethnic group. As people throughout the world intermingle to a greater extent, the distribution of the different blood types will become more uniform throughout the world.

All people belong to one of four inherited blood groups: A, B, AB, and O. The letters A and B refer to the kind of antigens found on an individual's red blood cells. An antigen is a protein or carbohydrate on the cell that triggers an immune response, such as the formation of antibodies.

Red Blood Cells:

- ABO system of antigens
- Rh system of antigens

ABO system:

- Type A antigen
- Type B antigen

Blood type	Antigen present
A	A
B	B
AB	A & B
O	neither A nor B

Antibodies:

- produced if antigen is not present
- produced because common intestinal bacteria have A- & B-like antigens
- produced by age of about 6 months

Blood type	Antigen	Antibody
A	A	anti-B
B	B	anti-A
AB	A & B	neither
O	neither	both anti-A & anti-B

If you mix anti-A antibodies with blood cells that have the A antigen OR mix anti-B antibodies with blood cells that have the B antigen, the results will be AGGLUTINATION (or clumping of red blood cells). This reaction can be used to type blood. You simply take two drops of 'unknown' blood and place a drop of anti-A antibody solution on one blood drop & a drop of anti-B antibody solution on the other blood drop. Then, look closely to see if any clumping occurs. If clumping occurs in the drop of blood where you added the anti-A antibodies, then you know that the A antigen is present (and, of course, if there is no clumping, then the A antigen is not present). If clumping occurs in the drop of blood where you added the anti-B antibodies, then you know that the B antigen is present (and, of course, if there is no clumping, then the B antigen is not present). Using this information, you can determine the blood type:

Drop of blood in which anti-A antibody was added	Drop of blood in which anti-B antibody was added	Blood type
Clumping	No clumping	A
No clumping	Clumping	B
Clumping	Clumping	AB
No clumping	No clumping	O

Type O blood is the most common blood type, followed by type A, type B, and, the least common blood type, AB.

Type O:

- universal donor
- no antigens = no clumping

Type AB:

- universal recipient
- no antibodies = no clumping

BLOOD TRANSFUSIONS

A transfusion is the infusion of a blood component through tubing connected to a needle that is inserted into a vein, usually in the arm. The amount and type of blood component transfused depends on the need of the patient.

A doctor may give a cancer patient a transfusion if he or she is having symptoms that may be related to low blood levels. First, lab tests such as a complete blood count (CBC) are done to make sure the patient's symptoms will be helped by a transfusion. These tests measure the levels of components within the blood such as red blood cells, white blood cells, and platelets. Coagulation (clotting) tests may also be done if abnormal bleeding is involved.

Blood Types

Not all blood is the same. People have different blood "types." These types are determined by substances called antigens on the surface of blood cells. The most important groups of antigens are called ABO and Rh. Each person has 1 of 4 possible ABO types (A, B, AB, or O) and 1 of 2 possible Rh types (Rh-positive or Rh-negative). These 2 factors combined yield 8 possible blood types.

Blood types are important when it comes to transfusions. If you receive a blood component transfusion that is not compatible with your blood type, your body's immune system could mount a defense against the donated blood, causing a transfusion reaction (described below), which can be serious or even life threatening.

To ensure no mistakes are made, donated blood is carefully "typed" (tested) both when it is collected from the donor and again once it is received by the hospital lab.

ABO blood types: Two antigens on blood cells (A and B) determine a person's ABO blood type (A, B, AB, or O). If you have type "A" blood, you have the A antigen on your red blood cells. Since you do not have B antigen on your cells, your body makes antibodies (immune system proteins) against the B antigen. These antibodies are in your plasma and would prevent you from getting either type B or AB red blood cells. You can receive type A or O red blood cell transfusions. If you donated blood, your red blood cells could be given to people with type A or AB blood.

If you have a "B" blood type, you have the B antigen on your red blood cells and have antibodies to the A antigen in your plasma. You can receive type B or O red blood cell transfusions. Your red blood cells can be given to people with type B or AB blood.

If you are an "AB" blood type, you have both the A and B antigens on your red blood cells and do not have antibodies to either of these antigens in your plasma. You can receive type A, B, AB or O red blood cell transfusions. Your red blood cells can be given only to other people with type AB blood.

