Clinical Surgery in General:
RCS Course Manual

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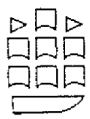

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17. Correction of preoperative, perioperative and postoperative anaemia: use of blood and blood products

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The administration of blood and blood products represents substitution therapy and can correct almost immediately and invariably the existing anaemia, thrombocytopenia, coagulopathy or hypoproteinaemia in the patient. However, the administration of blood and blood products is not without risk and should be carried out where the indications are clearly established, i.e. where the benefits to the patient outweigh the risks of transfusion. In this chapter indications for preoperative, perioperative and postoperative transfusion of blood and blood products will be presented, available products described, measures for monitoring the therapeutic effect discussed and adverse reactions to transfusion summarized. Note that in this chapter the term blood products is used for all therapeutic materials prepared from blood and includes both blood components and plasma products. The term blood components refers to red cell preparations, platelet concentrates, fresh frozen plasma and cryoprecipitate. Whole blood and blood components are administered to the patient as 'units', a unit having a quantity obtained from one blood donation. The term plasma products refers to all plasma protein preparations manufactured from large pools of donor plasma. The therapeutic potency of a plasma product is given in weight of protein (for example, a bottle of 20 g of albumin in 100 ml), or in units of activity (for example, a vial of 250 iu of factor VIII:C).

INDICATIONS FOR TRANSFUSION

Indications for transfusion of blood and blood products are based on the assessment of the impaired haematological status of the patient. Each of the main functions of blood — maintenance of intravascular volume, oxygen-carrying capacity, haemostasis and maintenance of oncotic pressure — may be impaired to a different degree in the patient with acute blood loss or chronic anaemia. Furthermore, each of the functions has a different 'critical level' which requires immediate corrective action if serious consequences or even death are to be prevented (Table 17.1). When critical levels for any of the blood functions are reached, and that may happen at any time before, during or after an operation, corrective action has to be taken by transfusion of blood, blood components or blood substitutes.

Table 17.1 Main functions of blood and their critical levels

Function	Blood constituents	Critical level (%)*
Maintenance of intravascular volume	Blood volume	60
Oxygen-carrying capacity†	Haemoglobin concentration	50
Haemostasis‡	Platelet count	10
	Concentration of coagulation factors	10
Maintenance of oncotic pressure	Concentration of plasma proteins (mainly albumin)	50

*Expressed as a percentage of normal function. Critical levels vary considerably in each patient and they should always be individually assessed.
†Several factors may affect oxygen-carrying capacity of haemoglobin; see also Table 17.2.
‡The third component of the haemostatic mechanism, the fibrinolytic system, has been excluded.

The main objective in the management of anaemia encountered in surgical practice is to ensure adequate oxygenation of tissues and par-

ticularly of the heart and the brain. Experience accumulated over the last few years has shown that that objective is achieved when the haemoglobin concentration is above 8.0 g dl^{-1}. That level of haemoglobin, at which a decision to transfuse the patient is usually made, is generally known as the 'transfusion trigger'. While the transfusion trigger can be useful as a pointer for action, it should never be used as an immutable value, as for example, a young patient with haemoglobin concentration substantially lower than 8.0 g dl^{-1} may tolerate the operation much better than an old patient with a higher haemoglobin level but with a failing heart or compromised cerebral circulation. It has to be appreciated that oxygen delivery to the tissues is a function of partial pressure of oxygen in the air, which is raised during anaesthesia and haemoglobin oxygenation; it is also dependent on the function of the lungs and cardiovascular system (Table 17.2). Although it is well documented that the level of haemoglobin and postoperative survival are inversely correlated, neither clinical observations nor laboratory experiments have been able to define the lowest 'safe' haemoglobin concentration. Therefore, it is mandatory to assess each patient individually and to consider the type and probable duration of anaesthesia and of operation before a decision to administer blood is made. In a proportion of patients anaemia may be associated with thrombocytopenia and/or defective coagulation. These patients will require, in addition to red cells, transfusion support with platelet concentrates and fresh frozen plasma.

