TRANSFUSION OF RED CELLS

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To many clinicians blood transfusion = transfusion of red cells

The term “blood transfusion” is often used rather loosely by doctors when what they really mean is the transfusion of red cells. Symptomatic of this linguistic laxity is that blood is often transfused without sufficient regard either to the specific requirements of the patient or to the potentially harmful effects of the transfusion. We therefore consider the red cell preparations generally available at present, the indications and some of the contraindications for their transfusion, the methods of infusion, and the side effects of transfusion of red cells that are not considered elsewhere in the series.

Red cell components

Comparison of red cell components

Component	Packed cell volume	Volume to be given	Main indication	Special precautions
Whole blood	.35 to .45	510 ml	Acute massive blood loss	Possible abnormalities of haemostasis if loss and replacement exceed twice the blood volume
Fresh blood	.35 to .45	510 ml	None proved	Blood that has not been microbiologically tested is unsafe
Red cell concentrates	.55 to .75	About 200 ml	Chronic blood loss or anaemia	None
Red cell concentrates in optimal additive solution	.50 to .70	Variable	Chronic blood loss or anaemia	Not to be used for neonates or exchange transfusion
Filtered blood	Variable	Variable	Non-haemolytic transfusion reactions and prevention of HLA immunisation before transplantation	Use within 24 hours of preparation
Washed red cells	Variable	Variable	Non-haemolytic transfusion reactions to plasma proteins	Use within 24 hours of preparation
Frozen, thawed, and washed red cells	Variable	Variable but usually <200 ml	Patients with rare antibodies	Use within 24 hours of preparation

A triple pack for collection of blood, with a unit of whole blood in the middle, a bag for plasma on the right, and a bag for collection of red cells into SAG-M (optimal additive solution) on the left.

- *Whole blood* is the complete collection of a single donation or “unit” of about 450 ml of blood into an anticoagulant solution. The unit contains effete, but still antigenic, granulocytes and platelets and all the plasma proteins, but as a result of storage there is loss of activity by the coagulant factors V and VIII:C and by complement.

Clinicians often request “fresh whole blood,” which is rarely available because of the time needed for collection, grouping, testing for harmful antibodies, microbiological screening, and despatching by the transfusion centre to the hospital. Red cell components supplemented by fresh frozen plasma and platelet concentrates are just as effective.

- *Red cell concentrates* comprise a unit from a single donor from which some or most of the plasma has been harvested by centrifugation or sedimentation.

- *Red cell concentrates in optimal additive solution*—The most commonly used solution in the United Kingdom is known as SAG-M, which contains sodium chloride 140 mmol/l, adenine 1.5 mmol/l, glucose 50 mmol/l, and mannitol 30 mmol/l. This permits removal of all of the plasma for the production of blood components while extending the shelf life of the red cells from four to five weeks. The packed cell volume is usually normal, but the absence of plasma proteins reduces the viscosity thus permitting easy and speedy transfusion. It is not used for neonates or for exchange transfusions.

- *Leucocyte depleted red cell components* have had most of the leucocytes and platelets removed. They are given to those patients who are already sensitised to HLA, granulocyte, and platelet antigens—for example, those who have had multiple transfusions and have had febrile reactions or those for whom exposure to these antigens is contraindicated, such as patients undergoing renal or bone marrow transplantation. Filters should be *leucocyte specific* to remove virtually all the white cells and platelets. *Microaggregate filters* remove only the larger aggregates of aged platelets, leucocytes, fibrin strands, cold insoluble globulin, and cellular debris; these deposits form in stored blood and can pass through the filter of the routine blood administration set. Microaggregate filters are used to minimise the risk of microembolisation when large volumes of blood are being transfused rapidly.

- *Washed red cells* are rarely used and have the plasma proteins as well as the leucocytes and platelets removed. They are given to patients with paroxysmal nocturnal haemoglobinuria and to those who have been immunised against plasma proteins—for example, patients deficient in IgA who have developed anti-IgA antibodies.

