HANDBOOK OF TRANSFUSION MEDICINE

BLOOD TRANSFUSION SERVICES OF THE UNITED KINGDOM

SECOND EDITION 1995

Editor: Brian McClelland

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CHAPTER I - ABOUT THE HANDBOOK

ABOUT THIS BOOK

Audience.

This book is for staff who are responsible for prescribing, supplying and administering blood products. Many people have an essential part in making sure that the right blood product is given to the right patient at the right time. They include:

- Medical staff who assess the patient and prescribe and order the product.
- Laboratory or pharmacy staff who receive the order and prepare the product, matching it to the patient's blood group where necessary.
- Transport and delivery personnel who deliver the product to the patient.
- Nurses, who have a critically important responsibility in carrying out the checks before the product is administered and observing the patient during and after the transfusion.

Evidence.

The effectiveness of much of today's blood transfusion practice has not been rigorously proved by clinical trials. It is therefore not possible to give a complete, evidence based guideline for practice. We have tried to use existing evidence about effective treatment. Where good evidence is not available, the contents reflect our best effort to give a balanced view of current opinion about good clinical practice in transfusion for patients in the United Kingdom.

It is important to emphasise that in other parts of the world, decisions about safe and effective practice have to take account of different local situations, for example epidemiology of infectious diseases, availability of intravenous fluids, and access to supplies of good quality blood products.

Key topics.

Most of the problems with transfusion that cause delays and may put the patient at risk are caused by poor communication or failure to follow procedures that should be well documented and in which staff should be well trained. Common problems include:

- Prescribing blood products that are not required by the patient or are not the most suitable for the patient's needs.
- Incomplete or inaccurate completion of request forms or sample tube labels.
- Delays caused by a failure to communicate accurately about when and where the blood is needed.
- Transfusion of blood products that were intended to be given to someone else (this *does* happen!)
- Failure to recognise and react effectively to evidence of adverse reactions that occur during transfusion.

Some rare complications of transfusion, such as the transmission of viral infections may only be recognisable many days or weeks after the blood product has been given. Clinical staff have the responsibility of recognising and reporting problems of this type to the supplier (usually the hospital transfusion department [HTD]). It is the task of the producer (the Blood Transfusion Service or other manufacturer of the blood product) to ensure that the products supplied are as safe and as effective as possible, and that reported adverse events are effectively followed up.

Feedback.

This second edition of the handbook has been improved by many comments and criticisms received from users of the first edition. The production team depend on readers of this edition to help improve the next revision.

Please use the enclosed card to send your comments, ideas and criticisms.

AUTHORSHIP

The people who prepared and evaluated this handbook are listed below, with their contact details. If you need specialist advice, you may find it useful to contact one of them. We will do our best to give an answer to your questions - and to include the important points in the next edition of the handbook.

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We thank many other colleagues who have commented on the text and assisted with references.

Local systems and procedures.

If you are not familiar with the local system for obtaining blood products, visit the blood bank. The clinical and the technical staff there will be able to explain the system. There is no substitute for talking with the people who are working to help you care for your patients.

Terminology.

Clinicians and laboratory people need to use the same language! Here is a simple glossary for ordering blood products that should help to avoid dangerous confusion. There is a full glossary on page .

Ordering blood products.

- **Emergency.** The patient needs blood now! Provided the hospital transfusion department staff understand this, they can usually respond very quickly by using a rapid compatibility procedure and organising quick delivery, (or you can arrange for someone to collect the blood).

- **As soon as possible (ASAP).** Don't use this phrase. Everyone can interpret it in a different way!

- **Unmatched or O neg (red cells).** Usually mean the same: find out and use the local language. The use of "Group O" red cells is covered on page .

- **Group-specific, homologous, ABO compatible (red cells).** All mean approximately the same: find out and use the local language. Red cell products described in this way are selected to be *compatible with but not necessarily the*

same as the patient's ABO blood type. They are not supplied as safe for any other patient.

Unmatched Group O blood should only be requested and used when the patient's life is thought to be at risk if there is *any* avoidable delay in giving blood. Group O negative blood is almost always in short supply. If it is used when it is not absolutely necessary, the supply for other real emergencies will be depleted.

Names of blood products.

In this book we have used the following convention.

- ***Blood products.*** Any therapeutic substances prepared from human blood.

- ***Blood components.*** Red cells
  Fresh frozen plasma
  Platelets
  Cryoprecipitate
  White cells
  Progenitor cells collected from peripheral blood ('stem cells').

- ***Plasma fractions.*** These are partially purified human plasma proteins made under pharmaceutical manufacturing conditions, including coagulation factors, immunoglobulins and albumin.

Names of other fluids.

The following short terms are used in the text.

- ***Crystalloid.*** Saline, Dextrose, Ringer's solution, etc.

- ***Saline.*** Sodium chloride injection 0.9% BP.

- ***Colloids.*** Dextran, modified fluid gelatin, hydroxyethyl starch. *(see BNF for details)*

The concept of blood component therapy.

It is useful for the prescriber to understand a few basic facts about how blood is collected and processed because this affects the safety and availability of the products. *Figure 1* illustrates the processing of blood from donor to patient. Blood is a raw material from which a range of therapeutic products including platelet concentrate, red cell concentrate and fresh plasma are made. Large amounts of plasma are also needed for the production of plasma fractions such as albumin, coagulation factors and immunoglobulins. In the United Kingdom most of the plasma is obtained from whole blood donations as shown in the figure. Some is obtained by plasmapheresis.

