JPAC Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee

PDF Generated 03/10/2022 08:16

**Transfusion Handbook**

**3.3: Blood products**

http://www.transfusionguidelines.org/transfusion-handbook/3-providing-safe-blood/3-3-blood-products

# 3.3: Blood products

These are classified as blood components prepared in the blood transfusion centre (red cells, platelets, fresh frozen plasma and cryoprecipitate) or plasma derivatives manufactured from pooled plasma donations in plasma fractionation centres (such as albumin, coagulation factors and immunoglobulins). Plasma derivatives are covered by the Medicines Act and, like any other drug, must be prescribed by a licensed practitioner. Since 1999, as a vCJD risk-reduction measure, all plasma derivatives used in the UK are manufactured using donations from countries with a low risk of vCJD.

## 3.3.1: Blood components

Whole blood is now rarely used for transfusion. Blood component therapy makes clinical sense as most patients require a specific element of blood, such as red cells or platelets, and the dose can then be optimised. Each component is stored under ideal conditions (e.g. red cells must be refrigerated, platelets must not) and the use of precious blood donations becomes more efficient. The use of blood components in clinical practice is covered in Chapters 7 to 10.

The process of producing blood components and plasma derivatives is summarised in Figure 3.1.

## 3.3.2: Labelling of blood components

### 3.3.2.1: Blood component labels

The content of blood pack labels attached at the transfusion centre is prescribed by the Blood Safety and Quality Regulations 2005 (BSQR). Key information is present in both eye-readable and barcoded form and allows the donor origin (via a unique donation number) and processing steps of the product to be traced as well as indicating the blood group, any special requirements (such as CMV negative or irradiated), expiry date and storage conditions. Work is in progress to review the content of blood component labels and improve their clarity. Up-to-date information is available in the Guidelines for the Blood Transfusion Services in the UK (http://www.transfusionguidelines.org.uk).

### 3.3.2.2: Blood compatibility labels

These are attached to the pack in the hospital transfusion laboratory and uniquely identify the patient for whom the component has been selected. At the final bedside check, the donation number and other details on the compatibility label must match those on the blood pack label and the patient details must exactly match those on the recipient's ID band (see Chapter 4 for detailed discussion of safe blood administration).

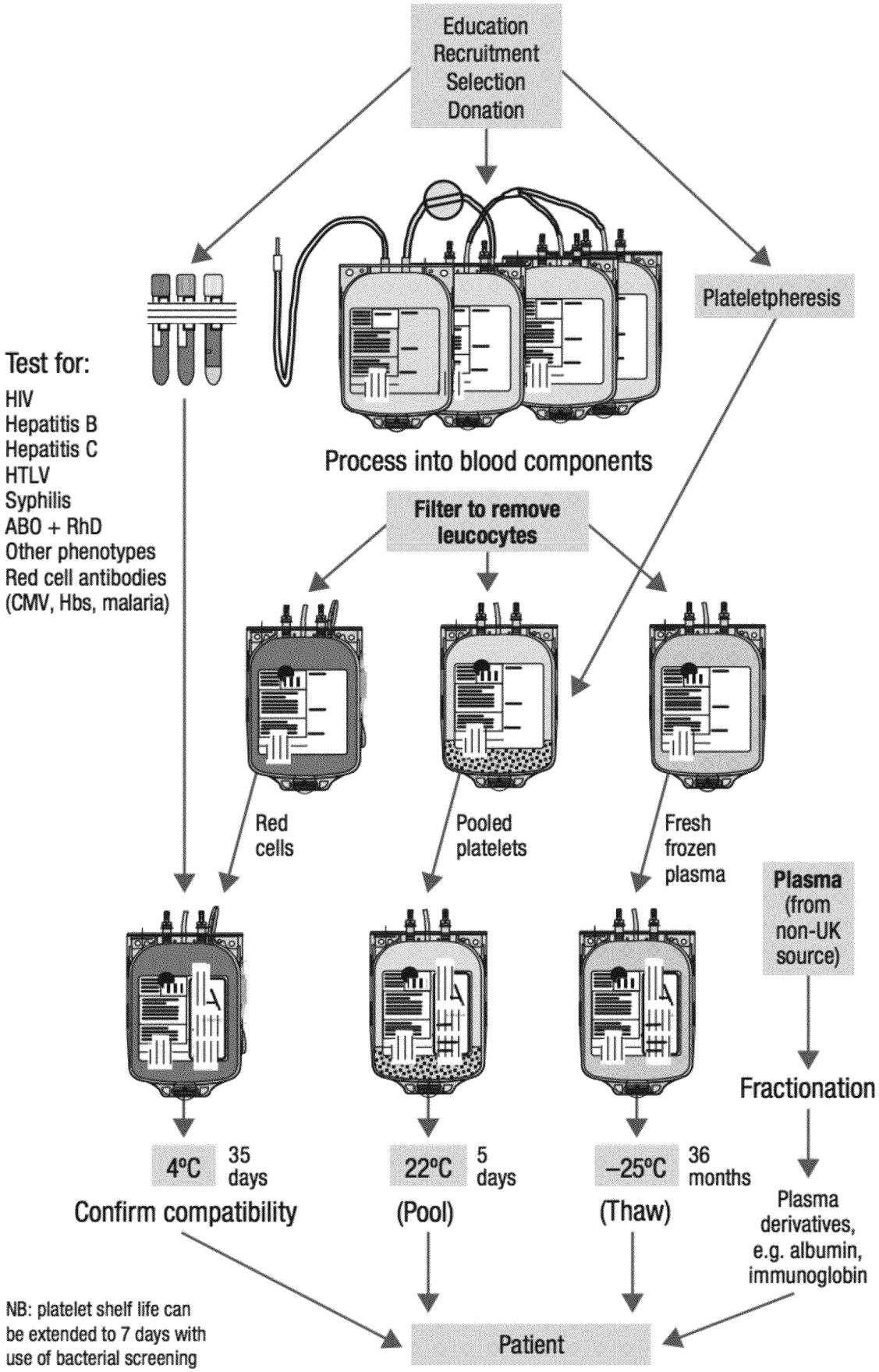
### 3.3.2.3: Specifications of blood components