- *Frozen and thawed red cells* have had all traces of leucocytes, platelets, and plasma proteins removed, but the red cell metabolic pathways are normal. These units are extremely expensive to prepare and thaw so they are usually given only to patients with rare blood groups or with antibodies against common antigens, such as Cartwright, Vel, or Getrich. They can safely be stored for up to 10 years.

- *Any product that requires an "open" procedure* (filtering, washing, and freezing) for preparation is at risk of bacterial contamination. Such products are therefore issued with a limited expiry time before which they must be transfused, otherwise they should be discarded.

Indications for transfusion of red cells

Normal red cells (left) and hypochromic macrocytic red cells of iron deficiency anaemia (right).

Give

- Whole blood
- Red cells in SAG-M
- Red cell concentrates
- Plasma expanders

The only true indication for the transfusion of red cells is the need to improve the delivery of oxygen to the tissues within a short time. A low haemoglobin concentration should not be the only reason for transfusion as many other factors are important; these include the patient's age and general state and the rate of fall of the haemoglobin concentration. A patient whose haemoglobin concentration falls suddenly feels ill and may well require transfusion. An equally low haemoglobin concentration (for example, 80 g/l), however, may be well tolerated by a patient whose body has had time to adapt because the fall has taken place gradually over weeks or months, so such patients are generally better treated in other ways.

- *Acute blood loss*—If blood is lost as a result of trauma or operation both red cells and volume replacement are needed. If more than half the blood volume is lost whole blood should be given; if less than half, red cell concentrates and plasma expanders may be given.

Normal red cells (left) and oval macrocytes of megaloblastic anaemia (right).

Sickle cell anaemia (left), and β thalassaemia major (right).

Give

- Red cell concentrates
- Filtered blood

Give

- Red cell concentrates
- Filtered blood

Match red cells for K and all Rh antigens

Give

- Blood that is as fresh as possible, and free of antibodies against cytomegalovirus

Plasmodium falciparum: ring forms (left) and schizont (right).

Method of transfusing red cells

Transfusion of less than two units of red cells is bad clinical practice.

• *Preoperative blood transfusion*—It is usually safer to correct anaemia with appropriate haematinics if its cause is known (see below). If preoperative anaemia cannot be corrected in this way (for example, if the operation is an emergency or the patient has failed to respond to haematinics) and the haemoglobin concentration is 80 g/l or less, the patient may be transfused. When the haemoglobin concentration is between 80 and 100 g/l each patient should be assessed individually before the decision to transfuse is made.

• *Iron deficiency anaemia*—Patients with iron deficiency should not be transfused unless they need immediate operation or have failed to respond to treatment with full therapeutic doses of oral iron. Transfusion for simple iron deficiency is an expensive and potentially hazardous way of raising the haemoglobin concentration, which—in the absence of other disease—will rise about 10 g/l/week with adequate oral treatment.

• *Megaloblastic anaemia*—Transfusion should be avoided in these patients as it can precipitate cardiac failure and death by increasing the strain on the heart.

• *Anaemia associated with chronic disorders*—Occasional patients with malignant disease, rheumatoid arthritis, or chronic inflammatory processes may not respond to haematinics and so may require blood transfusion.

• *Bone marrow failure*—Patients with bone marrow failure as a result of leukaemia, treatment with cytotoxic drugs, or malignant infiltration may require not only red cells but also other blood components.

• *Transfusion dependent patients*—Patients with severe thalassaemia syndromes and aplastic and sideroblastic anaemia require regular transfusions every four to six weeks to enable them to lead normal lives and—for children—to allow normal growth.

• *Sickle cell disease*—Some of these patients also require regular transfusions, particularly after strokes, for recurrent life threatening “chest syndromes” and during pregnancy. Selection of red cells for patients who are not of northern European descent requires additional screening, in particular for the Kell antigen and all the Rh antigens.