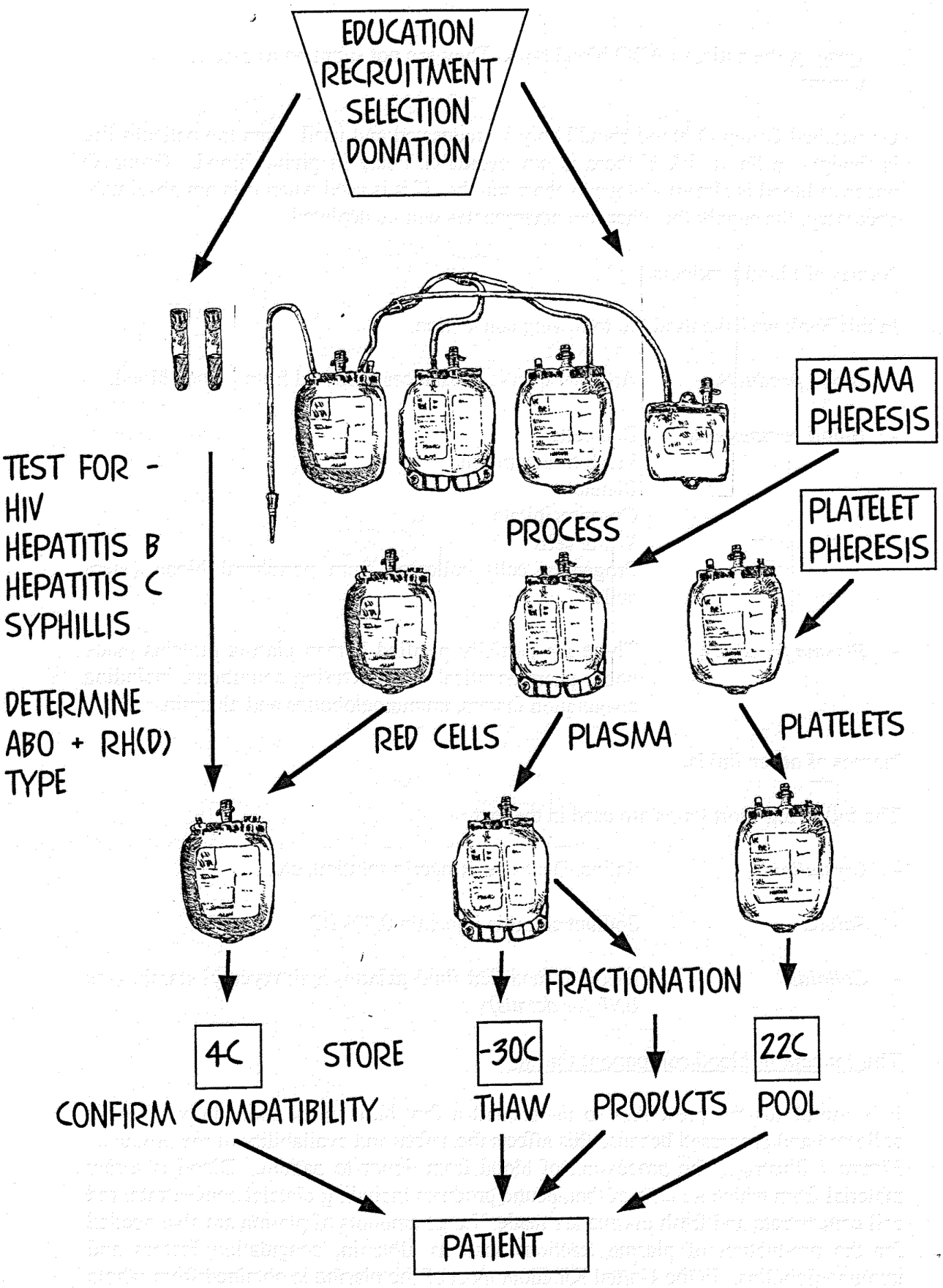


Figure 1. **FROM BLOOD DONORS TO BLOOD PRODUCTS**

Blood donors and blood donation testing.

Donors can give 450 ml whole blood, generally up to 3 times per year. Donors up to 60 yrs may alternatively give up to 15 litres of plasma per year by plasmapheresis: each donation provides 500-600 ml of plasma. Platelets and leucocytes can also be collected by cytapheresis.

The medical selection of donors is intended to exclude anyone whose blood might harm the recipient, for example by transmitting infection. In the UK every blood donation is tested for evidence of Hepatitis B, Hepatitis C, HIV-1, HIV-2 and Syphilis. In other countries, different tests for infection may also be needed, depending on the frequency of infection in the community. Each donation is tested to determine the blood group (ABO and Rh (D).

Table 1. BLOOD DONORS AND DONATION

- **Healthy persons aged 17-70 can volunteer.**

At each attendance donors complete a questionnaire or are interviewed to identify those

- who could be harmed by donating, or
- whose blood could harm a patient.

- **Donation may be**

- Whole blood: 2-3 times per year
- Plasma: up to 15 l/yr or
- Platelets: These donations are by apheresis. Transfusion of apheresis donations can offer safety benefits because fewer donations can provide an effective dose of blood component.

BLOOD DONATIONS FROM RELATIVES OR FRIENDS ("DIRECTED" DONATION)

Blood provided by a patient's relatives or friends specifically for that patient is called "directed" donation. This does not reduce the risk of virus transmission. Directed donations may on occasion be less safe since the donors may not be true volunteers and may have reasons for being reluctant to disclose information that should exclude them from donation.

There are occasional circumstances, such as neonatal alloimmune thrombocytopenia in which it may be safer to transfuse a mother's platelets to her baby. Other types of directed donation should be discouraged.

Irradiation.

Donations from blood relatives have caused fatal graft versus host disease. Therefore if a patient has to receive blood from a relative, any cellular blood component *must* be irradiated.

Preparation of blood components.

Blood is collected into sterile plastic packs which are centrifuged to separate red cells, platelets and plasma. (Figure 1) Plasma prepared in this way or obtained by plasmapheresis may be further processed into plasma fractions.

Manufacture of plasma fractions.

Plasma fractions are partially purified therapeutic preparations of plasma proteins. They are manufactured, in a large scale pharmaceutical process, from large volumes of plasma. Typically the plasma from up to 20,000 individual donations, about 5,000 kg of plasma, is processed by the addition of ethanol and exposure to varying temperature, pH and ionic strength conditions to precipitate different groups of proteins. Further purification and virus inactivation steps are carried out. The final products are freeze dried powders or solutions.

Since plasma from any one of the individual donors who contribute to each batch of products could potentially introduce infectious organisms, careful screening of every donation is vital. Even with screening, some viruses could find their way into the pooled plasma, so includes steps to inactivate any infectious agents which might escape detection.

Labels.

All blood products carry labels applied by the manufacturers. They give information that is important for staff who administer products and also allow the origins of the product to be traced. In addition, blood components usually have an additional label applied by the hospital blood bank. This should contain information that uniquely identifies the patient for whom the component has been selected. *An essential step before administering any blood component is to make sure that the details on this label (usually called the "compatibility label") match exactly with the identity of the patient (page). Figure 2 shows the main features of blood component labels.*

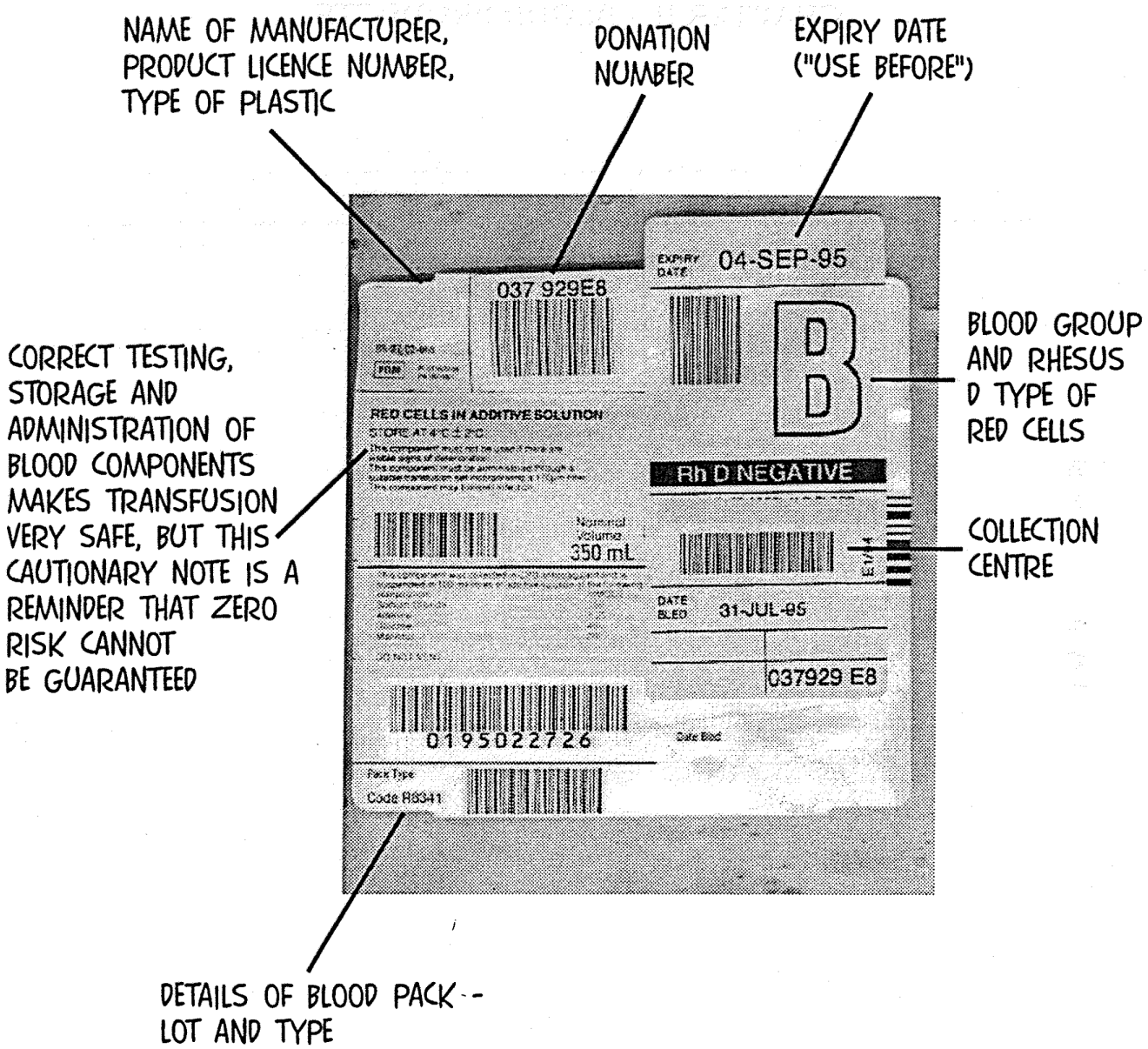


Figure 2. BLOOD COMPONENT LABEL: THE EXAMPLE SHOWN IS FOR RED CELLS IN ADDITIVE SOLUTION. IMPORTANT INFORMATION IS SHOWN IN BARCODE AS WELL AS CONVENTIONAL CHARACTERS TO HELP COMPUTERISED DATA ENTRY.