Table 17.2 Factors which may affect delivery of oxygen to the tissues.

Haemoglobin oxygenation
Partial pressure of oxygen in air
Haemoglobin concentration
Haemoglobin oxygen saturation
Haemoglobin affinity for oxygen
Effects of pH, 2,3-DPG and haemoglobins with high affinity for oxygen
Blood volume
Cardiac output
Peripheral vascular resistance
Lung function
Type and duration of anaesthesia
Type and duration of surgery

The use of albumin solutions is rather limited to specific indications, which will be discussed later.

PREOPERATIVE ANAEMIA

The determination of haemoglobin concentration — part of the preoperative assessment of the patient (see chapter 2) — will reveal the presence of anaemia (haemoglobin concentration less than 13.0 g dl^{-1} in men and 11.5 g dl^{-1} in women). Faced with the anaemic patient awaiting surgery, the surgeon should first ensure that the correct diagnosis of anaemia is made or at least that the samples required for the diagnosis have been collected. Second, he should decide whether to proceed with or defer the operation. Finally, he should decide whether the patient requires transfusion of blood. The decision to transfuse the patient should be based on the type and degree of anaemia and the urgency for surgery. Elective surgery should be delayed until haemoglobin concentration is raised to the level considered safe for the patient.

Anaemia is caused by the decreased production of red cells in the bone marrow, increased destruction of red cells in the circulation, or blood loss. Anaemia may be chronic or of sudden onset. In chronic anaemia compensatory mechanisms which increase oxygen delivery to the tissues are well developed; they are absent in acute anaemia. The current diagnosis of anaemia will most often make it possible to predict its progress and response to treatment. In the patient with functioning bone marrow an appropriate treatment will raise the haemoglobin concentration on average 1.0 g dl^{-1} per week.

Types of anaemia and their management are presented in Table 17.3. Anaemias of interest to the surgeon are described below.

Iron deficiency anaemia due to chronic blood loss is the most frequently seen type of anaemia. It is usually caused by blood loss from the gastrointestinal tract or kidneys and in women by menorrhagia. Once the measures to prevent further blood loss are taken, anaemia will respond well and quickly to treatment with oral iron.

Anaemia of chronic disease is often found in association with a number of chronic diseases. It is usually mild and unresponsive to treatment. A

Table 17.3 Main types of anaemia found by preoperative assessment and their management

Type	Management
Anaemia due to decreased production of red cells	Establish diagnosis, deal with the cause and prescribe oral iron preparations. Usually good response
Iron deficiency anaemia	
Nutritional or due to malabsorption	
Chronic blood loss	Establish diagnosis, deal with the cause and treat with parenteral vitamin B_{12}. Usually good response
Vitamin B_{12} deficiency	
Nutritional or due to malabsorption	
Pernicious anaemia	Establish diagnosis, deal with the cause and prescribe folic acid. Usually good response
Folic acid deficiency	Establish diagnosis and treat the primary disease. Usually poor response. Patients with renal disease respond to rhEPO*
Nutritional or due to malabsorption	Establish diagnosis and treat the primary disease. Variable response. Transfuse as required. Sometimes transfusion of platelets is also needed
Anaemia of chronic disease	
Anaemia due to bone marrow failure	Establish diagnosis. Transfuse as and when required
Aplastic anaemia, leukaemia, bone marrow infiltration with malignant cells	
Anaemia due to increased destruction of red cells	Establish diagnosis and treat primary disease. Avoid transfusion where possible
Inherited	
Haemoglobinopathies	
Thalassaemias	
Sickle cell disease	
Acquired	
Immune-mediated	
Non-immune haemolytic anaemias	
Anaemia due to blood loss	Remove the cause of bleeding where possible, transfuse where required
Acute	Manage as iron deficiency anaemia
Chronic	

*rhEPO, recombinant human erythropoietin.

severe degree of anaemia may occur in patients with renal failure and in these patients administration of recombinant human erythropoietin may raise the haemoglobin concentration to near normal values.