Whole blood donations of 405–495 mL (mean 470 mL) are collected into 63 mL of citrate phosphate dextrose (CPD) anticoagulant.

All blood donations are filtered to remove white blood cells (pre-storage leucodepletion) to leave $<1\times10^{6}$ leucocytes in the pack. This was introduced in 1998 as a vCJD risk-reduction measure but also reduces the incidence of febrile transfusion reactions and alloimmunisation to white cell (including HLA) antigens.

Indicative contents of commonly available components are noted below, based on quality assurance data from NHS Blood and Transplant (see http://www.blood.co.uk/hospitals/products for more detail and an up-to-date compendium). Blood components for neonates and intrauterine transfusion are discussed in Chapter 10.

**Figure 3.1 Production of blood components and blood derivatives**


Education
Recruitment
Selection
Donation
Plateletpheresis
Test for:
HIV
Hepatitis B
Hepatitis C
HTLV
Syphilis
ABO + RhD
Other phenotypes
Red cell antibodies
(CMV, Hbs, malaria)
Process into blood components
Filter to remove leucocytes
Red cells
Pooled platelets
Fresh frozen plasma
Plasma (from non-UK source)
4ºC 35 days
Confirm compatibility
22ºC 5 days
(Pool)
–25ºC 36 months
(Thaw)
Fractionation
Plasma derivatives, e.g. albumin, immunoglobin
NB: platelet shelf life can be extended to 7 days with use of bacterial screening
Patient

Red cells

These are used to restore oxygen carrying capacity in patients with anaemia or blood loss where alternative treatments are ineffective or inappropriate. They must be ABO compatible with the recipient (see Table 2.2). Clinical indications for red cell transfusion are discussed in Chapters 7 to 10.

Red cells in additive solution

In red cells in additive solution (Table 3.1) the majority of plasma is removed and replaced by 100 mL saline, adenine, glucose and mannitol additive solution (SAG-M).

**Table 3.1 Red cells in additive solution**

| | |
|---|---|
| Volume (mL) | 220–340 |
| Haematocrit (L/L) | 0.5–0.7 |
| Haemoglobin content (g) | >40 (in more than 75% of units tested) |
| Residual plasma (mL) | 5–30 |
| Storage temperature | 2–6°C |
| Shelf life | Up to 35 days from donation |

Irradiated red cells

Irradiated red cells are indicated for patients at risk of transfusion-associated graft-versus-host disease (TA-GvHD – see Chapter 8). The component must be irradiated by gamma or X-rays within 14 days of donation and it then has a shelf life of 14 days from irradiation.

