BLOOD TRANSFUSION

- Transfusion of blood and blood products has become common place since the first successful transfusion in 1818.
- 1492 – Pope innocent VIII receive a blood transfusion.
- 1665 – Richard Lower in Oxford canine transfusion.
- 1667 – Gean – Baptiste Denis – Sheep - human transfusions.
- 1818- James Blundell –Human Transfusion.
- 1901 – Karl Land Steiner – ABO system.
- 1914 – Albert Hustin – Sodium Citrate as anticoagulant .
- 1926- British Red Cross – Blood Transfusion Services.
- 1939 – Rhesus System was identified as major cause of transfusion reactions.

BLOOD & BLOOD PRODUCTS

- Blood is collected from donors who have been previously screened to exclude potential harmful conditions.
- A person can donate 450 ml of blood three times in a year.
- Each unit is tested for evidence of hepatitis B, hepatitis C, HIV-1, HIV-2, Syphilis.
- The ABO and Rhesus D Blood group is determined along with presence of irregular red cells and antibodies.
- The blood is then processed into subcomponents

Whole Blood :

- Now rarely available as it is an inefficient use of the limited resources
- Whole blood transfusion has significant advantage over packed cells, as it is rich in coagulation factor and if fresh, metabolically more active than stored blood.

Packed Red cells :

- Each unit is approximately 330mL with haematocrit of 50-70%.
- Stored in a saline – Adenine – Glucose –Mannitol (SAG-M) to increase shelf life to five weeks at 2-6^0 (CPD 2-3 weeks)

Fresh – Frozen plasma :

- FFP is rich in coagulation factors and is removed from fresh blood, stored at -40 to -50^{0}C with a shelf life of two years.
- First line therapy in the management of coagulopathic haemorrhage.
- Rh D positive FFP can be given to rh D – negative women although it is possible for sero conversion to occur with large volumes due to presence of RBC fragments.
- **Cryoprecipitate :** is a supernatant precipitate of FFP and is rich in factor VIII and fibrinogen.
- Stored at -30 C for two years of shelf life.
- It is given in low fibrinogen states where factor VIII deficiency

Platelets :

- Supplied as a pooled platelet concentrate and contain about 250 x 10^9/L.
- Stored on a special agitator at 20-24^{0}C with a shelf life of a only five days.
- Transfusions are given to patients with thrombocytopenia,or with platelet dysfunction who are bleeding or undergoing surgery.
- Patients who are on antiplatelet therapy such as aspirin or clopidogrel posses a problem to control haemorrhage during surgery.
- Aspirin therapy rarely produce problems but patients on clopidogrel who are actively bleeding and undergoing major surgery may require continuous infusion of platelets during the procedure.
- Arginine vasopressin or its analogues (DDAVP) may also be used.

Prothrombin Complex concentrtion (PCC) :

- Highly purified concentrates prepared from pooled plasma.
- They contain factors II, ix and x
- Factor VII may be included or produced separately.
- Indicated for emergency reversal of anticoagulant (Warfarin) therapy in uncontrolled haemorrhage.

Autologous blood :

- It is possible for patients undergoing elective surgery to donate their own blood upto three weeks before surgery for re-transfusion during the operation.
- During surgery blood can be collected in a cell – sever which washes and collect RBC and can be returned to the patient.

Indications for blood transfusion

Blood transfusion should be avoided if possible:

- Acute blood loss, to replace circulating volume and maintain oxygen delivery.
- Perioperative anaemia, to ensure adequate oxygen delivary during the perioperative phase.
- Symptomatic chronic anaemia, without haemorrhage or impending surgery.

Transfusion trigger :

- Historically patients were transfused to achieve Hb level >10g/dL, but now it has been shown,bnot only unnecessary but also associated with increased morbidity and mortality.
- A Hb level of 6g/dL is acceptable in patients who are not actively bleeding, not symptomatic or to undergo major surgery.
- There is some controversy about optimal level of Hb in patients with CV diseases, sepsis and traumatic brain injury.
- Conceptually a higher Hb improves oxygen delivery, but there is little clinical evidence to support this.