Haemoglobinopathies. Patients with sickle cell disease (HbSS, HbSC or HbS/thalassaemia) in general require exchange transfusion before major surgery, whereas intermediate and minor surgical procedures can be carried out safely without transfusion in the majority of patients. Particular attention should be paid to the hydration of the patient and to oxygenation during anaesthesia. Patients with sickle cell disease may develop painful crisis due to infarcts in tissues and organs, before, during or after an operation, which is best managed by symptomatic treatment, but occasionally may require blood transfusion.

Haemolytic anaemia. Patients with hereditary or long-standing acquired haemolytic anaemia are sometimes referred for splenectomy as the spleen is the major site of red cell destruction. Patients with long-standing haemolysis are prone to cholelithiasis and may be referred for cholecystectomy.

Patients with acquired autoimmune haemolytic anaemia may present a challenge to the blood bank to provide compatible blood for transfusion. When ordering blood sufficient time should be allowed for compatibility testing. Often blood issued for transfusion carries the warning that it is as compatible (or incompatible) as the donor's own red cells.

Anaemia due to acute blood loss, when severe, requires immediate restoration of circulatory volume with crystalloid solutions in the first instance and then colloid solutions afterwards. The decision to administer blood should be made after careful assessment of the patient's condition. Administration of albumin solutions as volume expanders is not recommended.

PERIOPERATIVE LOSS OF BLOOD

In a number of operations blood loss of varying magnitude may occur. Programmes to minimize the blood loss are based on meticulous surgical haemostasis and the use of pharmacological agents (ε-aminocaproic acid, tranexamic acid, desmopressin, aprotinin) to decrease the blood loss. However, supportive treatment with blood may be needed when excessive bleeding due to inadequate surgical haemostasis and/or breakdown of haemostatic mechanisms are encountered. With that in view it is customary to order in advance compatible blood according to the locally agreed maximum surgical blood order schedule (MSBOS). In addition, surgeons wishing to eliminate or decrease the use of homologous blood transfusion in the surgical patient should consider using one or several forms of autologous transfusion: preoperative blood donation, intraoperative and postoperative blood salvage and acute normovolaemic haemodilution (see below).

It is well recognized that it is difficult to estimate blood loss during surgery. Although there are a number of methods available for monitoring the patient's homeostatic and haemostatic states, none of these is wholly satisfactory (Table 17.4). In addition, the decision to transfuse blood may be influenced by the local policy and personal preferences of the surgeon or anaesthetist in relation to the type of operation, test used for monitoring blood loss and availability of blood and blood components. The management of blood loss and associated adverse reactions is best illustrated by descriptions of massive blood transfusion and cardiopulmonary bypass.

Massive blood transfusion

Massive blood transfusion is by definition transfusion of a volume of blood, greater than the recipient's blood volume, in less than 24 hours. It is used to combat hypovolaemic shock caused by profuse bleeding due to disease, trauma or surgical intervention.

Blood group-specific, compatible whole blood or red cell preparations can be transfused, usually using an in-line microaggregate filter. When a fast rate of transfusion is required a pressure infusor or a pump and blood warmer should be used. In massive blood transfusion, administration of fresh frozen plasma and platelet concentrates may also be required. These should be from the same blood group as the red cells. The following complications of massive blood transfusion can occur.

Cardiac abnormalities are usually ventricular extrasystoles, and rarely ventricular fibrillation progressing to cardiac arrest. They are due to the combined effect of low temperature, high potassium concentration and excess citrate with low calcium concentration. They can be prevented by using a blood warmer and a slower rate of transfusion, particularly in patients with hepatic or renal failure. Routine administration of calcium gluconate in massive transfusion has not been shown to be beneficial and may even be danger-

Table 17.4 Tests available for monitoring blood loss and substitution therapy with blood and blood products

Oxygen-carrying capacity of blood
Haemoglobin concentration
Packed cell volume (PCV)
Pulse oxymetry
Haemostatic functions
Whole blood coagulation time
Coagulation screen*
Prothrombin time (PT)
Partial thromboplastin time (PTT)
Thrombin time (TT)
Platelet count
Thromboelastography
Oncotic pressure of plasma
Serum total protein concentration*

* Samples for testing usually have to be sent to a main laboratory

ous unless calcium concentration in plasma can be monitored.