Washed red cells

Indicated for patients with recurrent or severe allergic or febrile reactions to red cells, and severely IgA-deficient patients with anti-IgA antibodies for whom red cells from an IgA-deficient donor are not available ( see Chapter 5). They are produced either manually (24-hour shelf life) or by a closed, automated system in which the red cells are sequentially washed to remove most of the plasma (<0.5 g residual plasma per unit) and then resuspended in 100 mL SAG-M (shelf life 14 days from washing).

Platelets

Platelet transfusion is indicated for the treatment or prevention of bleeding in patients with a low platelet count (thrombocytopenia) or platelet dysfunction. An adult therapeutic dose (ATD) of platelets is $>240\times10^{9}$ per transfusion.

Platelets have ABO antigens on their surface and may have reduced survival if transfused to an ABO-incompatible recipient, although this is not usually clinically significant. They are usually only available in groups O, A or B, with only a small number of group AB platelets produced.

Anti-A or anti-B antibodies in the plasma of platelet components may rarely cause haemolysis of the recipient's red cells, especially in babies and small children. Group O platelets should ideally only be given to group O recipients. Selection of platelets for patients of other ABO groups is summarised in Table 3.2. RhD negative platelet concentrates should be given to RhD negative patients where possible, especially to RhD negative women of child-bearing potential. When RhD-incompatible platelets have to be given, administration of anti-D immunoglobulin may prevent immunisation.

Platelets are produced in two ways (see Tables 3.2 and 3.3):

- Whole blood donations are centrifuged and the buffy coats (between the red cell and plasma layers) from four donations are pooled in the plasma of one of the donors (male, to reduce the risk of transfusion-related acute lung injury (TRALI) – see Chapter 5).
- An ATD of platelets is obtained from a single donor by apheresis (donors may give two or three ATDs at a single session).

The UK Blood Services aim to provide more than 80% of platelet doses by apheresis to reduce the exposure of patients to multiple donors (a vCJD risk-reduction measure).

Platelets are stored in temperature-controlled incubators (20–24°C) with constant agitation (refrigerated platelets are rapidly removed from the circulation). The recent introduction of automated bacterial screening has allowed some Blood Services to extend the shelf life from 5 to 7 days after donation.

**Table 3.2 Platelets from pooled buffy coats**

| | |
|---|---|
| Number of donors per pack | 4 |
| Mean volume (mL) | 300 |
| Mean platelets (×109 per unit) | 308 (range 165–500) |
| Anticoagulant | CPD |
| Storage | 20–24°C with agitation |
| Shelf life | 5 days (7 days if bacterial screening) |

**Table 3.3 Platelets from apheresis donation**

| | |
|---|---|
| Number of donors per pack | 1 |
| | |

| | |
|---|---|
| Mean volume (mL) | 199 |
| Mean platelets ($\times 10^9$ per unit) | 280 (range 165–510) |
| Anticoagulant | Acid citrate dextrose |
| Storage | 20–24°C with agitation |
| Shelf life | 5 days (7 days if bacterial screening) |

Irradiated platelets

Platelets may be irradiated to prevent TA-GvHD in susceptible patients. They retain their normal shelf life.

Platelets in additive solution

After 'washing' to remove most of the plasma the platelets are resuspended in 200 mL of platelet additive solution (PAS). This component is indicated for patients with recurrent severe allergic or febrile reactions to standard platelet transfusions. The shelf life is reduced to 24 hours after preparation and they must be ordered specially from the Blood Service. Some platelets are lost in the washing process and the component still contains around 10 mL residual plasma.

Human leucocyte antigen (HLA)-selected platelets

Indicated for patients refractory to random platelet components because of the development of HLA antibodies after previous transfusions (see Chapter 9). The Blood Services maintain a panel of HLA-typed platelet donors who donate by apheresis. The platelets are irradiated before issue to prevent TA-GvHD.