CHAPTER II - BLOOD PRODUCTS

BLOOD PRODUCTS

Essential Information.

The tables that follow summarise important information about the use, storage and content of blood products. More information is available in the 'further reading' section, or from your supplier of blood products.

Table 2. BLOOD PRODUCTS - VIROLOGICAL SAFETY

- **All donations of whole blood, plasma and platelets are tested to exclude the following viruses transmissible by blood: Hepatitis B, Hepatitis C, HIV1,2.**
- **Blood components are not routinely subjected to further manufacturing procedures to reduce risk of virus transmission.**
- **The exceptions are:**

  Virus inactivated plasma.
  Leucocyte filtered components (effective leucocyte filtration removes the risk of transmitting cytomegalovirus B, CMV).
  CMV antibody negative components (exclusion of components containing antibody removes the risk of transmitting CMV).

- **Plasma Fractions are subjected to further manufacturing procedures to remove or reduce the risk of transmission of Hepatitis B, Hepatitis C, HIV and other viruses.**

Table 3. BLOOD COMPONENTS - STORAGE AND ADMINISTRATION					
	Red Cells Red cells (Additive) Whole Blood	**Platelet Concentrate Recovered ("Random Donor")**	**Platelet Concentrate Apheresis ("Single Donor")**	**Fresh Frozen Plasma**	**Cryoprecipitate**
Storage temperature	2 to 6C	At 20 - 24C on a special agitator rack		-30C	-30C
Shelf life	35 days	5 days	5 days	1 year (frozen)	1 year (frozen)
Longest time from leaving controlled storage to completing infusion	5 hours	Depends on preparation method: consult supplier		4 hours	4 hours
Compatibility testing requirement	Must be compatible with recipient ABO and Rh (D) type	Preferably ABO compatible. Rhesus negative females under the age of 45 years should be given RhD negative platelets	Should be ABO compatible to avoid risk of haemolysis caused by by donor Anti A or Anti B		
Points to Note: Administration	• **Infuse through a blood administration set.** • **Record details of each blood component infusion in the patient's case record.** • **Follow local procedures or protocols for ordering and administering blood components.**				

Table 4. RED CELL PRODUCTS

	Red Cells	Red Cells, Additive Solution**	Red Cells, Buffy Coat Removed	Red Cells, Leucocyte Depleted	Whole Blood
Unit	← 1 Donation →				
*Volume ml	280 ± 60 ml	550 ± 70	280 ± 60	280 ± 60 ml	450 ± 45 ml blood
Haematocrit %	0.55 - 0.75	0.50 - 0.70		As for starting component why may be red cells in additive solution	0.35 - 0.45
Packed Red Cells ml per unit	← 120 - 250 →				
White Cells per unit	Sufficient to cause graft vs host disease, allo-immunisation and transfusion reactions.		<1.2 x 10^9	<5 x 10^6	Sufficient to cause Graft v Host Disease, alloimmunisation, transfusion reactions.
Content per unit *Sodium mmol Fresh* Expiry	15 10	20 15		As for starting components (red cell or red cells with additive solution)	50 55
*Potassium mmol Fresh Expiry	0.3 6	0.5 5			1 9
*Lactate mmol Fresh Expiry	← 1 10 →				
*Hydroxyl Fresh Expiry	5 12				20 55
Added Chemicals**	**Citrate Phosphate Dextrose Adenine (CPDA)**	**Adenine Mannitol Glucose Sodium Chloride (SAGM)**	**CPDA or SAGM**	**CPDA or SAGM**	**Citrate Phosphate Dextrose Adenine (CPDA)**
Points to Note:	Dose of 4 ml/Kg raises venous [Hb] by about 1g/dl	Not recommended for exchange or large volume transfusion of neonates	May reduce the risk of non haemolytic febrile transfusion reactions in patients who have reacted to previous transfusion	Can help to reduce the development of allo-antibodies to leucocyte antigens. An alternative to CMV negative product. Not an alternative to irradiated product.	The large volume of plasma increases risk of hyper-volaemia and cardiac failure in susceptible patients

* Typical values are given. Full product specifications are in the "Red Guide" [REF] and SNBTS Compendium [REF]

** Additive solutions are used to resuspend packed red cells after plasma is removed. They are designed to maintain the red cells in good condition during storage. There are various formulas. A widely used additive solution contains saline, adenine, glucose and mannitol (SAGM).

Table 6. FRESH FROZEN PLASMA - AND CRYOPRECIPITATE				
	Recovered (Random Donor) FFP	**Apheresis (Single Donor) FFP**	**Cryo Supernatant Plasma**	**Cryoprecipitate**
Unit	← **1 Donation** →			
Volume ml	150-300 plasma containing CPDA	500-600 ml of plasma containing CPDA	150-250 ml	10-20 ml
	← **Check local product specification.** →			
*Electrolytes: Solution mmol Potassium mmol Citrate mmol Lactate mmol Hydroxyl mmol	Content Per Unit: 35 1 4 1 12	Content Per Unit: 35 1 4 1 12	Content Per Unit: 35 1 4 1 12	Content Per Pool of 10 Units: 20 1 2 1 12
Fibrinogen Plasma clotting factors	2-5 mg/ml 0.7 unit/ml	2-5 mg/ml 0.7 unit/ml	Low content of fibrinogen Factor VIII and vWF factor	Fibrinogen 150-300 mg/pack Factor VIII 80-120 u/pack von Willebrand Factor
Other plasma proteins	← **As in slightly diluted plasma.** →			
Added chemicals	← **Citrate Phosphate Dextrose Adenine** →			
Points to Note: Prescribing	• **Risk of volume overload due to protein content.** • **Occasional severe anaphylactic reactions, especially with rapid infusion rates.** • **Infection risks are similar to those of other blood components.** • **Contain normal levels of plasma immunoglobulins: including red cell antibodies that can damage recipient's red cells.**			Use virus inactivated products in preference whenever it is possible.

* Typical values are given.

Table 5. PLATELET PRODUCTS					
	Platelets Recovered ("Random Donor")	**Leucocyte Depleted Apheresis Platelets**	**Apheresis ("Single Donor") Platelets**	**HL-A Compatible Apheresis Platelets**	**Crossmatched Apheresis Platelets**
Unit	1 Donation: or a pool of 4-6 units.	← 1 Donation →			
*Volume	40-60 ml of plasma	← Check local product specification. →			
Content of platelets	At least 55 x 10^9 per donation	← >240 x 10^9 →			
Content of white cells	<0.2 x 10^9/donation <0.8 x 10^9/pool	<5 x 10^6	← <0,8 x 109 →		
Points to Note: Prescribing		Can help to reduce development of allo-antibodies to leucocyte antigens. An alternative to CMV-negative product.		Donors are selected to match recipient for some HL-A antigens. May be effective in patients who do not respond to platelets due to HLA antibodies.	Donors are selected by a test for reaction with recipient's plasma. May be effective in patients who do not respond to platelets due to HLA antibodies.
		Contain at least 40 ml of a single donor's plasma, so haemolysis is a risk if the donors has potent red cell antibodies. Donor should be ABO compatible.			
	Adult dose 4-6 donations	← Adult dose: 1 donation →			

* Typical volumes are given.