Acidosis in the patient with severe renal or liver disease may be aggravated by the low pH of stored blood. In practice, acidosis is rarely a problem and administration of sodium bicarbonate after determining the 'base deficit' from measurements of blood pH and PCO_2 is rarely justified.

Failure of haemostasis. The usual clinical manifestations are failure of local haemostasis and, infrequently, a generalized bleeding tendency due to the lack of factors VIII:C, V and XI, as well as platelets in the stored blood. The diagnosis of bleeding due to massive transfusion must be confirmed by the laboratory, as other haemostatic defects have an identical clinical presentation but require different management (Table 17.5). Fresh frozen plasma, 1–2 units, corrects the abnormalities of coagulation and should be given prophylactically after every 10 units of blood. Platelet transfusion may be required when the platelet count is lower than $30 \times 109\ l^{-1}$, particularly if the patient is undergoing a neurosurgical procedure.

Adult respiratory distress syndrome (ARDS), also called non-cardiogenic pulmonary oedema (NPE), occurs in severely ill patients after major trauma and/or surgery. A tetrad of clinical features characterizes ARDS: progressive respiratory distress, decreased lung compliance, acute hypoxaemia and diffuse radiographic opacification of the lungs. The mortality is high; post-mortem studies show widespread macroscopic and microscopic thrombosis in the pulmonary arteries. The pathogenesis of ARDS is unclear, but agglutination of donor leucocytes, recipient leucocytes or both may be responsible for direct damage to alveolar lining cells; local disseminated intravascular coagulation, microvascular fluid leakage and embolization by leucocyte aggregates and microaggregates from stored blood all contribute. Management consists of stopping the transfusion, administering corticosteroids and providing supportive treatment to combat pulmonary oedema and hypoxia by using oxygen and positive pressure ventilation.

Jaundice almost invariably follows massive blood transfusion. However, serum total bilirubin rarely exceeds 40 μmol l^{-1} and haemoglobinaemia is slight. Investigation for a delayed haemolytic transfusion reaction is not indicated.

Transfusion in open heart surgery

Patients undergoing open heart surgery require cardiopulmonary bypass (CPB) for maintaining the circulation with oxygenated blood. CPB as a

Table 17.5 Differential diagnosis of haemostatic failure in massive blood transfusion

Condition or platelet disease	Laboratory tests: Prothrombin time	Partial thromboplastin time	Thrombin time	Platelet Count*
Massive blood transfusion	↑	↑	N	↓
DIC†	↑↑	↑↑	↑↑	↓↓
Vit. K deficiency	↑↑	↑	N	N
Haemophilias	N	↑↑	N	N
ITP‡	N	N	N	↓↓

*Platelet count rarely falls below $50 \times 10^9\ l^{-1}$.
†DIC, disseminated intravascular coagulation.
‡ITP, idiopathic thrombocytopenic purpura.
N, normal; ↑, moderately prolonged; ↑↑, markedly prolonged;

part of open heart surgery is a complex procedure and the demand for blood and blood products is variable in individual patients.

The blood required should be of the same blood group as the patient. In adults blood is not required for priming of the heart–lung machine but it is needed in neonates and small children. For post operative transfusion, any of the red cell preparations are equally satisfactory. Blood less than five days old is preferred to stored blood, but the latter can be used safely.

In most cases of open heart procedures 4 units of blood are initially cross-matched. An additional 2–4 units are required in repeated procedures. Blood components may be required for the correction of the haemostatic defect (see below). The use of albumin solutions either for priming the heart–lung machine or postoperatively has not been proved to be advantageous.