Perioperative red blood cell transfusion criteria

Hb level (g/dL -	Indications
< 6	Probably will benefit from transfusion.
6-8	Transfusion unlikely to be of benefit in the absence of bleeding or impending surgery
> 8	No indication for transfusion in the absence of other risk factors.

BLOOD GROUPS AND CROSS-MATCHING

- Human Red cells have on their cell surface many different antigens
- Two groups of antigens are of major importance – ABO and rhesus system.

ABO system :

- These are strongly antigenic and are associated with naturally occurring antibodies in the serum.
- Consists of three allelic genes – a, b & o which control synthesis of enzymes which add carbohydrate to the cell surface glycoproteins.

- A& B genes had specific carbohydrate while O gene is amorph and does not transform the glycoprotein.
- The system allows for six possible genotypes, although there are only four phenotypes.
- Blood Group O is “universal donor” type as it contain no antigen to provoke a reaction
- Conversely, group A B individuals are “Universal recipients” and can receive any ABO blood type as they have no circulating antibodies.

ABO blood group system

Phenotype	Genotype	Antigens	Antibodies	Frequency (%)
O	OO	O	Anti-A, anti-B	46
A	AA or AO	A	Anti-B	42
B	BB or BO	B	Anti-A	9
AB	AB	AB	None	3

Rhesus system : Rhesus D (RhD) antigen is strongly antigenic and is present in 85% of population.

Antibodies to the D antigen are not present in the serum of remaining 15% of population but the formation may be stimulated by the transfusion of Rh-Positive Red cells, or acquired during delivery of a Rh D positive baby.

Acquired antibodies are capable of crossing the placenta during pregnancy.

If antibodies are present in a Rh D negative mother, cause severe haemolytic anaemia and even death (Hydrops fetalis) in a Rh D fetus in utero.

Transfusion reactions :

- If antibodies present in the recipient's serum are incompatible with the donor's cells, transfusion reactions will result.
- This may be in the form of acute haemolytic reaction.
- Severe immuno-related transfusion reactions are mainly due to ABO incompatiblity, results in fatal intravascular haemolysis and MODs.
- Transfusion reactions with other antigen systems are usually milder and self limiting.

- Febrile transfusion reactions are non-haemolytic, usually caused by a graft versus – host response from leukocytes in transfused components. Symptoms - fever, chills or rigors.
- Blood transfusion should be stopped immediately.

Cross-matching :

- To prevent transfusion reactions, ABO and Rh typing of both donor and recipient blood must be cross-matched to ensure compatibility.
- The recipient’s serum is mixed with donor’s cells to confirm ABO compatibility and to test for Rh and any other blood group antigen-antibody reactions.
- Full cross-matching may take up to 45 min
  - In emergency “type specific “ blood is provided which only ABO/Rh matched and can be issued within 10-15 mnts.

- In emergency group O (universal donor) blood is given to group O negative females and group O positive males.
- When blood transfusion is prescribed it is essential to verify, correct patient will receive correct transfusion.
- Two health care persons should check the patients details and lable of the donor blood.
- Donor blood Serial Number should also be checked against the issue slip of the patient - which prevent severe and fatal ABO in compatibility reactions.

COMPLICATIONS OF BLOOD TRANSFUSION

Complications from a single transfusion

- Incompatibility, haemolytic reaction.
- Fibrile transfusion reaction.
- Allergic reactions
- Infection – Bacterial due to faulty storage

  - Hepatitis, HIV, Malaria

- Air embolism
- Thrombophlebitic
- Transfusion related acute lung injury (from FFP)

Complications from massive transfusion:

- Coagulopathy
- Hypocalcaemia
- Hyperkelaemia
- Hypokelaemia
- Hypothermia

In addition, patients who receive repeated transfusions over long periods of time (thalassaemia) may develop iron overload.