Table 7. HUMAN PLASMA FRACTIONS

	Human Albumin	Human Immunoglobulin		Clotting Factor Concentrates			
		For Intramuscular Use	For Intravenous Use	Factor VIII	Factor IX	Prothrombin Complex Concentrate	Others Include
Unit	Usually 20g as 500 ml of 5% solution or 100 ml of 20% solution	Varies with product and supplier.		Typically 250-500 iu in each vial			Factor VII Antithrombin III Fibrin Sealant [Recombinant Factor VIII] [Recombinant Factor VII] FEIBA (Factor VIII bypassing activity concentrate)
Active constituents include:	Human albumin	Human IgG - from a large pool of unselected donors - or from donors with high levels of anti RhD or anti-viral antibodies	Human IgG from a large pool of unselected donors	Factor VIII	Factor IX	Factors II IX, X. Factor VII contain some products.	
Other constituents include:	Sodium: 130-150 mmol/l Other plasma proteins. Stabilizer (sodium capryllate).	Other immuno-globulins and other plasma proteins	Other immuno-globulins and other plasma proteins. Sucrose, pepsin.	← Other human plasma proteins →			See supplier's information.
Main clinical uses	Hypoproteinaemic oedema with nephrotic syndrome. (20%) Ascites in chronic liver disease. (20%) Acute volume replacement (5%)	Prophylaxis of specific virus infections such as hepatitis A, B, Varicella Zoster. Prevention of Anti Rh (D) antibodies in at risk mothers.	Treatment of inherited and acquired deficiencies of antibody formation. Treatment of immunological disorders such as auto-immune thrombo-cytopenia purpura (AITP)	Treatment of haemophilia A.	Treatment of haemophilia B.	Replacement of multiple clotting factor deficiencies.	See supplier's information.
Points to Note: Prescribing	20% solution: hyperoncotic and expands plasma volume by more than the amount infused. 5% solution: use carefully - if patient is at risk of sodium retention.	← See Page →		← See Page → All these products should be used under the guidance of a specialist clinician.			
Storage	Store at room temperature.	Storage usually at 4°C but check manufacturers' information.					

CHAPTER III - PROCEDURES

PROCEDURES

Information for patients.

Explain the proposed transfusion treatment to the patient or relatives, and record in the case-notes that you have done so!

Patients or their relatives may be worried about the risks of transfusion. Some may wish to know more about the risks, about the need for transfusion and about alternatives such as autologous transfusion or drugs such as erythropoietin. Patients of the Jehovah Witness faith are strictly banned by their religious beliefs from receiving blood components, but may be prepared to accept plasma fractions or alternative treatments.

Research has shown that patients often have no recollection of being informed about treatment options, or feel that they have not had answers to questions that worry them. The balance of legal opinion is that a written record that the patient has been given information and that his or her questions have been answered is more valuable in a medicolegal case than the patient's signature on a consent form.

Answers to most patient's questions should be found in this book. We have also included an outline of an information sheet for patients on page . You should check if your hospital has a leaflet of this type and that your patients receive it.

Recording the reason for transfusion.

Before blood products are administered, the reason for transfusion (which should usually comply with local or national guidelines) should be written in the patient's case-notes. This is important. If the patient has a problem later on, that could be related to transfusion, the records should show *who* ordered the products, and *why*.

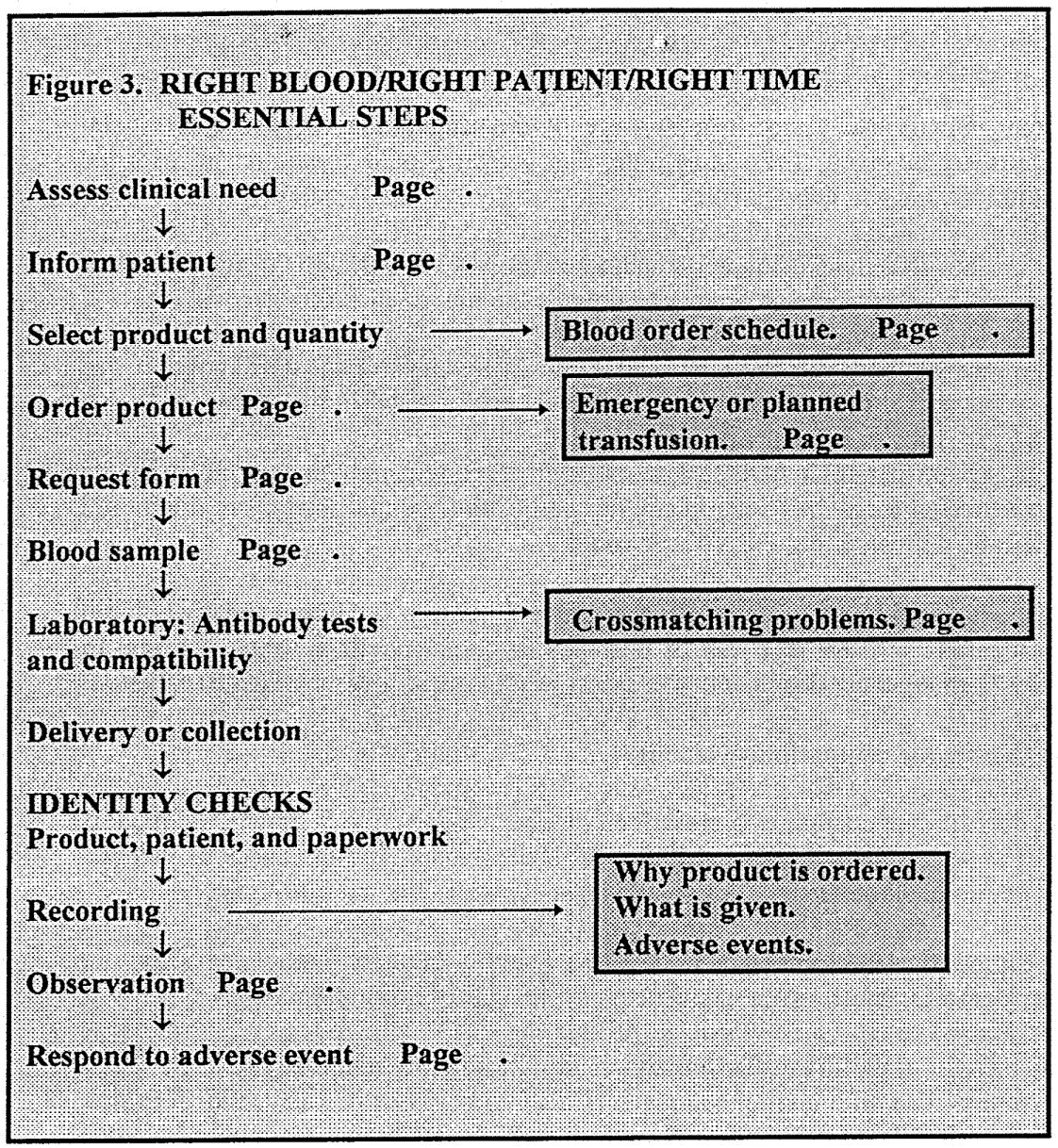
Ordering red cell products.

This section may seem to be very pedantic but experience everywhere shows that **dangerous or fatal transfusion errors are usually caused by failing to keep to the standard procedures.**

Acute **haemolytic** transfusion reactions are usually caused by transfusing red cells that are incompatible with the patient's ABO type. These reactions can be fatal. They usually result from errors made in identifying the patient when samples are being taken or when blood is being administered.

When ordering and giving blood products it is therefore essential to follow the local procedures. These should cover the steps outlined in Figure 3.

Figure 3. RIGHT BLOOD/RIGHT PATIENT/RIGHT TIME
ESSENTIAL STEPS



Ordering blood in an emergency.

This will often be done in the emergency admissions unit. There may be several unconscious patients who need blood quickly. Often many staff are involved. It is very easy to make mistakes, so procedures must be clear, and simple and everyone must know them.