Bleeding associated with CPB is rare in the patient operated on for the first time. It is due to activation and loss of platelets and coagulation factors in the extracorporeal circulation, failure of heparin neutralization by the first dose of protamine, activation of fibrinolysis in the oxygenator and pump, and/or disseminated intravascular coagulation in patients with poor cardiac output and long perfusion times. The differential diagnosis of bleeding associated with CPB is presented in Table 17.6.

Management of bleeding associated with CPB requires: administration of 4–8 units of platelet concentrates when the platelet count is less than $30 \times 10^9 l^{-1}$; transfusion of 2–4 units of fresh frozen plasma to correct the loss of coagulation factors; neutralization of excess heparin by protamine (1 mg of protamine neutralizes approximately 100 iu of heparin); administration of tranexamic acid (or a similar antifibrinolytic agent) when hyperfibrinolysis is confirmed by laboratory testing; treatment of disseminated intravascular coagulation, in the first instance by correcting the underlying cause (e.g. poor perfusion, oligaemic shock, acidosis, infection, etc.), and then by transfusion of fresh frozen plasma and platelet concentrates as required.

Autologous transfusion

Autologous transfusion is the administration of the patient's own blood collected prior to, during or after an operation. Indications for autologous transfusion are, first, provision of blood for the patient with antibodies to one of the high-frequency antigens (public antigens) who is awaiting elective surgery and for whom it is not possible to

Table 17.6 Differential diagnosis of bleeding associated with cardiopulmonary bypass

Cause of bleeding	Laboratory tests				
	Prothrombin time	Partial thromboplastin time	Thrombin time Without protamine	Thrombin time With protamine	Platelet count
Loss of platelets	N	N	N	N	↓↓
Depletion of coagulation factors	↑↑	↑↑	N	N	N or ↓
Excess of heparin	↑	↑↑	↑	N	N or ↓
Hyperfibrinolysis	↑	↑	↑↑	↑↑	N or ↓
DIC*	↑↑	↑↑	↑↑	↑↑	↓

*DIC, disseminated intravascular coagulation.
N, normal; ↑, moderately prolonged; ↑↑, markedly prolonged; ↓, moderately decreased; ↓↓, markedly reduced.

collected using a cell separator (also equivalent to 6 single units). Single units contain on average 75×10^9 platelets. Platelet concentrates are administered to thrombocytopenic patients who are bleeding or receiving prophylactic treatment. In surgical practice platelet concentrates are used for treating severe bleeding after cardiopulmonary bypass and massive transfusion as well as in preparation for surgery of patients with qualitative disorders of platelets — Glanzmann's thrombasthenia, Bernard–Soulier syndrome, etc..

Platelet concentrates have a shelf-life of five days when kept in packs for extended storage, at temperatures between 20 and 24°C, preferably in an incubator and continuously agitated on an agitator. Usually 6 units of platelet concentrate are administered as one dose for an adult patient, and using a rule of thumb 1 unit of platelet concentrate, with at least 50×10^9 platelets, will increase the platelet count 1 hour after transfusion by $10^{10}\,l^{-1}\,m^{-2}$ body surface.

Fresh frozen plasma (FFP) for clinical use is separated from single units of blood and rapidly frozen within 6 hours after collection. It contains all the constituents of fresh plasma (except platelets). FFP is used for supporting failing coagulation in disseminated intravascular coagulation, deficiency of vitamin K-dependent coagulation factors, overdose of oral anticoagulants, liver disease, massive blood transfusion, cardiopulmonary bypass and treatment of congenital deficiencies of factors V and XI. Although 2–4 units are usually administered to the patient, the volume and frequency of administration should be assessed for each patient separately. FFP, kept in a deep-freeze at a temperature below –30°C, has a shelf-life of one year.

