/ 17 – Blood Products & Blood Transfusion

Resources: Essential Surgery, 5th ed., 'Blood Transfusion.'

Blood products available for transfusion incl.: RBCs, platelets and coagulation factors (frozen plasma [FP], cryoprecipitate, factor concentrates.)

- Specialised blood products incl.:
  - Irradiated blood products
    - Prevent proliferation of donor T-cells in potential or actual bone marrow transplant recipients.
    - Used for immunocompromised Pz. Or for Pz. On purine analogue chemotherapy, intrauterine transfusions, Hodgkin lymphoma
  - CMV-negative blood products
    - For transplant recipients, neonates, AIDS patients and seronegative pregnant women.

- **Laboratory aspects of blood transfusion**:
  - Donated blood (1 U = 500 mL) is fractionated into the aforementioned blood components
    - Centrifugation separates whole blood into RBCs and platelet-rich plasma. Platelet-rich plasma can be further fractioned into platelets and plasma.
      - Multiple units must be pooled together to obtain therapeutic amounts
      - **Fresh plasma** (FP) is plasma frozen within 24h of collection
      - **Cryoprecipitate** is the high molecular weight precipitate generated when FP is thawed at low temperatures.
  - Blood grouping and compatibility testing:
    - Transfusion practice aims to minimise the risk of transfusing ABO incompatible blood and involves two steps: (1) determining the patient's ABO and Rhesus groups, and (2) screening the patient's blood for antibodies.
      - This is simply tested by **Cross-Matching** (Donor Blood x Patient's serum). This procedure is also used in determining the organ compatibility in transplantation medicine.

Potentially lethal side effects of blood transfusion mean that a decision to transfuse blood or blood products must be based on clear indications and after considering alternatives.

Indications include:

- Initial restoration of circulating volume in haemorrhage & maintenance of BP – Plasma substitutes
- Substantial haemorrhage or Severe anaemia – Packed or concentrated red cells
- Resuscitating patients w. traumatic or septic shock – Human albumin solution
- Deficiency of clotting factors – Fresh frozen plasma (FFP)
- Thrombocytopaenia – Platelet concentrates
- Specific coagulation deficiencies – Cryoprecipitate

Blood Type	Antigen (RBC)	Antibody (Plasma)	Receive	Donate
A	A	b	A, O	A, AB
B	B	a	B, O	B, AB
AB	AB	------	A, B, AB, O	AB
O	------	ab	O	A, B, AB, O

- In an emergency (e.g. obstetric haemorrhage) where group-compatible blood is unavailable, group O, Rh -ve blood can be given.

Box 9.1 Types of transfusion and indications for their use

Whole blood

Very rarely used because of the demand for separate blood components. Whole blood carries greater risks of adverse reactions owing to the presence of leucocytes

Packed or concentrated red cells (the most common transfusion product)

For use in substantial haemorrhage and severe anaemia. Whole blood is collected then centrifuged to separate the red cells (and platelets and plasma). Packed/concentrated red cells are then suspended in a preservative solution ready for reinfusion. A bag of red cells is approximately 300 ml and raises the haemoglobin concentration by approximately 1 g/dl

Human albumin solution, available as 4.5% and 20% solutions

Albumin is expensive and is derived from human donor blood. In terms of efficacy, mortality and cardiorespiratory function, there is little evidence that albumin solutions are better than plasma substitutes or normal saline for resuscitating patients with **traumatic** or **septic shock** or requiring large perioperative volume replacement

Transfusion of albumin solutions should probably be restricted to patients with hypoproteinaemic oedema with nephrotic syndrome or with ascites in chronic liver disease. Other uses are difficult to justify in the absence of scientifically proven benefit

Fresh-frozen plasma (FFP)

Plasma is separated from fresh whole blood and then frozen. FFP contains near normal amounts of all clotting factors and other plasma proteins. It should be blood group compatible when possible and should not be used simply for volume replacement. FFP is often used to replace clotting factors exhausted during major haemorrhage (due to a combination of consumption of clotting factors by attempted haemostasis and the lack of clotting factors in transfused blood). This is likely when blood loss exceeds 1.5 times the blood volume, and the loss has been replaced rapidly with red cells and crystalloids or colloids. Clotting studies usually demonstrate a coagulopathy

FFP is also used to replace deficiencies of coagulation factors when there is continued bleeding and the necessary specific factor concentrates are unavailable. This may occur in liver disease, thrombotic thrombocytopenic purpura (TTP) and acute disseminated intravascular coagulation (DIC)