If you have type "O" blood, you have neither A nor B antigens on your red blood cells, and your plasma has antibodies to both A and B antigens. You can only receive type O red blood cell transfusions. Your red blood cells can be given to people with type A, B, AB, or O blood, which is why you are sometimes called a "universal donor."

Rh factor: Blood is either Rh-positive or Rh-negative, depending on whether the red blood cells have Rh antigens on their surface. A person that has type A, Rh-positive blood is called "A positive," whereas a person with type O, Rh-negative blood would be "O negative."

If you have Rh-positive blood, you can receive Rh-positive or Rh-negative red blood cell transfusions. People with Rh-negative blood, however, should only receive Rh-negative red blood cells, unless there is an emergency.

Other antigens: There are other antigens on red blood cells that can lead to transfusion reactions, but these are rare because people do not make antibodies against them unless they have had a transfusion before. Plasma transfusions follow a different set of rules (based on the antibodies in the plasma):

- People with type O blood can receive any type of plasma.
- People with type A blood can receive A or AB plasma.
- People with type B blood can receive B or AB plasma.
- People with type AB blood can receive only AB plasma.
- The Rh type is usually not a factor in plasma transfusions.

For platelet and cryoprecipitate transfusions, matching the blood type of the donor to the recipient is usually not critical, although labs usually try to match them if possible. This is especially important in patients who have already had many transfusions or who have had transfusion reactions in the past.

Crossmatching

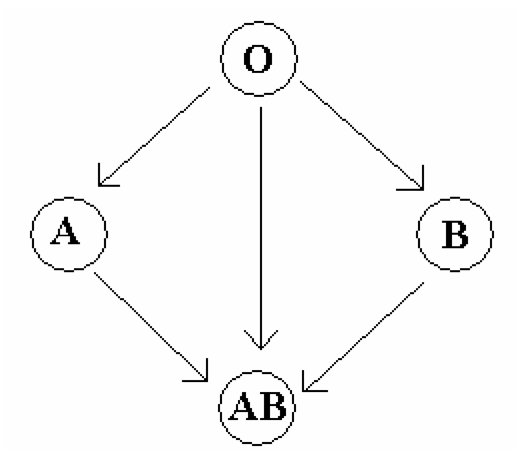
Before a person can receive a transfusion of packed red blood cells, a lab test called a crossmatch must be done to make sure that the donor blood is compatible with (matches) the recipient. A unit of the proper ABO and Rh type is selected, and a drop of donor blood is mixed with a drop of plasma from the patient. If no problems are encountered, a crossmatch takes about 30 minutes. Another test called an antibody screen is done to see if a patient's plasma contains antibodies other than ABO and Rh. If this is the case, some units of donor blood may not match, even if they have the same ABO and Rh types.

A crossmatch is usually not necessary for a platelet or plasma transfusion, unless the platelets appear to be contaminated by red blood cells.

Getting a Transfusion

Most blood transfusions are given in the hospital or in outpatient clinics. The medicines acetaminophen (Tylenol) and diphenhydramine (Benadryl) are given before a transfusion to help prevent transfusion reactions in people who have had previous reactions. Otherwise, there is usually no need for medicine before a transfusion. Blood or blood products are then infused through a vein, usually in the arm. The patient is watched carefully for the signs and symptoms of a transfusion reaction, and vital signs are taken at regular intervals. Each unit of blood or blood product is usually transfused over a couple of hours.

When blood transfusion is needed



Some of the different conditions that require transfusion of blood or blood products include:

- **Blood loss** - that is severe enough to affect blood volume and circulation.
- **Severe anemia** - where the blood can't carry sufficient oxygen to the cells of the body.
- **Thrombocytopenia** - spontaneous bleeding caused by too few platelets or blood clotting factors.
- **Severe infections** - the immune system isn't strong enough to fight off particular diseases.
- **Clotting factor deficiencies** ex hemophilia.

Different types of blood collection

The different ways in which blood is collected include:

- **Homologous** - whole blood is collected from the donor, separated into different components, and transfused into compatible recipients.