Cryoprecipitate and single coagulation factor concentrates are rarely used in surgical practice. The properties, indications for use and monitoring of

Table 17.7 Blood and blood components and indication for use

Component	Volume/unit (ml)	Main indications for use	Special precautions
Whole blood (PCV* 0.35–0.45)	510	Acute massive blood loss	Possible abnormalities of haemostasis if loss and replacement exceed twice the blood volume
Red cells (PCV 0.55–0.75)	280	Anaemia	None
Red cells in OAS† (PCV 0.50–0.70)	350	Anaemia	Not to be used for neonates and exchange blood transfusion
Filtered red cells (PCV variable)	Variable	Non-haemolytic febrile transfusion reaction Prevention of HLA immunization	None
Platelet concentrates from random donors	50	Thrombocytopenia Qualitative disorders of platelets	None
obtained by plateletpheresis	250	As above	For patients with platelet refractoriness should be HLA matched
Fresh frozen plasma	200	Replacement of all coagulation factors Reversal of warfarin effect Thrombotic thrombocytopenic purpura	Allergic reactions; circulatory overload
Cryoprecipitate	20	von Willebrand's disease Hypofibrinogenaemia Factor XIII deficiency	Allergic reactions

*PCV, packed cell volume.

†OAS, optimal additive solution.

therapeutic effect of these preparations are described in textbooks of haematology and blood transfusion.

Albumin is available as 5% and 20% solutions in a variety of dose units. The indication for administration of 5% albumin is the replacement of plasma proteins and expansion of plasma volume, as in hypoproteinaemia following burns (after the first 24 hours) and as a part of the replacement fluid in large-volume plasma exchange. Opinions are divided whether albumin solutions play a role in restoration of circulatory volume in haemorrhage shock, but the view that administration of colloid and crystalloid solutions is better for that purpose (and it is certainly cheaper) is gaining popularity. The indication for use of 20% albumin is solely the replacement of plasma proteins in severe hypoproteinaemia in renal or liver disease, after large-volume paracentesis, following massive liver resection and in some cases of Gram-negative septicaemia.

Plasma substitutes are colloid and crystalloid solutions which are used for maintaining the circulatory volume following acute haemorrhage, shock, burns and septicaemia. Plasma substitutes have no oxygen-carrying capacity and lack haemostatic properties. Crystalloid solutions have no plasma oncotic activity and colloid solutions possess it only temporarily as their half-life in circulation is rather short (Table 17.8). The use of plasma substitutes in an emergency 'buys time' necessary for provision of compatible blood and appropriate blood products.

ADVERSE CONSEQUENCES OF BLOOD TRANSFUSION

In general, transfusion of blood and blood products is a safe and effective mode of treatment. However, a small proportion of patients will suffer from transfusion side effects and a few may be in danger from having potentially catastrophic reactions of transfusion. The main undesirable consequences of transfusion are transfusion reactions due to antigen/antibody binding and subsequent destruction of the target cell, modulation of the immune system of the recipient, graft-versus-host disease and transmission of diseases (Table 17.9).

Immediate haemolytic transfusion reaction (HTR) is almost always due to ABO incompatibility between the transfused red cells and the recipient. Over 90% of HTR is due to clerical error in the identification of the patient or the unit of blood.

Severe HTR is characterized by anxiety, chest pain, back pain, headache, dyspnea, rigors, vomiting, diarrhoea, restlessness, tachycardia, hypotension, shock, unexplained bleeding and renal shutdown, which occur in quick succession. In the anaesthetized patient persistent hypotension and unexplained oozing from the wound may be the only signs. Haemoglobinaemia and haemoglobinuria are present. Diagnosis is based on finding the clerical error, visual inspection of serum and urine and laboratory testing. Management consists of stopping the transfusion, administration of hydrocortisone 100 mg and an intravenous antihistamine (i.e. chlorpheniramine 10 mg), maintenance of blood volume and urinary flow with intravenous fluids, and in the presence of disseminated intravascular coagulation intravenous administration of heparin.

Moderate HTR presents less dramatically than severe HTR, while mild HTR presents with a mild degree of fever only and often passes unnoticed.

