TRANSFUSION MEDICINE
Blood transfusion refers to transfer of blood or blood components from a donor to a recipient

PRINCIPLES
- Blood donation should always be voluntary.
- Never give transfusion unnecessarily.
- Blood transfusion should follow components policy.

BLOOD DONATION
- Donor must be fit & healthy.
- It should not harm the donor
- It should not transmit any disease to the recipient

Before blood donation the donor should be subjected to
1. Detailed Medical history (Questionnaire Form)
2. Limited physical examination

Questionnaire form:
1. Name of the donor
2. Gender
3. Age: 18-65 year
4. Weight: > 50 kg
5. Occupation: driving bus, plane or train, heavy machine or crane operator, scaffolding, etc. because delayed faint would be dangerous
6. Last donation: not less than 2 months
7. Frequency of donation: maximum 3 times/year for females and 4 times/year for males
8. History of blood transfusion: defer 6 months
9. Major surgery: defer 6 months
10. Those with history of heart disease, active pulmonary disease (active T.B), diabetes, hypertension, or hyperthyroidism are generally deferred from donation.
11. History of blood diseases such as leukemia, lymphoma, thalassemia major, sickle cell anemia and polycythemia should be deferred from donation.
12. History of abnormal bleeding tendency should also be deferred
13. History of epilepsy is generally a cause of deferral
14. History of infectious diseases
15. AIDS patients, AIDS contacts, homosexuals, drug abusers, those with multiple partners, hemophiliacs receiving products of human origin; all should be indefinitely deferred.
16. Patients with history of jaundice or viral hepatitis A are deferred one year. Patients with Hepatitis B (HBs Ag +ve) or Hepatitis C are deferred permanently.
17. Malaria: those infected are not accepted as blood donors.
18. Brucellosis: deferred for 2 years from last febrile episode.
19. EBV infected patients are deferred for 2 years.
20. Syphilis: patients with this disease are considered as permanent deferral.
21. Drugs: patient on certain drugs (anticoagulants, antihypertensive, insulin) are not accepted as donors.
22. Pregnancy: not allowed. Accepted 3-6 months postpartum
23. Donor consent: written consent
Physical Examination: this should be simple, brief and includes:

1. General appearance
2. Temp: not more than 37°C
3. Pulse: 50-100 beats/min
4. Blood pressure: normal
5. Weight: at least 50 Kg
6. Hb level: more than 13.5 g/dl for males and 12.5 g/dl for females

Anticoagulants
ACD (Acid citrate dextrose)
    Shelf life of blood 21 days
CPD (Citrate phosphate dextrose)
    Shelf life of blood 28 days
CPD-A (Plus Adenine)
    Shelf life of blood 35 days (used now)

Blood donation is taken by an aseptic technique into plastic packs designed to hold 450 ml ± 45 ml of blood, mixed with 63 ml of anticoagulant. The ratio of anticoagulant to blood must be maintained at the optimal level of 1:7. The citrate anti-coagulates the blood by combining with blood calcium.

Mandatory tests on blood units
1. ABO & Rh grouping
2. Test for HIV Ab
3. Test for HBs Ag
4. Test for HCV Ab
5. Test for syphilis
6. Screening for atypical antibodies.

Compatibility testing
Before giving blood to the patient compatibility testing should be done which includes:
1. ABO & RH typing of the donor and the recipient blood
2. Screening of the donor & the recipient sera for unexpected antibodies
3. Cross matching the donor & the recipient blood by cross matching the donor cells & the recipient serum.