- **Aphaeresis** - only the necessary components, such as plasma or platelets, are taken from the blood of the donor by a special machine; the bulk of the blood is given back.
- **Autologous** - prior to a scheduled operation or transfusion, the patients donate blood specifically for their own use. This reduces the possible risks of incompatibility or infection.
- **Directed or designated** - prior to a scheduled transfusion, the patient requests that only blood collected from family members or friends be used for transfusion.

Transfusion complications

Occasional complications caused by blood transfusions can include:

- **Fluid overload** - this common side effect can be lessened by slowly introducing the donated blood.
- **Allergic reaction** - the most common complication. The recipient's immune system treats the donated blood products as a threat. Symptoms include itching, dizziness, headache and difficulties in breathing.
- **Haemolytic reaction** - occurs if the recipient is given the wrong type of blood. The transfused red blood cells are killed off. Symptoms include a feeling of pressure in the chest, back pain and difficulties in breathing. Haemolytic reaction can sometimes be life threatening.
- **Graft versus host disease** - where the donated white blood cells destroy the recipient's cells. The symptoms include low blood pressure and fever. It is also life threatening.

Donating blood

A blood donor needs to:

- Be aged between 16 (18 in Tasmania) and 70 years.
- Weigh at least 45kg.
- Be in good health, including normal temperature and blood pressure.
- Meet guidelines designed to protect the donor and the people who will receive their blood.

Where to get help

- Your doctor
- Your surgeon

Things to remember

- A blood transfusion generally means the transfer of blood from one person to another.

- The donated blood must match the recipient's blood type, or complications will occur.
- The different types of blood transfusion include whole blood or particular blood components.

HIV / AIDS BLOOD TRANSFUSION

HIV Human Immuno deficiency virus

AIDS Acquired Immuno Deficiency syndrome

HIV is the most dreaded virus disease at present confronting the entire world. HIV is transmitted through several ways with two most important routes viz 1. abnormal sexual contact 2. Blood transfusions.

HIV invariably results in AIDS disease which has no treatment and which is always fatal. So in order to prevent transmission of HIV virus to a normal person the blood must be carefully screened for presence of HIV or its antibodies.. Therefore HIV positive blood should not be used for transfusion. Similarly a voluntary blood donor whose blood becomes HIV donor should be allowed to donate blood.

BLOOD COAGULATION

Blood coagulation is a process that changes circulating substances within the blood into an insoluble gel. The gel plugs leaks in blood vessels and stops the loss of blood. The process requires **coagulation factors**, **calcium** and **phospholipids**.

- The coagulation factors (proteins) are manufactured by the liver.
- Ionized calcium (Ca^{++}) is available in the blood and from intracellular sources.
- Phospholipids are prominent components of cellular and platelet membranes. They provide a surface upon which the chemical reactions of coagulation can take place.

Coagulation can be initiated by either of two distinct pathways.

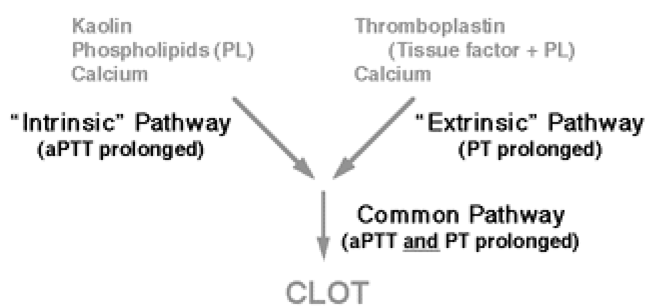
- The ***Intrinsic pathway*** can be initiated by events that take place within the lumen of blood vessels. The Intrinsic pathway requires only elements (clotting factors, Ca^{++}, platelet surface etc.) found **within**, or **intrinsic to** the vascular system.
- The ***Extrinsic pathway*** is the other route to coagulation. It requires Tissue Factor (tissue thromboplastin), a substance which is "extrinsic to", or not normally circulating in the vessel. Tissue Factor is released when the vessel wall is ruptured.

