- Platelets plug without the formation of a clot is enough to prevent bleeding from minor injuries. This occurs daily even in healthy individuals.
- Platelets count ranges from 150,000 to 400,000.
- Dense granules in platelets also contain minimal amounts of histamine and epinephrine.
- 4 steps in clot formation: vasoconstriction, platelets adhesion, platelets aggregation, fusion.
- Factor VIII is a very large protein. It has 3 functional components:
  - (VIII:C): important in the coagulation process.
  - (VIII:Ag): important for platelets aggregation.
  - (VIII:vWF): important for platelets adhesion.
- ADP released form platelets granules:
  - Causes platelets to adhere to each other.
  - Causes the platelets to swell and the projections to appear on their surfaces.
  - With thrombasthenin and enzymes released from platelets, contributes to irreversible fusion of aggregated platelets.
- Ca^{2+} is needed in very small amounts in the coagulation process, especially if compared to that needed in muscles, for example.
- In vitro, blood coagulation can be prevented using EDTA, oxalate or citrate. These bind to Ca^{2+} thereby, block most of the coagulation process.
- Because factor XIII stabilize fibrin fibers, it's called fibrin stabilizing factor.
- Fibrinogen is water soluble; fibrin fibers are not.
- Tenase (so called because it enzymatically acts on factor 10) is the complex which cleaves factor X to form factor Xa. This complex constitutes of:
  - In the extrinsic pathway: tissue factor, factor VIIa and Ca^{2+}.
  - In the intrinsic pathway: phospholipids, factor IXa, factor VIIIa and Ca^{2+}.
- Factor VII is activated by binding to tissue factor followed by its cleavage by different proteases. Ca^{2+} is needed in VII activation.
- Because of clot retraction phenomenon, blood left in a tube for 2 hours shrinks by 50%.
- Factor XII stimulates the production of kallikerin which converts plasminogen to plasmin.
- Coumadins, like warafarin, are used in vivo only; heparin can be used in vivo and in vitro.
- Another way to prevent coagulation is by non-wettable surfaces (tube covered by wax, polystyrene or silicon). They cause rapid cooling and thus, delay the formation of thrombokinase.

- The following table is IMPORTANT.

	Hemophilia A	**Hemophilia B**	**von Willebrand**
Platelets count	Normal	Normal	Normal
Bleeding time	Normal	Normal	Prolonged
Factor VIII:C	Low	Normal	Low
Factor VIII:Ag (aggregation)	Normal (Normal)	Normal (Normal)	Low (Impaired)

- Antigens found on the surfaces of RBCs are also found in salivary glands, pancreas, kidneys, liver, lungs, testes, semen, amniotic fluid.
- The most important antigen in minor blood groups are MM, MN, NN, PP, Pp, Kell, Lewis, Lutheran.
- Capital letter is used to denote dominant trait while small letter is used to denote recessive trait. For example, a person who has the genotype Nn has the phenotype of blood group N and Rh positive and minor group N.
- In Europe, 85% of the population is Rh positive.
- Distribution of blood group in America:
  1. A 41%, B 10%, AB 4%, O 45%, Rh-positive 85%.
  2. The Rh is positive 90% in black people, 99% in Chinese, 100% in Indian, 97% in Jordanian.

- An Rh negative mother develops antibodies in some cases:
  1. If she married an Rh positive man, the embryo may be Rh positive (the exact probability depends on whether the father is homozygous (100%) or heterozygous (50%)). During pregnancy, some of the fetal RBCs may reach the mother's blood. This causes the production on antibodies against D (Rh) antigen.
  2. If the mother received Rh positive blood before pregnancy, she either develops antibodies which respond to even small amounts of Rh antigen or becomes sensitive to that antigen which is less dangerous.
  3. Placental defects (e.g. inflammation) make it leaky so that RBCs from the Rh+ fetus pass to the maternal blood. The danger is proportional to the degree of leakiness.
  4. Placental squeezing during delivery also causes some of the fetal RBCs to pass to the maternal blood.
- In the above mentioned conditions, hemolysis occurs. It could be:
  - Mild (erythroblastosis fetalis): small amounts of RBCs pass to the maternal blood resulting in the production of antibodies which pass to the fetal blood causing mild hemolysis. The fetus can be rescued by receiving Rh- blood (not from the mother because it contains antibodies against Rh)

- Moderate (Icterus graves neonatorum or kernicterus): the infant is born at term with jaundice or becomes so within 24 hours. Neurological lesions involving the basal ganglia may result in mental retardation.
- Severe (hydrops fetalis): the infant either dies in uterus or within 24 hours because of anemia, jaundice and edema.