- For each patient, the crossmatch sample tube and the blood request form must be clearly labelled with the EMERGENCY ADMISSION NUMBER. Use the patient's name only if you are sure you have this right!

- If you have to send another request soon for the same patient, use the same identifiers that you used on the first request so the hospital transfusion department staff know they are dealing with the same patient!

- It may help if one person takes charge of ordering blood especially if several patients are involved at the same time; that person should communicate with the hospital transfusion department.

- Tell the hospital transfusion department how quickly the blood is needed for each patient. This allows the laboratory to provide the blood when it is needed.

- Make sure that both you and the hospital transfusion department staff know

  - *who* is going to bring the blood to the patient
  - *where* the patient will be. For example if your patient is just about to be transferred for a CAT scan in another part of the hospital, make sure the blood will be delivered to the CAT scan room!

- The hospital transfusion department may send Group O Rhesus negative blood, especially if there is a risk of mistakes in patient identification. During an acute emergency, this may be the safest way to avoid a mismatched transfusion.

Request forms for compatibility testing.

It is the doctor's responsibility to prescribe blood products and to complete the request form. In some hospitals the responsibility for taking samples from conscious patients is delegated to phlebotomists. They should be specifically trained for this work.

- The blood request form should be clearly and accurately completed with the patient's family name, given name, date of birth and/or hospital number.

- Patients who at the time of admission cannot be reliably identified *must* be given an identity band with a unique number. This number *must* be used to identify this patient until full and correct details are available and are properly communicated to the hospital transfusion department.

- The quantity of blood product required and the time at which it is needed should be written on the request form. The timing of blood ordering for planned procedures should comply with local rules, and the quantity requested for elective surgical patients should be guided by the local surgical blood ordering schedule.

- All the details requested on the form should be completed. It should be signed by the clinician with his or her name in *legible* capitals.

Blood samples for compatibility testing.

- At the time of taking the sample the conscious patient must be asked to state his/her surname, family name, and date of birth.

- This information must be checked against the patient's identification bracelet to make sure that the details entered on the request form are identical.

- The blood sample should be taken according to the hospital laboratory manual and the correct sample tube must be used (for adults, usually 10 ml, no anticoagulant).

- The sample tube must be accurately *labelled at the patient's bedside when the blood sample is being taken.* Sample containers must not be pre-labelled before the specimen is obtained because of the risk of putting the patient's blood into the wrong tube.

- In the case of unconscious patients a medical practitioner should complete the request form and take the sample.

The hospital transfusion department staff are acting correctly if they refuse to accept a request for compatibility testing when either the request form or the sample is inadequately identified. At least 5% of samples arrive with labelling or form filling errors. This wastes time for all concerned and can contribute to serious errors.

Blood ordering for planned procedures.

Blood ordering schedule or tariff.

The blood order for a planned procedure should reflect the clinical team's actual blood use for the particular operation. Many operations very rarely need blood component transfusion so there is no need to crossmatch blood as a routine.

The type and screen procedure should be used for procedures where red cell transfusion is only rarely required.

For procedures that often need red cell transfusion, the standard blood order should be based on the actual use of blood for patients who have recently undergone that operation, not taking account of the occasional patient who has unusually severe blood loss.

- **Type and screen, (also called "group and hold" or "group and save").** In the laboratory, the patient's ABO and Rh (D) type are determined and the patient's serum is screened for IgG antibodies that can damage red blood cells at 37°C. The patient's serum sample is then held in the laboratory, usually for 7 days. If red cells are required within this period they can be provided safely for the patient after a further rapid test to exclude ABO incompatibility. Using this method the hospital transfusion department will usually need about 15 minutes to have blood ready for issue to the patient.

  With this approach there is no need to hold units of blood as an "insurance" for a patient who is unlikely to need them. As a result we can make better use of the donated red cells.

- **Red cell compatibility testing (crossmatching).** In addition to the group and screen, the patient's serum sample is usually tested by the hospital transfusion department for compatibility with the red cells of the units of blood to be transfused.* Compatible units of blood are then labelled specifically for the patient and can be kept available for immediate release. The laboratory will usually reserve these units only for 48 hours after the initial request.

  If the patient needs further red cell transfusion a fresh sample should be sent for crossmatching. This is specially important if the patient has had a recent red cell transfusion completed more than 24 hours ago. Red cell antibodies may appear very rapidly as a result of the immunological stimulus given by transfused donor red cells.

Crossmatching problems.

When the patient's sample is found to contain a clinically significant red cell antibody further tests are needed to identify the antibody so that red cell units of a suitable blood type can be provided.

Every effort will be made by the transfusion department to provide blood that is compatible to avoid the risks of haemolytic transfusion reaction or of stimulating the patient's antibody to a high level. These tests may be complicated, and can cause considerable delay in providing red cells.

When this occurs, non urgent transfusions and surgery should be delayed until suitable red cell units are found, to avoid risks to the patient.

However, when a patient needs transfusion urgently and it is difficult to find compatible red cell units the doctor responsible for the transfusion department should [1]be asked to advise on the risk of a life-threatening reaction if a red cell unit is given that is not fully compatible. *This risk must be balanced with the risk of delaying transfusion when a patient's life may be placed at risk from blood loss that urgently requires restoring the oxygen carrying capacity of the patient's blood.*

Storage, release and collection of red cells for transfusion.

Red cells must be stored in a special, designated refrigerator. It is the responsibility of the hospital transfusion department to maintain these refrigerators and to specify the procedures to be followed when removing red cell units from them.

Crossmatched units of blood may be held within the hospital transfusion department or delivered to another blood refrigerator. In either case, the written procedure for removing red cell units for a patient should state:

- Who is authorised to collect red cell units from the refrigerator.

[1] * In some EU countries this procedure is not routine, but other checks are used instead.

- The details that must be checked against the labels of the units being collected.

- The record that must be made of collection (and return) of the units, including:

  - the identity of the patient for whom blood is collected
  - the unique number of the red cell pack (Fig 2)
  - the time of collection
  - the name of person collecting the unit
  - the time of returning units to the refrigerator if they are not transfused.

Crossmatched red cell units will be collected by the transfusion laboratory if they have not been used within 48 hours of the time for which they were originally requested. *They must be kept in the blood refrigerator except when actually being transfused.*

Administering blood products.

The procedures for infusing blood components should be defined by the hospital transfusion department with the medical and nursing staff. The written procedures should be available to all staff who have to administer transfusions. Responsibility for ensuring that the procedures are kept up to date and available, and for staff training must be defined by the hospital's management.

Identity checks.

Follow local procedures for the checks to be undertaken and the staff who may perform them. The checking must involve two people, one of whom should be a Registered nurse or doctor.

The hospital transfusion department should provide with the red cell units a compatibility report stating the patient's full identity, the patient's ABO and Rh (D) group and the unique donation number and group of each unit which has been supplied. The compatibility label on each unit should show:

- Family name of patient
- Given name
- Date of birth and/or hospital number
- Patient's ABO and Rh (D) group
- Unique donation number
- Time for which blood is requested.

Occasionally red cells will be supplied that are of a different ABO group from the patient's but that are compatible - e.g. red cells of Group A are safe for a patient of Group AB. In this event (usually due to shortage of a particular group) the hospital transfusion department should inform the clinician responsible and also record the fact on the document that accompanies the blood units. Before starting the infusion, check that there are NO discrepancies between:

- Information on the patient's identity band, the compatibility label, and the compatibility report. Patients who can communicate should be asked to state their identity.
- The ABO and Rh (D) group on the blood pack, on the compatibility label and in the compatibility report.
- The donation number given on the blood pack, on the compatibility label and on the compatibility report.

If any discrepancies are found, the unit must not be transfused. If there is any suspicion that the contents of the pack appear abnormal (e.g. evidence of leakage, unusual colour or signs of haemolysis) the unit must not be transfused and the hospital transfusion department must be informed immediately.

Always check that:

- The expiry date on the blood pack has not been passed.
- There is no sign of leakage from the pack.

Record keeping.