Some patients with sickle cell disease require exchange transfusions for emergencies such as severe hypoxia, stroke, and priapism. The aim is at reducing the amount of haemoglobin S to less than 20% of the total while steadily raising the total haemoglobin concentration to 120–145 g/l.

• *Haemolytic disease of the newborn* may also be an indication for exchange transfusion when the neonate has severe hyperbilirubinaemia or anaemia (see chapter on haemolytic disease of the newborn and its prevention).

• *Other indications* for exchange transfusion include selected cases of severe *Plasmodium falciparum* malaria and meningococcal septicaemia.

• *Immune mediated haemolysis*—These patients should not be allowed to become compromised by severe anaemia. The selection and testing of red cell units before transfusion should not, however, be undertaken without the advice of a haematologist.

The volume of red cells required by a patient should be calculated by the clinician before ordering the blood. In adults, transfusion of less than two units of red cells is bad clinical practice because it can be avoided; a rise of about 10 g/l of haemoglobin may be expected from each unit of red cells transfused.

Technique of transfusion

Preparation for transfusion: close clamp (A), then mix blood thoroughly, pull tabs to expose outlet port, remove coupler cover (B), and insert into outlet.

Remove protective cover from needle adapter (C), open clamp (D). Invert blood pack and squeeze to fill filter chamber (E) completely and drip chamber (F) by about a quarter. Close clamp (D). Suspend pack. Attach adapter (C), open clamp (D), allow blood to fill set, and expel air. Close clamp (D).

Preparation for using Y type giving set: close clamp (A). Remove one coupler cover (B). Insert coupler into pack of solution and suspend container. Open clamp (A) on lead below solution. Open clamp (C) on adjacent lead. Close clamp (A) when chamber (E) is full. Squeeze and release drip chamber (E) until a quarter full.

Remove protector from needle (F) and attach needle. Remove lower clamp to fill with solution and expel air. Puncture vein. Mix blood in pack and close all clamps. Pull apart tabs, remove coupler cover (D) from unused lead, insert into outlet port and suspend blood pack. Close clamp (A) under saline container and open clamp (C) under blood pack. Open lower clamp and adjust flow rate.

The ordering and administration of blood must comply with certain minimum requirements (see chapter on testing before transfusion, and blood ordering policies).

(1) All samples and requests for blood must contain accurate identification of the patient's name, date of birth, address, and hospital index number (special arrangements must be made for emergencies).

(2) A procedure for ordering blood that consists either of grouping and screening the patient's serum for unusual antibodies or of compatibility testing to establish that the blood is indeed compatible with the patient's own serum. In the first instance blood is not set aside for the patient, whereas in the second instance specific units are labelled and held in readiness for that patient.

(3) Release and collection of blood must depend on the local system but must include checking against the agreed method of documenting the patient's details.

(4) Blood should be stored correctly only in designated refrigerators with alarms. If a unit is taken from a blood refrigerator and transfusion is not started within 30 minutes that blood is no longer suitable or safe for use.

(5) Before administration of the blood the patient's identity must be checked according to the local procedure and the unit to be given should also be checked to make sure that the compatibility label shows all the details given in (1) above, together with the unique number of the unit and the time for which the blood has been requested—no discrepancies should be accepted.

(6) Drugs must never, under any circumstances, be added to blood.

Blood should be infused through special sterile giving sets designed for the procedure and containing standard 170 μ m filters. The best veins for cannulation are those on the dorsum of the hand and in the forearm. When large volumes of blood are to be transfused in a short time a blood warmer may be required. Blood must never be warmed in a sink of hot water or on a radiator.

The patient should be monitored during and after transfusion by carefully laid down procedures, the least of which are the checking and recording of blood pressure, pulse rate, and temperature every 30 minutes. It is advisable to observe the patient closely during the first 5 to 10 minutes of each unit in case of a severe unexpected reaction. In severely ill and elderly patients measurement of the central venous pressure allows prevention of circulatory overload from rapid transfusion.