- The should be injected with antibodies against Rh+ erythrocytes 72 hours after delivery of an Rh+ infant even if no threat was observed.
- AB blood type is a general recipient while O is a general donor.
- When transferring blood from a donor whose blood group is O, for example to a recipient whose blood group is A or B or AB, usually (but not always), antibodies against A or B antigens from the donor result in mild immune reaction that has no clinical manifestation. However, this immune reaction may cause significant agglutination. Cross matching test is performed to test whether the transfusion procedure is safe.
- Antibodies have 2 to 10 sites to bind antigens. This is what causes agglutination.
- When the need for blood transfusing is to supply the patient with platelets, fresh blood is favored. However blood stored up to 3 days can be transfused.
- When the need for blood transfusing is to supply the patient with WBCs, fresh blood is required because WBCs, especially neutrophils which are the most abundant WBCs, have short life span.

You may be wondering whether ABO incompatibilities are also a cause of hemolytic disease of the newborn. For example, a woman with type O blood has natural antibodies to both the A and B antigens. If her fetus is type A or B, this theoretically should cause a problem. Fortunately, it usually does not, partly because the A and B antigens are not strongly expressed in fetal erythrocytes and partly because the natural antibodies are of the IgM type, which do not readily cross the placenta. IgG

Indications of blood transfusion:

1. to restore the Blood Volume, e.g. in haemorrhage.
2. to provide Red Blood Cells, e.g. anaemias.
3. to increase Blood Coagulability in haemorrhagic diseases, e.g. haemophilia & purpura.
4. to replace infant's blood with Rh.-ve blood in erythroblastosis foetalis.
5. to supply antibodies to raise the general resistance of the body.
6. to provide White Blood Cells, e.g. in leucopenia (= decreased W.B.Cs).
7. to supply plasma proteins in hypoproteinaemia.

- K^+, SO_4^{2-}, PO_4^{3-}, and proteins are found in higher levels **inside the cells**
- Na^+ and Cl^- are found in **higher levels** outside the cells.
- Proteins concentration in the plasma is 16meq/L while it's 1 in the interstitial fluid. Therefore, proteins contribute to only 0.5% of the osmolality of the plasma which is 290mOsmol/Kg.
- Water comprises:
  - 83 % of blood.

- 82.7 % of the kidneys
- Only 10 % of adipose tissues.

- Of total body weight, 18% is skin; 41.7% is muscles; 16% is bones.
- Fluids intake is equal to fluids output = 2.6L/day.
  - **Intake**: 1L ingested as fluids; 1.2L or as food in Middle East (this number is much lower in Europe); 0.4L from the metabolism.
  - **Output:** 1.5L in urine (highly variable depending on the volume of fluids ingested); 0.5L in expired air, 0.45L in sweat glands; 0.15 in feces.
- In hypertonic dehydration, water leaves the cell while in hypotonic dehydration, water enters the cells.
- Additional cause of water intoxication is ADH administration.
- Alcoholics tend to drink plenty of water when alcohols are not available because this causes disorientation of the cells.
- Lymph contents:
  - Proteins.
  - Lymphocytes which prevent foreign bodies from entering the circulation.
  - Fat
  - Clotting factors which may cause lymph coagulation. However, lymph coagulation is mild because platelets are not present.
- The average rate of flow through the lymph vessels is 3L/day, compared with 7200L/day through blood vessels.
- Along the way, lymph percolates through lymph nodes where it's filtered.
- **In sheet 10 (pages 15 and 16), there are 2 important applied examples on blood grouping.**

Corrections

- **Page 18 (**Promotes ADH and aldosterone actions) > (Increases ADH and aldosterone secretion).
- **Page16 (**the last 2 points are not correct)
  - Blood is stored at 4^{o} c in packs containing ACD (acid citrate dextrose). Citrate is the anticoagulant while dextrose (glucose) is the metabolic substrate.
  - This method of storage allows blood to be stored up to 5 weeks that is when transfused, more than 70% of RBCs remain viable.
  - If, for example, transfused blood had been stored for 2 weeks, measuring the viable RBCs in the patient the next day would show that 80% of transfused RBCs are viable and only 1% hemolyze daily.