Objectives of crossmatch are:
1. Assurance of the ABO compatibility
2. Recognition of clinically significant antibodies

Standard routine crossmatch:
1. **Saline tube:** mix donor cells with recipient’s serum. Leave the tube at room temperature (18-25°C)
2. **Albumin tube:** add albumin to the mixture of the donor cells and recipient’s serum at 37°C to detect warm-reacting antibodies
3. **Indirect antiglobulin test (indirect Coombs test):** at 37°C to detect antibodies in the recipient’s serum that coat or cause sensitization of the donor red cells
COMPLICATIONS OF BLOOD TRANSFUSION:
Incidence of transfusion reactions is about 2-5%. It is mostly of mild degree. Fatal complications are uncommon (1: 100,000 – 1: 500,000). Complications can be divided broadly into:

1. **Immunological complications**
2. **Nonimmunological complications**

**IMMUNOLOGICAL COMPLICATIONS:**
1. **Sensitization to red cells antigens.**
Because the ABO and RhD antigens are the only Ags matched between donors and recipients, there is a possibility of sensitization to other red blood cells Ags. In clinical practice this sensitization could lead to:
   - A. Hemolytic disease of the newborn if the recipient is a female.
   - B. Difficulties in compatibility testing if the recipient required further transfusion.
   - C. Hemolytic transfusion reaction.

2. **Hemolytic transfusion reaction (HTR).**
Most of the cases are due to clerical or administrative error, rarely due to laboratory error. This reaction is caused by premature destruction, *almost always* of the donor cells by antibodies present in the recipient. The HTR could be immediate or delayed.

**Immediate HTR:**
This is the most dangerous type. It is usually caused by ABO incompatibility. The antibodies are IgM in type that bind to the red cells and cause complement activation leading to *intravascular lysis* of the red cells with production of the anaphylatoxins, the C3a & C5a liberated during complement activation. The C3a and C5a will cause smooth muscle contraction, platelets aggregation, increased capillary permeability, release of vasoactive amines and hydrolases from mast cells and granulocytes with hypotension.

**Sign & Symptoms**
- Occur within minutes to 1 hour from the start of transfusion
- Heat in the vein
- Throbbing headache
- Flushing of the face
- Chest tightness
- Nausea and vomiting
- Lumber or loin pain
- Hypotension and tachycardia
- DIC, hemoglobinuria (passing red urine), acute renal failure, collapse and death in severe cases.

Less commonly the hemolysis is *extravascular* caused by removal of C3b & IgG coated red cells by the macrophages in the liver and spleen. Symptoms are less rapid in onset and occur usually after 1 hour with fever, jaundice and unexplained decrease in Hb. Renal failure is rare.

**Management of immediate HTR**
- Stop transfusion immediately. Keep the IV line open.
- Maintain the circulating blood volume, restore the blood pressure and urinary outflow:
  - Give normal saline (20-30 ml/ kg body weight) to maintain the systolic BP > 100 mg Hg
  - Give Diuretics: e.g. Frusemide up to 1 mg/kg body weight intravenously to restore urinary flow > 100 ml/hour
- Collect blood samples from vein opposite to infusion site in 3 tubes:
  1. EDTA blood for CBP
  2. Citrated blood for coagulation studies
  3. Clotted blood for serological studies
- Collect the next urine sample and 24-hour urine post-transfusion check for Hb-uria
- Check the label and the number on the blood unit
- Check the crossmatch form for any error

Tests and measures to be done in the laboratory:
- Check the ABO & Rh group of the recipient and the donor samples again
- Examine the post-transfusion blood sample for hemolysis
- Check the donor unit for hemolysis
- Do Coomb’s test on recipient post-transfusion sample
- Repeat cross match with both pre- & post-transfusion samples
- Screen pre- & post-transfusion samples and donor plasma for antibodies
- Check the Hb level
- Coagulation screening test for the possibility of DIC
- Bacteriological evaluation: inspect the donor unit for hemolysis or clot. Blood from the giving set and the blood unit should be cultured
- Biochemical studies: test for hemoglobinemia and for raised serum bilirubin
- Check the urine for hemoglobinuria

**Delayed HTR:**
This is manifested usually 7-10 days after transfusion and is caused by antibodies, which are present in low titer and are not detected at time of crossmatch. So this reaction is neither predictable nor preventable. The antibodies are caused by sensitization due to previous pregnancy or transfusion. Sign and symptoms include: fever, jaundice and lowering of Hb.