The person administering a blood product must enter in the casenotes the number and blood group of the unit and the time at which the transfusion commenced. They must sign to indicate that the pre-administration checks have been performed. This document is part of the patient's permanent record.

Observe the patient.

The following should be observed and recorded.

- Baseline pre-transfusion observation of pulse, blood pressure and temperature.
- Periodic check of pulse and temperature throughout the transfusion. This should be more frequent if there are unexpected symptoms or signs.
- Repeat observation of pulse, blood pressure and temperature at the end of the transfusion.
- Recording of the patient's fluid balance throughout the transfusion episode.

Observe the patient specially carefully during the first 15 minutes of the transfusion. If the patient starts to complain of pain at or near the transfusion site, distress, or loin pain, it can be the first indication of a transfusion reaction.

Clinical features and management of acute transfusion reactions are on page .

Time limits for infusion.

There is a risk of bacterial proliferation when blood components are kept at ambient temperature. For this reason a blood component transfusion must be started within 30 minutes of removing the pack from refrigeration and be completed within 5 hours of starting the transfusion. See Table 3 for other blood components.

Blood administration sets.

For red cells, plasma and cryoprecipitate.

Blood must be infused through a giving set containing an integral 170 micron filter. The set must be changed at least 12 hourly during red cell infusion.

For platelets.

A fresh blood administration set, primed with saline should be used to infuse platelets.

For paediatric patients.

Special paediatric sets should be used.

Filtration of red cells and platelets.

Microaggregate filters.

There is no evidence from controlled trials that these offer clinical benefit. Common, but unproven indications are for massively transfused patients, transfusion for multiple trauma, and during cardiopulmonary bypass. Some patients who require long-term red cell replacement have febrile transfusion reactions, and microaggregate filtration of stored red cells may reduce or prevent these reactions.

Leucocyte depleting filters.

The technology and application of these filters is still evolving. They are useful in preventing the onset of febrile transfusion reactions in red cell transfusion dependent patients and also in avoiding further reactions, if less costly options are not successful.

The use of effectively leucocyte depleted red cells and platelets can reduce the development of anti-leucocyte antibodies in multiply transfused patients but only if all transfused units are filtered. Many clinicians believe this delays or avoids "refractoriness" to platelet therapy. This remains controversial.

Blood warmers.

There is no evidence that warming blood is beneficial to the patient when infusion is slow. At infusion rates greater than 100 ml/minute case reports suggest that cold blood could cause cardiac arrest. Keeping the patient warm is probably more important than warming the infused blood. Blood warmers can be dangerous if they malfunction. They must have a visible thermometer and an audible warning and be properly maintained. Red cells and plasma exposed to temperatures over 40°C may cause severe transfusion reactions. Blood products must NOT be warmed by improvisations such as putting the pack into hot water, in a microwave, or on a radiator.

Use of a blood warmer is advised for adults receiving infusion of blood at rates greater than 50 ml/kg/hour, for children receiving volumes greater than 15 ml/kg/hour and for infants undergoing exchange transfusions. A blood warmer is also indicated when transfusing a patient who has clinically significant cold agglutinins.

Do not add other pharmaceuticals to blood products.

No other infusion solutions or drugs should be added to any blood component. They may contain additives such as calcium which can cause citrated blood to clot. Dextrose solution (5%) can lyse red cells. Drugs should never be added to any blood product. If there is an adverse reaction it may be impossible to determine if this is due to the blood, to the medication which has been added or to an interaction of the two.

If a crystalloid or colloid solution have to be given at the same time as blood components it should normally be given through a separate IV line.

Adverse reactions.

Any adverse reaction thought to be related to the transfusion should be assessed as described on page - and the clinical details and actions taken should be recorded in the case-notes.

Autologous transfusion.

In some situations a patient can be transfused with their own blood that has been collected and stored in advance of a planned operation. There are theoretical advantages in this way of reducing the risk of immunological incompatibility or transmission of some infectious agents. There are detailed guidelines in the UK for carrying out this procedure. *(Further reading)*

Red cells can be stored for up to 5 weeks using standard hospital transfusion department conditions. Medical selection must ensure that patients are fit for this procedure. Suitable patients can "lay down" 2-4 units of blood pre-operatively. The blood must be tested, labelled and stored to the same standard as donor blood. Before

transfusion, autologous blood units must be ABO and Rh(D) grouped and compatibility checked to avoid the consequences of any possible clerical errors. These "autologous" donations should **not** be transfused to anyone other than the patient who provided the donation. *Do not attempt to collect autologous blood units without the advice and help of the hospital transfusion department or transfusion centre.*

There are important practical limits to the application of pre-deposit auto-transfusion.

- Not all patients are fit enough or live near enough to hospital to have 450 ml blood withdrawn several times before a planned operation.
- Auto-transfusion does not reduce the risk of bacterial infection hazards that may result from collection or storage problems. Nor does it reduce the risk of procedural errors that can cause ABO incompatible transfusion.
- Autologous units will often be left unused unless collection is restricted to patients undergoing operations that are very likely to involve a need for transfusion.
- Although "pre donation" appears safe, there has been no systemic assessment of the risks.
- The cost of the procedure is reported to be high in relation to the gains in patient safety.
- There is new evidence that potentially dangerous mistakes occur quite frequently.

Certain categories, such as young fit individuals requiring elective major surgery with inevitable blood losses are likely to benefit most from pre-deposit autologous transfusion.

Immediate pre-operative bleeding and isovolemic haemodilution.

This procedure may be useful in cardiothoracic surgery and other major procedures such as orthopaedic operations in young people. Immediately before operation, after induction of anaesthesia, blood is withdrawn with fluid replacement and stored in the operating theatre. After surgery, the patient's blood can be reinfused. This procedure allows the patient's haematocrit to be reduced to a level selected for optimal capillary perfusion, reduces red cell losses during surgery, and provides fresh autologous blood for reinfusion when needed.

Intra-operative blood salvage.

During surgery blood shed into the operative field can be collected by suction, mixed with anticoagulant (unnecessary if the patient is heparinised) and reinfused through a filter. Using special equipment, the red cells can be washed before reinfusion. Because of concern about the risk of contamination, cell salvage is not advised in the

presence of systemic sepsis, bacterial contamination of the operation field, or malignant disease.

Long term blood storage of autologous blood.

Red cells can be stored for long periods at very low temperatures. Cryo-preservation is expensive and the facilities are available in only a few centres. It should be reserved for patients with rare blood groups or with red cell antibodies that make it very difficult to find compatible donor blood.

Therapeutic apheresis.

Therapeutic apheresis is the removal of blood or a blood component intended to benefit the patient's condition. The simplest procedure is therapeutic venesection in which whole blood (200-450 ml) is periodically withdrawn. This is indicated for some patients with haemochromatosis and polycythaemia. More commonly, cells or plasma are selectively removed using a cell separator. Methods for selective removal of plasma constituents (e.g. cholesterol, autoantibodies) are still at the experimental stage of development.

Good venous access is essential as a rapid blood flow is required for processing. Some machines can operate using a single vein but usually separate cannulae are required for blood withdrawal and return.

Plasma exchange.

Therapeutic plasma exchange combined with other medical treatment contributes effectively to management of conditions show in Table 8.

Table 8. INDICATIONS FOR THERAPEUTIC PLASMA EXCHANGE (PLASMAPHERESIS)

- **Hyperviscosity syndromes eg myeloma, Waldenström's macroglobulinaemia.**
- **Rapidly progressive glomerulo-nephritis.**
- **Goodpasture's syndrome.**
- **Guillain-Barré syndrome.**
- **Familial hypercholesterolaemia.**
- **Wegener's vasculitis.**
- **Thrombotic thrombocytopenic purpura.**

Plasma exchange has been used in many other conditions such as myasthenia gravis, pemphigus, SLE, other autoimmune disorders and in maternal Rh(D) sensitisation during pregnancy. Its effectiveness has not been proved in these conditions and in many cases objective monitoring is difficult. The potential risk and the high cost of plasmapheresis should be taken into account before using it in these conditions.