Delayed haemolytic transfusion reaction. Haemolysis of the transfused red cells in the recipient's circulation which occurs one to three weeks after transfusion is due to an anamnestic antibody re-

Table 17.8 Plasma substitutes: colloid volume expanders (given in percentages)

Product	Mol. w	Concentration	Half-life in circulation (h)
Modified gelatin	35 000	3–4	5
Hydroxyethyl starch	450 000	6	24
Dextran 70	70 000	6	24

Table 17.9 Adverse consequences of blood transfusion

Immune response to cellular and plasmatic alloantigens:		
Clinical syndromes following repeated transfusions		
Red cell antibodies	—	haemolytic transfusion reaction
HLA antibodies	—	non-haemolytic febrile transfusion reaction
	—	platelet refractoriness
Platelet-specific antibodies	—	platelet refractoriness
	—	post-transfusion thrombocytopenia
	—	neonatal immune thrombocytopenia
Anti-IgA*	—	anaphylactic shock
Immunomodulation (e.g. reduced disease-free interval after resection of carcinoma of the colon)		
Graft-versus-host disease (caused by transfusion of live lymphocytes)		
In immunosuppressed patients (e.g. patients receiving tissue or organ transplants		
In immunocompetent patients (transfused with blood donated by first-degree relatives)		
Transfusion of viruses†		
Hepatitis B virus		
Non-A, non-B hepatitis (including hepatitis C virus)		
Cytomegalovirus		
Epstein–Barr virus		
HIV 1 and 2		
HTLV I and II		

*Only seen in some individuals with IgA deficiency.
†Transfusion of *Treponema pallidum* (syphilis) is exceedingly rare in the UK. In tropical areas the transmission of *Plasmodium* species (malaria) and in South America transmission of *Trypanosoma cruzi* (Chagas' disease) presents a serious problem.

sponse, most often against antigens in the Rh system. Jaundice, progressive anaemia, fever, arthralgia and myalgia are commonly encountered. Diagnosis is easily established by a positive direct antiglobulin test (DAT) and a positive antibody screen.

Usually no treatment is required, but when hypotension and renal failure are present the patient should be treated symptomatically. Blood transfusions should be avoided but when necessary compatible red cells should be administered. Patients with delayed haemolytic transfusion reaction have an increased risk of thrombosis and should be considered for administration of prophylactic subcutaneous heparin.

Non-haemolytic febrile transfusion reaction (NHFTR) usually occurs within hours after the onset of transfusion. NHFTR occurs in multi-transfused patients with antibodies against HLA antigens or granulocyte-specific antibodies. The reaction is due to pyrogens, released from granulocytes damaged by complement in an antigen/antibody reaction. It presents with a rise of temperature with flushing palpitations and tachycardia, followed by headache and rigors. In severe forms of NHFTR, cough, breathlessness and respiratory distress may ensue. Diagnosis is made clinically and confirmed by laboratory tests showing absence of haemolysis. Management of NHFTR consists of administration of antipyretics (aspirin or paracetamol) and in patients with severe symptoms 100 mg of hydrocortisone i.v. can also be given. Prevention in patients who repeatedly suffer from NHFTR is achieved by administration of blood filtered using one of the specific leucocyte depletion filters (Sepacell R-500, Pall RC-100).

Platelet refractoriness is the term used to describe the failure of platelet transfusion to raise the platelet count in the recipient. It represents one of the serious manifestations of alloimmunization to HLA and platelet-specific antigens. Diagnosis of platelet refractoriness and management of the patient are usually in the province of the haematologist.

Transfusion reactions associated with plasma proteins are urticaria and anaphylactoid reactions. Urticaria is one of the most common transfusion reactions and consists of circumscribed areas of cutaneous oedema. It is caused by the degranula-

tion of mast cells in the skin and subsequent release of histamine. Urticaria is easily recognizable clinically and it is treated by administration of an antihistamine drug. Severe urticaria recurring with each transfusion can be prevented by administration of chlorpheniramine or transfusion of washed red cells or frozen and thawed red cells, free of plasma proteins.

Anaphylactoid reaction is a term used to describe an immediate hypersensitivity reaction. It is a rare reaction which occurs in individuals with IgA deficiency who have anti-IgA due to previous immunization. The clinical manifestations vary from mild erythema, pruritus, urticaria and angio-oedema of lips to severe oedema of the larynx or epiglottis, and bronchospasm, hypotension and shock. The mainstay of treatment is administration of adrenaline, as well as maintenance of unimpeded breathing and treatment of hypotension.