Human platelet antigen (HPA)-selected platelets

HPA-1a/5b negative platelets are kept in limited numbers at strategically placed stock-holding units in the UK and are used for babies with neonatal alloimmune thrombocytopenia (NAIT) (see Chapter 10).

Plasma

Plasma is obtained from whole blood donations or component donation by apheresis. Only male donors are used to reduce the risk of TRALI. The UK Departments of Health recommend that patients born on or after 1 January 1996 should only receive plasma sourced from countries with a low risk of vCJD. Imported plasma is treated with a pathogen reduction process, such as methylene blue or solvent detergent treatment, to reduce the risk of viral transmission.

Plasma components of the same ABO group should be transfused to patients wherever possible. If ABO-identical plasma is not available, the selection criteria given in Table 2.2 are recommended. Plasma components do not need to be matched for RhD group as they contain no red cells or red cell stroma. They do not cause TA-GvHD and irradiation is not required.

Fresh frozen plasma (FFP)

Plasma is frozen soon after collection to maintain the activity of blood-clotting factors. It can be stored for up to 36 months at –25°C or below. Standard UK FFP is issued as single-donor packs which must be thawed before use, usually in a purpose-designed waterbath. Thawed units of FFP can be stored for up to 24 hours at 4°C before transfusion. Clotting factor levels vary widely between normal healthy donors and this variability is reflected in the concentrations found in individual packs of FFP.

FFP (see Table 3.4) is indicated for the treatment of patients with bleeding due to multiple clotting factor deficiencies such as disseminated intravascular coagulation (DIC). It may also be used in patients with inherited clotting factor deficiencies (e.g. Factor V deficiency) where a clotting factor concentrate is not yet available. The recommended dose is 12–15 mL/kg (minimum of four units in a 70 kg adult). However, much larger doses may be needed to produce 'therapeutic' levels of coagulation factors and volume overload is a significant clinical problem. FFP is no longer indicated for the reversal of warfarin, as a specific and effective antidote is available (prothrombin complex). FFP carries a significant risk of severe allergic reactions (see Chapter 5) and should not be used as a plasma volume expander.

**Table 3.4 Fresh frozen plasma**

| | |
|---|---|
| Number of donor exposures per pack | 1 |
| Mean volume (mL) | 274 |
| Mean Factor VIIIc (IU/mL) | 0.83 (specification >0.7) |
| Anticoagulant | CPD |
| Storage | <–25°C |
| Shelf life | 36 months (24 hours at 4°C after thawing) |

Pathogen-inactivated fresh frozen plasma

Solvent detergent treated FFP (SD-FFP) is available as a licensed medicinal product (Octaplas®, Table 3.5). It is prepared from pools with a maximum of 1520 donations and the SD process inactivates bacteria and most encapsulated viruses, including hepatitis B and C and HIV. Donations are sourced from countries with a low risk of vCJD and a prion-reduced version, Octaplas LG®, is now licensed in the UK. The pooling process leads to more standardised concentrations of clotting factors in each pack and probably explains the significantly reduced incidence of severe allergic reactions and TRALI in haemovigilance reports. SD treatment reduces the concentration of fibrinogen and Factor VIIIc by 15–20%, but levels remain within the defined specification. Levels of Protein S, an anticoagulant factor, are around 30% lower and this may be important in patients with an increased risk of thromboembolism. UK guidelines recommend imported SD-FFP for plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP – see Chapter 11).

**Table 3.5 Solvent detergent plasma (Octaplas®)**

| | |
|---|---|

| | |
|---|---|
| Number of donor exposures per pack | Maximum 1520 donors per batch |
| Volume (mL) | 200 (standardised) |
| Mean Factor VIIIc (IU/mL) | 0.8 (specification >0.5) |
| Mean fibrinogen (mg/mL) | 2.6 (range 1.5–4.0) |
| Anticoagulant | Sodium citrate |
| Storage | <–18°C |
| Shelf life | 4 years (transfuse immediately after thawing) |
| Based on data from Octapharma AG (http://www.octapharma.co.uk) | |

Methylene blue treated FFP (MB-FFP) is a single-donor pathogen-reduced component available through the UK Blood Services. The process inactivates encapsulated viruses and bacteria. In the UK, the methylene blue process is used to treat packs of FFP imported from low vCJD risk countries, providing a single-donor component that is preferred by some neonatologists and paediatricians. MB-FFP has a reduced activity of fibrinogen and Factor VIII. The clinical significance of this is uncertain, although some studies in cardiac surgery have suggested the need for bigger transfusions to achieve the same therapeutic effect. Like all single-donor FFP components, the content of clotting factors varies between individual packs.