The replacement fluid for plasma exchange, is usually 4.5% albumin, saline or a mixture of these. **Fresh frozen plasma should be used only for the specific**

CHAPTER IV - CLINICAL APPLICATIONS OF BLOOD PRODUCTS

indication of Thrombotic Thrombocytopenic Purpura (TTP) because of the risk of virus transmission and acute anaphylactic reactions. FFP may occasionally be needed to correct a deficiency of coagulation factors at the end of a plasma exchange.

Thrombotic thrombocytopenic purpura.

This rare and serious condition often responds to infusion of fresh frozen plasma (FFP). Because large volumes of FFP may have to be given over a long period, plasma exchange, using FFP to replace the patient's plasma, is often used.

Cytapheresis (removal of blood cells).

Leucapheresis may help to alleviate symptoms and signs caused by very high cell counts in leukaemic patients (usually chronic granulocytic leukaemia) until chemotherapy takes effect. Plateletpheresis is occasionally used in patients with very high platelet counts causing bleeding or thrombosis. Erythrocytapheresis (red cell exchange) is occasionally needed in the management of malaria, sickle-cell crisis, polycythaemia or following a transfusion error in which Rh (D) positive blood is given to an Rh (D) negative female of child-bearing age.

Table 9 . COMPLICATIONS OF THERAPEUTIC APHERESIS.

- **Anaphylactic reactions to fresh frozen plasma.**
- **Volume overload.**
- **Hypovolaemia.**
- **Air embolism.**
- **Haemolysis.**
- **Extracorporal clotting.**
- **Citrate toxicity.**
- **Coagulopathy.**
- **Vasovagal attacks.**

Progenitor cell (stem cell) collection by apheresis.

Progenitor cells can be collected from a patient's own peripheral blood by apheresis. This procedure is an effective alternative to the collecton and reinfusion of autologous bone marrow, and avoids the need for the patient to have marrow aspirated under general anaesthesia.

This procedure must be carried out by a specialist team, because the preparation of the patient, the cell collection, and the laboratory procedures to process, store and prepare the patient's cells for reinfusion must be very carefully planned and coordinated. There is a detailed clinical guideline published by BCSH. (*Further reading*)

CLINICAL APPLICATIONS OF BLOOD PRODUCTS

Principles.

The following section deals with clinical situations that often involve the use of one or more blood products. Some general principles that apply to most clinical decisions about transfusion are given in Table 10.

Table 10. MINIMISE THE NEED FOR DONOR BLOOD PRODUCTS.	Page
• Transfusion carries risks; some of these are specifically due to the use of allogeneic blood (i.e. blood from another person). • Good clinical practice requires that blood products should be prescribed only when the benefit to the patient is likely to outweigh any risk. • Prescribing decisions should be based on the best available clinical guidelines, modified according to individual patient needs. The rationale for prescribing should be part of the patient's record. • For some patients in some clinical situations it may be safer to use the patient's own blood (autologous transfusion). • "Wastage" of a patient's blood can be minimised in many ways that can reduce the need for transfusion: - Minimise blood taken for laboratory use. - Transfuse to meet clinical need rather than responding to a laboratory result. - Use the best methods to minimise blood loss during surgery. - Salvage and reinfuse surgical blood losses during procedures where this is appropriate. - Use alternative approaches e.g. Desmopression, Aprotinin, Erythropoietin. - Stop anti-coagulants and anti-platelet drugs before planned surgery. - Use non-blood fluids for resuscitation.	

Perioperative red cell transfusion.

When should red cell transfusion be given?

In the past surgeons and anaesthetists have often used the "rule of thumb" that a patient whose haemoglobin level has fallen below 10 g/dl (haematocrit <30%) needs red cell transfusion. There is no clinical evidence to support this generalisation. Some patients tolerate profound haemodilution during surgery without morbidity attributable to lack of red cells. Clinical studies do not support the general application of the "10g/30%" rule. Experimental evidence is that in healthy humans cardiac output does not increase sharply until the haemoglobin falls well below 7g/dl. However, in some older or "fragile" patients, especially with cardiovascular disease, moderate haemodilution may contribute to myocardial ischaemia.

Conservative use of red cell replacement is appropriate in fit patients, especially the young, who are usually very tolerant of haemodilution, and for whom long term complications of avoidable transfusion are potentially important.

There is however little to commend the aggressive avoidance of red cell transfusion in elderly patients. Evidence of cardiovascular and respiratory disease should lead to caution in allowing haemoglobin to fall to a low level. In all patients with substantial blood loss, priority should be given to maintaining circulatory volume by giving adequate fluids and to maintaining oxygen supply (page).

Transfusion management of acute blood loss. (Table 11)

This section refers to situations where rapid infusion of substantial volumes of fluid together with red cell replacement is likely to be required over a few hours, as a result of major bleeding.

Table 11. PRINCIPLES OF TRANSFUSION MANAGEMENT OF ACUTE BLOOD LOSS

- Restore circulating fluid volume to correct hypoperfusion.
- Achieve surgical control of bleeding.
- Maintain adequate blood oxygen transport capacity.
- Request early coagulation screen. The results may help to guide blood component therapy should bleeding persist after attempted surgical haemostasis.

Insert a large IV cannula, obtain blood samples, and first infuse crystalloid as rapidly as possible until an acceptable systolic blood pressure is restored.

% Loss of Blood Volume	Equivalent Adult Fluid Volume	Replacement Fluid
<20%	Up to 1 litre	- Crystalloid (eg 0.9% saline)
>20%	More than 1 litre	- Red Cells - Fluid: Crystalloid and/ or colloid

Notes:

1. To estimate blood volume: = 70 ml/kg in adults: 80 ml/kg in infants.
2. If bleeding continues after attempted surgical haemostasis and when coagulation tests or platelets count are abnormal, platelets, FFP or cryoprecipitate or combinations of those may be needed: the dose should be estimated and the effect monitored by clinical evidence of reduced bleeding, coagulation screen and platelet count.
3. Clinical trials in humans have not demonstrated that albumin solutions or colloids are superior to crystalloids for resuscitation.
4. Dextran and HES (Table 12) should be limited to 1.5 litre per 24 hours in an adult (according to manufacturers' data sheets).
5. Avoid saline in patients with severe liver disease for whom sodium overload is a special risk. Also take care with 5% Albumin in these patients for the same reason.
6. Clinical observations that should be routinely monitored and recorded throughout the management of an episode of bleeding are pulse, systolic blood pressure, central venous pressure, urine output (catheter)*. Criteria for the use of additional invasive monitoring procedures such as pulmonary arterial wedge pressure should be set in local protocols.
7. The type of crystalloid or colloid to be used and the source of supply should be specified in local protocols.

Table 12. NON PLASMA COLLOID VOLUME EXPANDERS					
Product	**Source**	**Concentration of solution**	**Number average Mol. wt.**	**Intravascular persistence**	**Approximate frequency of severe acute reactions**
Modified	Heat-degraded cattle bone gelatine	3-4%	35,000	50% of infused volume persists 4-5 hours	1 in 10,000 infusions
Hydroxy-ethyl starch (HES)	Maize starch, chemically modified	6%	450,000 or 265,000	Similar to or longer than Dextran 70	1 in 20,000 infusions
Dextran 70	Bacterial product	6%	70,000	50% of infused volume persists 24 hours	1 in 10,000 infusions
Dextran 40	Bacterial product	10%	40,000	Shorter than Dextran 70	1 in 50,000 infusions

Transfusion support of major bleeding problems.

Acquired haemostatic problems.

Haemostatic failure can be triggered by hypovolaemia, tissue damage, hypoxia and sepsis.

Normal haemostasis involves pro-coagulant proteins (the coagulation cascade), the platelets, the fibrinolytic system, and the blood vessel wall. Acquired haemostatic disorders arise frequently in hospital practice. Blood component therapy is often required. Prescribing should be based on correct interpretation of clinical features and laboratory tests.