Regardless of whether the Extrinsic or Intrinsic pathway starts coagulation, completion of the process follows a common pathway. The common pathway involves the activation of factors: X, V, II, XIII and I. Both pathways are required for normal hemostasis and there are positive feedback loops between the two pathways that amplify reactions to produce enough fibrin to form a lifesaving plug. Deficiencies or abnormalities in any one factor can slow the overall process, increasing the risk of hemorrhage.

The coagulation factors are numbered in the order of their discovery. There are 13 numerals but only 12 factors. The following are coagulation factors and their common names:

- Factor I - fibrinogen
- Factor II - prothrombin
- Factor III - tissue thromboplastin (tissue factor)
- Factor IV - ionized calcium (Ca++)
- Factor V - labile factor or proaccelerin
- Factor VI - unassigned
- Factor VII - stable factor or proconvertin
- Factor VIII - antihemophilic factor
- Factor IX - plasma thromboplastin component, Christmas factor
- Factor X - Stuart-Prower factor
- Factor XI - plasma thromboplastin antecedent
- Factor XII - Hageman factor
- Factor XIII - fibrin-stabilizing factor

The liver must be able to use Vitamin K to produce Factors II, VII, IX, and X. Dietary vitamin K is widely available from plant and animal sources. It is also produced by normal intestinal flora.



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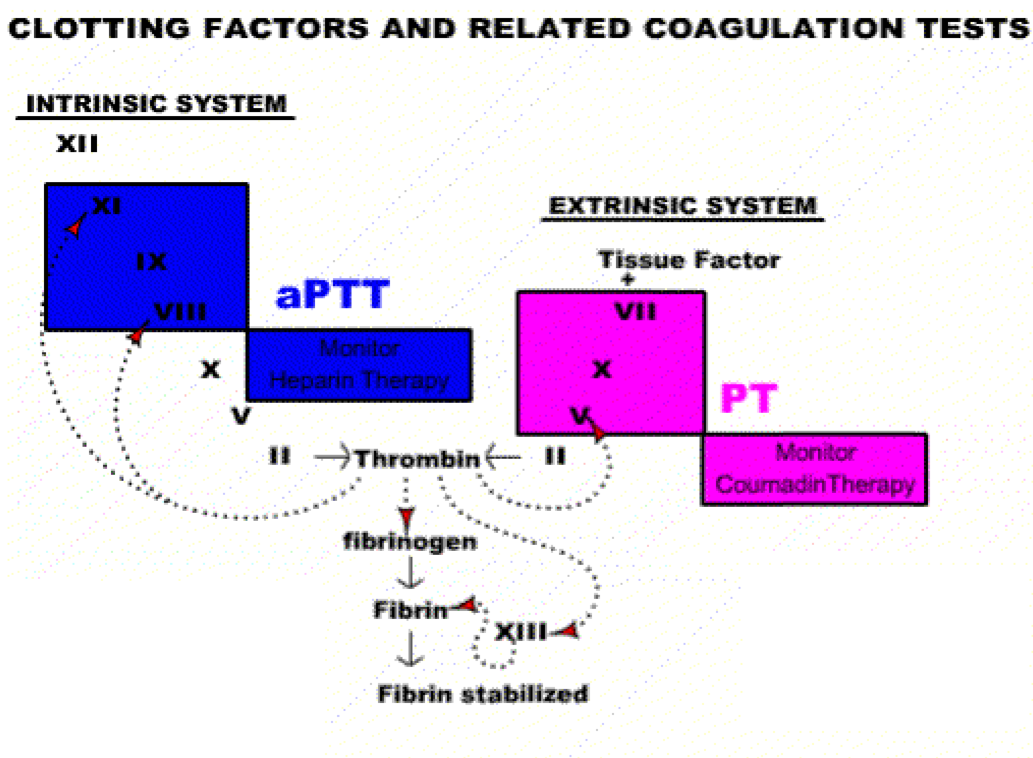

BLOOD CLOTTING is a normal important physiological phenomenon which is responsible for controlling the bleeding. If this does not occur patient may die of bleeding itself. Even defeiciency or absence of any of 13 clotting factors may result in uncontrolled bleeding.

Exs of diseases that resuilt from deficiency of blood clotting factors

FACTOR DEFECIENT	DISEASE
FACTOR VIII	HEMOPHILIA
FACTOR IX	CHRISTMAS DISEASE

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