Each unit of RBC contain approximately 250mg of iron.

Management of coagulopathy : Not necessary if there is no active bleeding or haemorrhage is not anticipated (surgery).

However, coagulopathy following massive transfusion must be managed aggressively.

Standard guidelines:

- FFV if PT or PTT > 1.5 times normal.
- Cryoprecipitite if fibrinygen < 0.8 g /L
- Platelets if platelet count < 50 x 10^9/ mL
- Pharmacological adjuncts to blood component therapy – antifibrinolytics such as tranexamic acid and aprotinin are commonly administered.
- Recombinent factor VIIa is also used in the treatment of non-surgical haemorrhage.

Blood substitutes : are an attractive alternate to the costly process of donating, checking, storing and administering blood and due to the immunogenic and potential infectious complications associated with transfusion.

Several oxygen carrying blood substitutes under investigation in animal are in early clinical trials.

Blood substitute or either biomimetic or abiotic.

Biomemetic substitutes memic the standard oxygen carrying capacity of the blood and are Hb based.

Abiotic substitute are synthetic oxygen carriers, primarily per fluorocarbon based.

Varies engineered molicules are under clinical trials.

Haemostasis – Natural attempt of haemostasis or stoppage of bleeding starts immediately at the site bleeding.

The first step of haemostasis is local release of a humoral agent known as **thromboxane** which is a powerful constrictor of vascular smooth muscle and promote aggregation of platelets results in spontaneous sealing of the injured vessel.

Platelets are essential components of haemostasis, contain contractile protein – thrombosthenin which allows the platelet plug to contract and reinforces the contracted vessel.

Next mechanism in haemostasis is formation of fibrin clot, a process known as coagulation.

Coagulation sequence leads to the formation of thrombin, which splits fibrinogen to form insoluble fibrin under the influence of factor XIII to form a tough clot.

Another important aspect of coagulation is **fibrinolytic process** which prevents formation of intravascular fibrin.

Strong proteolytic enzyme known as fibrinolysin breakdown fibrin into much smaller soluble fragments.

This is formed from **plasminogen,** a circulating precursor present in vascular endothelium.

Plasminogen and circulating plasminogen activators are selectively absorbed on fresh fibrin.

Congenital abnormalities of haemostasis :

Commonest congenital abnormalities are Haemophilia Christmas disease and Von Willebrand's disease.

Haemophilia (A) : Sex linked inherited disorder carried by recessive gene manifests only in males and asympatically transmitted through female carriers.

It involves due to total lack of factor VIII activity.

Clinical features : Clinical manifestations vary considerably – Bleeding after slight trauma is the main problem.

Repeated haemorrhages into the joints are more common.

Spontaneous retroperitoneal bleeding with severe abdominal pain, tenderness and paralytic ilieus.

Renal bleeding causes haematuria.

Death is usually results from bleeding into the CNS.

Recurrent haemarthoarthrosis may result in permanent damage to the articular cartilates, and disorganisation of the joints.

Treatment : Cryoprecipitate is a rich source of factor VIII.

Periodic infusions will increase the level of factor VIII.

If any operation has to contemplate, should be performed only after raising the factor VIII to normal level.

Alternative forms of therapy include transfusion of fresh blood or fresh frozen plasma.

Christmas disease (haemophilia-B) – Second most congenital disorder of coagulation due to deficiency of factor IX.

Clinical manifestations are like haemophilia-A, but milder than it.

Treatment : Transfusion of fresh frozen plasma.

No definite substitute of factor IX is available. Treatment is Less effective.

Cryoprecipitate may be used.

Von-Willebrand's disease – 3rd most common. cong.

Clinical manifestation vary in severity, bleeding is more from mucous membrane than from musculo-skeletal system.

Associated with low levels of plasma factor VIII compliment and factor VIII related antigen.

There are also platelet abnormalities.