Platelet concentrates

Used for platelet exhaustion during major haemorrhage (e.g. ruptured abdominal aortic aneurysm) and in thrombocytopenia. Indicated if the platelet count is $<50\times10^9$/L, or massive blood loss is occurring. Platelets should be avoided in autoimmune platelet disorders except in the presence of life-threatening haemorrhage

Cryoprecipitate, fibrinogen and other specific clotting factor concentrates

Used for various specific coagulation deficiencies, e.g. severe hypofibrinogenaemia, haemophilia. These should only be used in consultation with a haematologist

Plasma substitutes

These are solutions of macromolecules with colloid osmotic pressure and viscosity characteristics similar to plasma. Gelatin solutions (e.g. Haemaccel, Gelofusine) and etherified starch solutions (e.g. hetastarch) are used for initial restoration of circulating volume in haemorrhage or burns and to maintain volume, blood pressure and renal perfusion intraoperatively where blood transfusion is not indicated

- Storage and useful life of blood products:
    - Packed red cells (RBCs)
        - Stored btw. 2^{O} to 6^{O}C and have a shelf life of 35 days. As they age pH changes & K^{+} leaks out of the cells, making the packages more dangerous than useful.
        - Empty blood packs should be retained for 48 h for examining and testing in the event of a transfusion reaction.
        - 1 U of packed RBCs increases the Hb level by 10g/L
    - Platelets
        - Stored at 20 to 24°C
        - If an increase in the platelet count is not seen post-transfusion, then autoantibodies (i.e. ITP), alloantibodies, consumption (bleeding, sepsis), or hypersplenism may be present.

Red Blood Cells (RBCs)	
Indication for RBC transfusions	• Hb < 70 g/L (maintain Hb between 70 to 100 g/L during active bleeds.) • Consider maintaining a higher Hb for Pz. w.: 1. CAD/Unstable coronary syndromes 2. Uncontrolled, unpredictable bleeding 3. Impaired pulmonary fct. 4. Increased O_2 consumption.
Blood transfusion & elective surgery	• Blood is expensive and its use carries risks. **Blood samples must be always labelled in the presence of the patient**! • In elective surgery, patients fall into one of three categories: 1. Transfusion not anticipated (e.g. hernia repair), 2. Transfusion possible but unlikely (e.g. cholecystectomy), or ▪ **Group & Save**: Send blood for ABO and Rhesus grouping and Atbs. screening, and retain serum for compatibility testing if required later 3. Transfusion probable (e.g. major arterial reconstruction). ▪ Patients in this category req. multiple units for the operation. The blood is prepared a day or so before the OP.
Blood transfusion necessity	• The volume of blood req. and the rate of transfusion depend on age, and the indications for transfusion and the patient's general and cardiovascular condition. **I. Volume & rate in haemorrhage** ▪ **Class I & Class II haemorrhage**: normally req. only crystalloids/colloids except in pre-existing anaemia. ▪ **Class III haemorrhage**: req. Red cell transfusion ▪ **Class IV haemorrhage**: req. rapid volume replacement w. crystalloids/colloids, followed by Red cell transfusion (4 units via a blood warmer). If bleeding continues, further red cells should be accompanied by fresh-frozen plasma (FFP) to prevent coagulopathy. Repeat coagulation screens are needed after every 4 units. If bleeding persists, recombinant activated factor VII is occasionally recommended. **II. Volume & rate in anaemia** ▪ If transfusion proves necessary in anaemic patients, it should be given at least 2 days before surgery to maximise its beneficial effects and to allow fluid balance to stabilise. ▪ It's older patients that are less tolerant of anaemia unless it is chronic and little operative blood loss is expected.

Platelets	
Indications	• Thrombocytopaenia w./w.out bleeding (use pooled platelets) • Procedures assoc. w. blood loss and major surgeries • Platelet dysfunction and marked bleeding • Potential bone marrow transplant recipients (use single donor platelets) • Pz. w. HLA antibodies (use HLA matched platelets)
Relative contraindications	• TTP, HIT • Post-transfusion purpura • HELLP

Coagulation factors	
Product	**Indication**
Frozen plasma (FP)	Depletion of multiple coagulation factors (e.g. sepsis, TTP/HUS, liver disease), Emergency reversal of life-threatening bleeding secondary to warfarin OD
Cryoprecipitate	Emergencies (Haemophilia A, von Willebrand disease, Hypofibrinogenemia)
vWF	Von Willebrand disease
Factor VIII concentrate	Haemophilia A
Factor IX concentrate	Haemophilia B
Recombinant factor VIIa	Factor VII deficiency w. bleeding/surgery Haemophilia A or B w. inhibitors Glanzmann thrombasthenia
Prothrombin complex concentrate	Reversal of warfarin therapy or vit. K deficiency in bleeding patient
Activated prothrombin complex concentrate	Urgent reversal of direct thrombin inhibitors.