Cryoprecipitate

Cryoprecipitate (Table 3.6) is made by thawing UK donor FFP at 4°C, producing a cryoglobulin rich in fibrinogen, Factor VIII and von Willebrand factor. It was developed as a treatment for haemophilia but this use has now been replaced by Factor VIII concentrate. Cryoprecipitate is mainly used as a more concentrated, hence lower volume for infusion, source of fibrinogen than FFP. It is available from the Blood Services as single-donor packs or as pools of five donations. The recommended adult therapeutic dose is two pools of five units (or one unit per 5–10 kg body weight), which will typically raise the plasma fibrinogen by about 1 g/L. Cryoprecipitate produced from imported MB-FFP is now available. Because of a lower concentration of fibrinogen, pools of six donations are issued.

**Table 3.6 Cryoprecipitate**

| | Cryoprecipitate packs | Cryoprecipitate pools |
|---|---|---|
| Number of donors | 1 | 5 |
| | | |

| | | |
|---|---|---|
| Mean volume (mL) | 43 | 189 |
| Fibrinogen (mg /pack) | 396 (specification >140) | 1552 (specification >700) |
| Factor VIIIc (IU /pack) | 105 (specification >70) | 454 (specification >350) |
| Storage | <–25°C | <–25°C |
| Shelf life | 36 months (use within 4 hours of thawing, do not refrigerate) | 36 months (use within 4 hours of thawing, do not refrigerate) |

Granulocytes

Although their clinical effectiveness is controversial, transfusion of granulocytes (neutrophils – phagocytic white blood cells) may be indicated in patients with life-threatening soft tissue or organ infection with bacteria or fungi and low neutrophil counts, usually in the setting of severe, prolonged neutropenia after cytotoxic chemotherapy.

There are two main granulocyte-rich components available: buffy coats derived from whole blood donations and granulocytes collected by apheresis from individual donors. Because of contaminating red cells, granulocyte components must be ABO and RhD compatible and crossmatched with the recipient. They are irradiated before issue to prevent TA-GvHD. Daily transfusions are given, with monitoring of response, until recovery of bone marrow function.

Individual buffy coats

These buffy coats (Table 3.7) contain large numbers of red cells and the Hb/haematocrit of the recipient must be monitored. Usefully, the high platelet content may reduce the need for platelet transfusions. The recommended dose is ten buffy coats daily for adults
(10–20 mL/kg for smaller children and infants).

**Table 3.7 Buffy coat (granulocytes)**

| | |
|---|---|
| Mean volume per pack (mL) | 60 (10 packs = 600 mL) |
| Mean granulocytes ($\times 10^9$/pack) | 1.0 (10 packs = $1 \times 10^{10}$) |
| Haematocrit (L/L) | 0.45 |
| Platelets ($\times 10^9$/pack) | 70 |

| | |
|---|---|
| Storage | 20–24°C |
| Shelf life | To midnight on day of collection |

Pooled buffy coats (granulocytes pooled buffy coat derived in additive solution and plasma)

This component (see Table 3.8) was introduced in the UK in 2012. Although the manufacturing process is more complicated, it has the advantages of lower volume, less red cell and plasma contamination and resuspension in male donor plasma and additive solution to reduce the risk of TRALI. The dose is two packs (20 donations) for an adult and 10–20 mL/kg for children.

**Table 3.8 Granulocytes pooled buffy coat derived in additive solution and plasma**

| | |
|---|---|
| Mean volume per pack (mL) | 207 (175–250) mL |
| Mean granulocytes ($\times 10^{10}$/pack) | 1.0 ($1 \times 10^{10}$) |
| Haematocrit (L/L) | 0.15 |
| Platelets ($\times 10^{9}$/pack) | 499 (equivalent to 2.5 adult transfusion doses) |
| Storage | 20–24°C (not agitated) |
| Shelf life | To midnight on day following collection |

Apheresis granulocytes

The collection of a therapeutic dose of apheresis granulocytes (Table 3.9) requires the donor to be pre-treated with steroids and/or injections of granulocyte colony stimulating factor (G-CSF). Hence, their collection is restricted to directed donors (usually a relative) for an individual patient, rather than UK Blood Service volunteer donors, and the component is only available in certain clinical centres.