The rate of transfusion is dependent on the reason for transfusion and may vary from 4 hours/unit in a patient with chronic anaemia to 5-10 minutes/unit (until the systolic blood pressure reaches 100 mm Hg) in a patient with acute blood loss. Transfusion of a unit of blood should normally be completed in four hours.

Blood infusion sets are calibrated to deliver 1 ml in 20 drops, and a steady infusion rate can be calculated. The fastest rate at which blood can be transfused by gravity alone is 60 ml/minute. If a faster rate is required then either multiple leads or transfusion under pressure (manual or with a pressure cuff or pump) may be used.

Exchange transfusion in adults is a laborious procedure, which should be carried out isovolaemically—that is, without pronounced changes in the patient's blood volume. Ideally, venous access should be at two sites to permit simultaneous venesection and transfusion. When this is difficult then a single catheter with a three way tap may be used for alternate

removal and infusion in 20-50 ml aliquots. The exchange should ideally be carried out within a closed system.

In patients with sickle cell disease it is important to remember that the blood removed has a lower packed cell volume than the blood being transfused. To achieve less than 20% haemoglobin S in a total haemoglobin concentration of 120-145 g/l a total exchange requires removal and transfusion of 1.25 times the patient's blood volume. (Blood volume (ml)=weight (kg)×70.) In children this can be done in three divided daily exchanges, but adults normally require four procedures in each of which about two to three units are removed and three are transfused daily.

Problems associated with transfusion of red cells

The problems associated with transfusion of red cells are discussed in detail in other chapters, so we mention them only briefly.

Immediate problems

- Circulatory overload occurs when blood is transfused too rapidly for compensatory fluid redistribution to take place or if there is impaired cardiac function. The central venous pressure rises and in severe cases left ventricular failure develops.
- Potassium leaks out of red cells during storage, and this hyperkalaemia is exacerbated by keeping the blood for too long at room temperature.
- Massive transfusion can cause hypothermia, citrate toxicity, acid load, and depletion of platelets and coagulation factors.
- Haemolytic reactions cause fever, tachycardia, loin pain, restlessness, rigors, vomiting, diarrhoea, headache, dyspnoea, hypotension, shock, and ultimately acute renal failure, and bleeding as a result of disseminated intravascular coagulation.
- Non-haemolytic reactions can present as urticaria and fever and rarely as severe anaphylaxis.

Medium term problems

- Local phlebitis may develop if plastic cannulas are left in the same site for too long. Occasionally there is infection by staphylococci or corynebacteria.
- The hypertension or convulsion syndrome has been described occasionally in patients with sickle cell disease and β thalassaemia major who have regular transfusions. The patients develop severe diastolic hypertension with headache and there is a risk of subarachnoid haemorrhage and fits, probably as a result of the release of vasoactive substances during the storage of the blood.
- Infection may be transmitted by transfusion.

Long term problems

- Iron overload—Every unit of blood contains 250 mg of iron that the body is unable to excrete. Regular frequent transfusions can lead to a build up of iron in the body resulting in pigmentation, poor growth, hepatic cirrhosis, diabetes, hypoparathyroidism, cardiac failure, arrhythmias, and eventually death. Iron chelation treatment should therefore be considered for these patients before serious damage to organs occurs.

Conclusion

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Red cell transfusions are labour intensive and expensive but frequently life saving. In a few patients, however, they can result in potentially fatal complications. It is therefore essential that they are given appropriately.

Give

- Frusemide (20 mg intravenously with each unit)
- Oxygen
- Morphine

- Use units in less than 8 hours
- Give dextrose/insulin if potassium concentration rises

- Warm the blood
- Give plasma and platelet components
- Monitor serum calcium concentration

- Stop transfusion
- Keep line open with saline
- Check identification of patient and unit

Always seek advice from haematologist in charge of the blood bank

- Change the site every 48 hours
- Treat infections

- Reduce blood volume
- Give anticonvulsant and antihypertensive drugs

- Give desferrioxamine by subcutaneous infusion over 8 to 10 hours for 5 to 7 days a week