Immunomodulation. There is now little doubt that transfusions of blood can cause immunosuppression in the recipient. This effect of transfusion was used for the benefit of recipients of kidney transplants before the introduction of cyclosporin into the treatment schedules. However, adverse effects of blood transfusion have been reported in patients after surgical removal of malignant tumours (shortened disease-free interval). Furthermore, several reports have highlighted increased incidence of postoperative infections in patients transfused before or during operation. Detailed discussion on immunomodulation is beyond the scope of this chapter.

Graft-versus-host disease (GVHD) is caused by engraftment of donor lymphocytes in severely immunosuppressed or immunodeficient recipients as well as in premature babies. It can also occur in immunocompetent recipients who are transfused with blood donated by first-degree relatives (directed donations). In most instances manifestations of GVHD are mild but in immunocompetent patients the disease is often fatal. To abolish the capacity for engraftment of donor lymphocytes it is recommended that blood, platelet and granulocyte concentrates are irradiated with 15–30 Gy before administration to patients likely to develop GVHD.

Transmission of infectious diseases. While the transmission of bacterial and parasitic infections by transfusion is exceptionally rare in the UK, the transmission of viruses is the focus of interest of the public and medical profession alike. Transfusion services maintain a safe blood supply by a rigorous process of selection of prospective blood donors and by the use of specific microbiological screening tests for markers of the disease. In addition, safety of the fractionated plasma products is enhanced by the use of viral inactivation procedures. A description of the manifestation

Table 17.10 Estimates of virus transmission rates by transfusion of blood and blood components*

Virus	Incidence of carriers†	Tests Available	Tests Used	Estimate of units required for transfusion
Hepatitis B virus	1 : 1000	Yes‡	Yes	20 000
Non-A, non-B viruses§	1 : 1700	Yes	Yes	20 000
Cytomegalovirus	1 : 2	Yes	No¶	10(**)
Epstein-Barr virus	9 : 10	Yes	No	Most recipients are immune
HIV 1 and 2	1 : 25 000	Yes	Yes	1 000 000
HTLV I and II	1 : 20 000	Yes	No	1 000 000(**)

*Transmission of viruses by plasma products is excluded; all plasma products undergo viral inactivation in production.
†Seen in first-time blood donors following self-exclusion of those in risk categories, donating blood in London, February 1992.
‡Test for HB_s antigen.
§Includes hepatitis C virus; test for anti-HCV is reactive in about 80% of carriers capable of trasmitting non-A, non-B hepatitis.
¶Test is used to provide anti-CMV negative blood for patients in 'at risk' groups: recipients of kidney transplants, recipients of bone marrow transplants, preterm babies of less than 1500 g weight and pregnant women. Patients with AIDS who are anti-CMV negative can be also considered as at increased risk from acquiring CMV infection.
**Only about 1 in 5 recipients negative on testing will seroconvert following transfusion of a unit of blood found positive on testing.

and management of the viral diseases which can be transmitted by transfusion can be found elsewhere and only the estimates of risk of transmission are discussed below.

The risk of transmission of a viral disease depends, in addition to a vigorous selection procedure, on the incidence of carriers (individuals who are healthy but harbour the virus), availability of a screening test and its sensitivity and specificity, the use of the test for screening purposes, and the susceptibility to infection of the recipient (Table 17.10). It is mandatory in the UK to test for markers of hepatitis B virus (HBV), hepatitic C virus (HCV), human immunodeficiency virus types 1 and 2 (HIV 1 and 2) and for *Treponema pallidum*.

It can be seen from Table 17.10 that the incidence of most of the viral infections in the general population is low; donor selection procedures are effective and the screening for disease markers is highly successful. The absolute number of infections transmitted by blood transfusion is exceedingly small. However, the risk of transmitting a disease still remains and has to be taken into account when the decision to transfuse the patient is made.

FURTHER READING

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