**Table 3.9 Apheresis granulocytes**

| | |
|---|---|
| Mean volume per unit (mL) | 312 |
| Granulocytes per unit | $>1 \times 10^{10}$ |
| Haematocrit (L/L) | 0.23 |

| | |
|---|---|
| Platelets ($\times 10^9$ per unit) | 111 |
| Storage | 20–24°C |
| Shelf life | 24 hours from collection |

Plasma derivatives

These are licensed medicinal products manufactured from human plasma donations. Some of the main products used in hospital practice are listed below but the reader is referred to the British National Formulary (BNF – http://bnf.org/bnf) and the individual Summary of Product Characteristics for more detailed information about formulation and clinical indications. Although these products are manufactured from large donor pools, sometimes thousands of donations, all now undergo multiple pathogen inactivation steps to eradicate transfusion-transmitted viruses. Since 1999, all plasma derivatives used in the UK are derived from imported plasma (a vCJD risk-reduction measure).

Human albumin solution

Human albumin solution (HAS) contains no clotting factors or blood group antibodies and crossmatching is not required. The clinical indications for HAS are controversial. Crystalloid solutions or synthetic colloidal plasma substitutes are alternatives for use as plasma expanders in acute blood or plasma loss. HAS should not be used to 'correct' the low serum albumin level often associated with acute or chronic illness. Side effects include occasional severe hypersensitivity reactions. HAS is available in two forms:

- Isotonic solutions (4.5 and 5.0% in volumes of 50 to 500 mL): Often used to replace subacute plasma volume loss caused by burns, pancreatitis or trauma, and as a replacement fluid in plasma exchange.
- Concentrated solutions (20% in volumes of 50 and 100 mL): Indications may include initiating diuresis in hypoalbuminaemic patients with liver cirrhosis or nephrotic syndrome, removal of large volumes of ascites in patients with portal hypertension and to assist the reduction of high bilirubin levels by exchange transfusion in the newborn (unconjugated bilirubin binds to albumin).

Clotting factor concentrates

Single-factor concentrates are available for the treatment of most inherited coagulation deficiencies except Factor V and Factor II (prothrombin). Most patients in the UK with severe haemophilia A are now treated with recombinant Factor VIIIc, which carries no risk of viral or prion transmission.

Fibrinogen concentrate (Factor I) is, at present, only licensed in the UK for the treatment of congenital hypofibrinogenaemia but there is encouraging international experience of its effectiveness in the much more common setting of acquired hypofibrinogenaemia (e.g. DIC, traumatic haemorrhage, massive transfusion). Many coagulation experts believe that it will replace the use of cryoprecipitate for this purpose in view of its ease of administration, convenience of storage and standardised fibrinogen content.

Prothrombin complex concentrate (PCC) contains Factors II, VII, IX and X. It has replaced FFP as the recommended treatment for rapid reversal of warfarin overdose, with elevated international normalised ratio (INR) and severe bleeding, in view of its superior efficacy, ease of administration and lower risk of severe allergic reactions or fluid overload. Modern formulations of PCC do not contain activated clotting factors and have a low risk of causing thrombotic complications. PCC may also be used to treat bleeding due to the coagulopathy associated with liver disease. The dose for reversal of warfarin is 25–50 IU/kg.

Immunoglobulin solutions

These are manufactured from large pools of donor plasma:

- Normal immunoglobulin: contains antibodies to viruses that are common in the population. Intramuscular normal immunoglobulin may be used to protect susceptible contacts against hepatitis A, measles or rubella. High-dose intravenous immunoglobulin is used as replacement therapy in patients with severe immunoglobulin deficiency and in the treatment of autoimmune diseases such as idiopathic thrombocytopenic purpura (ITP).
- Specific immunoglobulins: made from selected donors with high antibody levels to the target of treatment. Examples include tetanus, hepatitis B and rabies immunoglobulins as well as anti-D immunoglobulin for the prevention of maternal sensitisation to RhD in pregnancy (see Chapter 9).