**3. Febrile reaction due to WBC and platelets antigens.**
- Most common immunological reaction
- Seen in patients having multiple blood transfusion or pregnancy
- Caused by Ab to WBC & platelets HLA Ags (Usually WBC)
- The onset of the reaction is delayed 30-90 min after start of transfusion
- The main symptom is fever

**Management:**
- Slow the transfusion
- Give antipyretic
- No need to terminate the transfusion
- If symptoms recur in patients requiring repeated transfusions, the patient should be checked for WBC or platelets antibodies and if these are present, leukodepleted blood (by using WBC filters) should be used.

**4. Reaction to platelets Ag (Post-transfusion Purpura).**
- Seen in women with history of multiple pregnancies or in those with history of multiple blood transfusions
- Caused by Abs to platelets Ags
The reaction occurs 7-10 days after transfusion
- The main feature is purpura due to thrombocytopenia (caused by destruction of the platelets by the Abs)
- It is usually self-limiting

5. Reaction due to plasma protein antibodies.
- Majority are due to Anti IgA antibodies
- Main symptom is urticaria
- Treatment is by antihistamine
- Rarely more severe anaphylactic reaction occur which should be treated urgently with adrenaline and any next transfusion should be IgA deficient blood

NON-IMMUNOLOGICAL COMPLICATIONS:
1. Reaction due to bacterial pyrogens or bacteria.
   Although rare complication, it has very high mortality rate characterized by sudden onset of high fever, shock and bleeding due to DIC. Blood may be contaminated by cold-growing organisms (pseudomonas or colon-aerogenes group). These microorganisms utilize citrate as the primary source of carbon, which leads to citrate depletion and hence clotting of blood. Visual inspection of the blood units may reveal clots and indicate the presence of contamination.
   The infusion of large number of gram-negative microorganisms results in a serious reaction i.e. endotoxic shock. The latter is accompanied by fever, marked hypotension, pain, vomiting and the development of profound shock. The reaction may start with shaking chills following a latent period of 30 minutes or more. As little as 10 ml of blood may contain sufficient microorganisms to produce the reaction.
   Management
   - Do direct examination & culture of the blood from the patient and the blood unit
   - Give antibiotic IV
   This complication could be prevented by:
   - Ensuring aseptic technique in the preparation of blood packs and anticoagulant
   - Aseptic condition in blood donation
   - Packs should not be opened for sampling and the unit should be transfused within 24 hour if any open method has been used
   - Blood should be kept in accurately controlled refrigerator at 2-6 ºC
   - Avoid leaving blood at room temperature.
   - Inspect all blood units for signs of contamination as clotting or hemolysis.

2. Circulatory overload.
Transfusion generally increases blood volume except in those who are actively bleeding. This increase in blood volume may be dangerous in the elderly with a compromised cardiovascular function, pregnancy and in those with severe anemia

   Prevention:
   - Blood should be given slowly over 4 hr.
   - Give diuretics at the start of transfusion. No more than 2 units should be given within 24 hours.
   - Blood should be given during the day-time and the patient should be followed carefully.
If signs and symptoms of overload & pulmonary edema occur:
- Transfusion should be stopped
- Patient propped upright
- Give diuretics IV

3. **Thrombophlebitis.** This is a complication of indwelling venous cannulae and is not specifically related to blood transfusion.

4. **Air embolism.** This is now a rare complication of transfusion therapy due to the introduction of plastic bags, which provide a closed system. Only large volumes of air, and not the entry of a few bubbles, result in a clinically significant air embolism. Symptoms include pain, cough, and sudden onset of dyspnoea. The treatment includes clumping off the administrating tube.