Hazards and complications of blood transfusion

Febrile non-haemolytic transfusion reaction (FNHTR)

- A leucocyte incompatibility usually results in a febrile reaction, but this is a rare reaction since universal leucodepletion of blood products.
- A temp.^{O}C rise > 1 and shivering during or after transfusion indicates FNHTR.
- Symptoms usually subside after stopping the transfusion for 15-30 min and administering antipyretics and antihistamines.

Haemolytic reactions

- A major ABO incompatibility causes massive haemolysis, which can be lethal.
- Almost all haemolytic reactions are caused by human error and incompatible transfusion.
- **Clinical features**:
    - Rapidly developing pyrexia at the onset of infusion
    - Dyspnoea, constrictive feeling in the chest, intense headache
    - Severe loin pain
    - Hypotension
    - Acute oliguric renal failure w. haemoglobinuria (due to obstruction of tubules w. haemoglobin).
    - Jaundice
    - DIC w. spontaneous bruising & haemorrhage
- **Dx.**:
    - Blood tests – Hyperbilirubinemia
    - +ve Coomb's
- **Tx.**:
    - Halt transfusion
    - Resuscitated
    - Induce osmotic diuresis w. mannitol (to treat oliguria)

Allergic reactions

- **Clinical features**:
  - Fever
  - Skin rashes & Pruritus
  - Wheals or angio-oedema
  - Anaphylaxis (rare)
- **Tx.**:
  - Halt transfusion
  - Antihistamines

Infection

- Infections may arise from three source:
  I. The donor
  II. Contamination during blood preparation & storage
  III. Giving set/Cannula site
- Donated blood can be screened for most significant transmissible infectious agents, however diseases acquired too recently for the Atbs. response to develop cannot be detected.
- Generally, the most common/dangerous diseases transmitted via transfusion are:
  - **I. Viral infections**
    - Hepatitis (HBV, HCV and HDV)
      - Patients needing multiple transfusions need to be vaccinated against HBV prior to a surgery.
    - HIV
    - HTLV
    - Herpes viruses (CMV, EBV)
      - With CMV, there is a high risk only among premature neonates. Leucodepletion is an efficient way of reducing the risk.
  - **II. Bacterial infections**
    - Syphilis
    - Brucellosis
    - Contaminants
  - **III. Protozoal infections**
    - Malaria
    - Chagas disease
    - Babesiosis
  - **IV. Prions (esp. vCJD)**

Transfusion-Related Acute lung injury (TRALI)

- Transfusion of particularly plasma-containing products may be followed by an acute and rapid onset of shortness of breath and cough.
- There is typically a 'white-out' on CXR.
- Treated like ARDS – see *'Post-OP Complications – Respiratory Complications'*
- The injury is caused by donor antibodies reacting with the patient's leucocytes

Other complications of blood transfusion

- Immunosuppression
- Fluid overload
- Delayed transfusion reactions
  - PTP (Post-transfusion purpura) – This is a rare life-threatening complication caused by platelet-specific alloantibodies. Symptoms usually occur after a week w. the patient dev. thrombocytopaenia and bleeding
  - Transfusion-associated graft vs host disease – When the donor's lymphocytes recognise the recipient's cells as foreign, a graft vs host disease may be initiated. Irradiation of blood products is needed to inactivate T-cells likely to cause GvHD in susceptible patients (i.e. patients w. defective cell-mediated immunity.)

Reducing the need for blood bank transfusion

Considering the risks & the financial implications of blood transfusion, we should try to reduce the need for transfusion.

- **Non-transfusion methods**
    - Preoperative
        - Tolerating lower [Hb]
        - Iron therapy for iron deficiency anaemia
        - Tx. w. EPO before or after the OP
    - Intraoperative
        - Using gelatin or crystalloid solutions for hypovolaemia
- **Autologous transfusion** (Preoperative autologous donation, Acute normovolaemic haemodilution, Intraoperative cell salvage & post-OP cell salvage)