5. **Hemosiderosis.** Each unit of blood contains approximately 200 mg of iron. Repeated transfusions over many years, in the absence of blood loss, cause deposition of iron initially in the reticuloendothelial system. After 50 units in adults, and lesser amount in children, the liver, myocardium and endocrine glands are damaged. This major problem, in thalassemia major and other severe chronic refractory anemias, could be prevented by giving chelating agents to iron.

6. **Complications of massive transfusion.**
These tend to occur in cases of replacement the total blood volume within 24 hours (for adult about 10 units/24 hours). This could lead to:

1. **Dilution of platelets.** As blood stored in refrigerator at 1-6 °C for more than 48 hours has no functional platelets. Transfusion of 8-10 units of blood to an adult will lead to thrombocytopenia (low platelets). It follows that any patient receiving many blood units should be monitored through platelets count and judged on his clinical condition. Some give one platelets unit for every 4 blood units. Others give platelets transfusion if platelets count becomes less than 100,000/µL if there is bleeding or surgical intervention.

2. **Dilution of coagulation factors.** This occurs if blood stored more than 14 days is given. Blood stored less than 14 days has adequate level of most of the coagulation factors except factor V and VIII, as they are the most labile factors.

3. **Metabolic changes.**
- **Citrate toxicity.** This is not a problem except in a very rapid transfusion (one unit every 5 minutes) or in infants, especially if premature, having exchange transfusion with blood stored in citrate for longer than 5 days.
- **Hyperkalemia and hypocalcaemia.** These are usually transient and rapidly corrected.

4. **Hypothermia:** Cardiac irregularities, in particular ventricular fibrillation, may result from transfusion of large quantities of cold blood.

7. **Transmission of Infection.**
Diseases transmitted by blood could be classified as follows:

1. **Bacterial:**
   - Syphilis
   - Brucellosis

2. **Protozoal:**
   - Malaria
   - Toxoplasmosis

3. **Viral:**
   - Hepatitis viruses
   - HIV, HTLV I, HTLV II
   - EBV
Syphilis:
- The agent is *Treponema pallidum*
- Donor is infective during the early spirochetemia phase i.e. before the development of the antibodies
- Blood products implicated: fresh blood and components
- Viability in blood: the bacteria are unlikely to survive more than 3 days at 4-6 °C, so transmission of syphilis by blood is a rare complication.
- It is more likely to be transmitted by platelets concentrate because of its storage at room temperature and its short shelf life.
- Prevention:
  - Mandatory screening of all donor units by VDRL or TPHA
  - Exclusion of high-risk group.

Brucellosis:
- The agent is *Brucella abortus*
- Viability in stored blood: months
- Incubation period: 6 days- 4 months
- Reports of transfusion related brucellosis: mainly in children, splenectomized or immunocompromized.
- Prevention: deferment from blood donation of infected patients for 2 years after cure.

Malaria:
- The gent is Plasmodia species (*P. vivax, P. ovale, P. malariae, P. falciparum*)
- Viability: viable in stored blood at 4 °C at least 1 week; in case of *P. falciparum* up to 2 weeks
- Blood product implicated: products containing red cells
- Incubation period: *P. vivax* & *P. falciparum* 1 week- 1 month; *P. malariae*: months
- Prevention: In endemic areas: prophylactic treatment of donors with chloroquine 48 hours before donation or single dose of chloroquine to the recipient 24 hours before transfusion.

AIDS (Acquired immune deficiency syndrome):
- The agent is Human immunodeficiency virus HIV type I & II
- Blood product implicated: whole blood (cellular& plasma blood components)
- Incubation period: mean incubation period is 4.5 yr
- Prevention:
  - Education through the media
  - Self –exclusion of high risk group
  - Screening all donors for HIV antibodies

Hepatitis Viruses
**Post transfusion hepatitis** could be caused by the following viruses
1. *Hepatitis viruses (A, B, C,)*
2. *Cytomegalovirus (CMV)*
3. *Epstien-Bar virus (EBV)*
Prevention: - Tests to screen for Hepatitis B surface antigen (HBs Ag) and HCV Abs
  - Exclusion of high risk group