Disseminated Intravascular Coagulation (DIC) refers to a spectrum of bleeding problems that are seen in such patients. Activation of the coagulation and fibrinolytic systems leads to deficiencies of coagulation proteins, fibrinogen, and platelets. The clinical presentation can range from major bleeding with or without thrombotic complications to a compensated state detectable only on laboratory testing.

Treatment should focus on correcting the cause of DIC. Replacement with blood products is indicated when there is bleeding with acute DIC. Platelets, fresh frozen plasma, and cryoprecipitate should be given to correct thrombocytopenia and clotting factor deficiencies. Control of bleeding is the goal; laboratory test results help to select the blood products that may be effective and to monitor the doses needed.

Neonates, patients with marrow disorders or liver disease and patients taking anticoagulants, aspirin or other non steroidal anti-inflammatory drugs are more likely to develop haemostatic problems because their platelet function is impaired and/or

their haemostatic factor production is reduced. Where possible, seek advice from the hospital haematology or transfusion department physicians when managing these problems.

Blood component replacement.

Dilution effect.

When there is no pre-existing haemostasis problem, replacement of up to 1 blood volume (8-10 units of blood in an adult) with red cells and non-plasma fluids is unlikely to cause haemostatic problems due simply to dilution.

Platelets.

In an adult, platelets should be given if there is severe microvascular bleeding (MVB) with a platelet count below 50-100 x 10^9/l, (especially if more than 15 units of blood have been transfused) or if laboratory results suggest there is disseminated intravascular coagulation (DIC).

There is no evidence that giving platelets or plasma prophylactically to patients undergoing large transfusions reduces the risk of MVB. *Routine prophylactic use of these products for major surgery is not recommended.*

Fresh frozen plasma (FFP) and cryoprecipitate.

FFP should be used only where there is microvascular bleeding with laboratory results that show abnormal coagulation. If the fibrinogen level is below 1 g/l and DIC has been diagnosed with severe bleeding the fibrinogen level should be raised by giving cryoprecipitate, (initially at least 15 packs containing in total 3-4 gm fibrinogen).

Laboratory tests of haemostasis.

These can help to identify the need for blood components to control microvascular bleeding. The platelet count, Prothrombin Time Ratio (INR) or Activated Partial Thromboplastin Time (APTT) should be monitored during large transfusions to help guide replacement.

Other complications of large volume transfusions.

The problems described below are rarely due to transfusion alone and cannot be avoided simply by attention to transfusion practice. However, transfusion should be managed so as to avoid making the problems worse.

Hypocalcaemia.

The citrate anticoagulant in some blood components (Table) binds ionised calcium. This could lower plasma ionised calcium levels, but usually rapid liver metabolism of citrate prevents this. In neonates and patients who are hypothermic, the combined effects of hypocalcaemia and hyperkalaemia may be cardiotoxic. If there is ECG or clinical evidence of hypocalcaemia, 5 ml of 10% calcium gluconate (for an adult) should be given

IV. If necessary the dose should be repeated till the ECG is normal. Note that red cells in additive solution contain only traces of citrate.

Hyperkalaemia.

The plasma or additive solution in a unit of red cells or whole blood stored for 4-5 weeks may contain 5-10 mmol of potassium. In the presence of acidaema and hypothermia this additional potassium can lead to cardiac arrest. This problem is best prevented by keeping the patient warm.

Hypothermia.

Rapid transfusion of blood at 4°C can lower the core temperature by several degrees. The best safeguard is to keep the patient warm. A blood warmer should be used in adults receiving large volumes of blood at rates above 50 ml/kg/hr (in children above 15 ml/kg/hr).

Acid base disturbances.

Despite the lactic acid content of transfused blood, [1-2 mmol/unit of red cells, 3-10 mmol/unit of whole blood] fluid resuscitation usually *improves* acidosis in a shocked patient. In practice, transfused citrate can contribute to metabolic *alkalosis* when large volumes of blood components are infused.

Adult respiratory distress syndrome.

The risk is minimised if good perfusion and oxygenation are maintained and over-transfusion is avoided. The use of albumin solutions to maintain a plasma oncotic pressure >20 mmHg is often stated to be important but controlled studies have not proven any advantage of albumin solution over crystalloid fluids for resuscitation. The use of microaggregate filters when stored blood is transfused is often advised but the benefits remain unproven. These filters may offer benefit for patients with pre-existing lung disease.

Avoidable haemostatic problems in the elective surgery patient.

If a patient admitted for elective surgery or an invasive procedure is found to have thrombocytopenia or an abnormal coagulation screen (prolonged PT or APPT) the procedure should be postponed while the cause of the abnormality is identified. If a congenital bleeding disorder is found, the patient must be managed in conjunction with a Haemophilia Centre.

If the platelet count is below 80 x 10^9/l before starting a procedure likely to cause significant blood loss, or bleeding in a critical site, e.g. CNS, it must be investigated before starting the procedure and treated along the lines given on page .

Warfarin.

Unless it is contra-indicated to do so, warfarin anticoagulation should be stopped before elective major surgery in time to allow the prothrombin time ratio (INR) to approach normal. This should be guided by a local protocol for preoperative anticoagulant management.

Aspirin.

A single dose as low as ½ tablet (300 mg), impairs platelet function for several days. Aspirin should be stopped at least 7 days before planned surgery unless there is a specific reason for continuing it. When an aspirin-induced platelet defect contributes to abnormal bleeding, platelet transfusion is likely to be effective.

Transfusion for acute gastrointestinal bleeding.

In the UK, gastrointestinal bleeding occurs in 50-150/100,000 of the population each year. It is the direct cause of 3,500 deaths per year and accounts for about 8% of medical admissions to hospital.

Blood replacement for patients with GI bleeding is summarised in Table 13. Special points in managing patients with bleeding from varices associated with chronic liver disease are given in Table 14.

Table 13. USE OF FLUIDS AND BLOOD PRODUCTS IN MANAGING PATIENTS WITH ACUTE GASTROINTESTINAL BLEEDING.			
Severity	**Clinical Features**	**IV Infusion**	**End Point**
Severe	•History of collapse and/or • Shock - systolic BP <100 mmHg - pulse > 100/min	• Replace fluid rapidly (Table) • Ensure red cells are available quickly; use local emergency transfusion protocol • Transfuse red cells according to clinical assessment and Hb/Hct (Table).	Maintain urine output >40 ml/hour and systolic BP >100mHg. Maintain haemoglobin above 9 g/dl
Significant	Resting pulse >100/min and/or haemoglobin less than 10 g/dl.	Replacement fluid. Order compatible red cells (4 units).	Maintain haemoglobin above 9 g/dl.
Trivial	Pulse and haemoglobin normal	• Maintain intravenous access until diagnosis is clear. • Send patient sample for red cell group and antibody screen.	
No evidence of bleeding	May have 'coffee grounds' or altered blood in vomitus. Faecal occult blood negative.		

Table 14. REPLACING GASTROINTESTINAL BLOOD LOSS IN PATIENTS WITH CHRONIC LIVER DISEASE.

Features	Transfusion Management	End Points
• Bleeding is often but not always from oesophageal varices and is often severe. Other causes such as peptic ulcer are not uncommon and must be excluded.	Insert one or two large bore cannulas. A central line may be indicated.	Systolic pressure >100 mmHg Haemoglobin 9 g/dl urine output > 40 ml/hr.
• Bleeding from varices usually recurs if there is no intervention to control the varices or to reduce portal pressure. The prognosis depends on the severity of the liver disease.*	Ensure red cells are available quickly use local emergency transfusion protocol: order 4-6 units.	CVP 0-5 mmHg (not higher)
• Hepatic failure may follow variceal bleeding, but usually recovers if bleeding can be stopped and recurrence prevented.[1]	Crystalloids should be used carefully. Saline should be avoided as sodium retention is usual and leads to ascites.	
• Thrombocytopenia is usual. The platelet count may fall below 50 x 10^9/l. Provided the platelet count is above 50 x 10^9/l, bleeding is unlikely to be controlled or prevented by platelet transfusion.	Platelet transfusion is rarely needed. If there is continued bleeding with a platelet count below 50 x 10^9/l, platelet transfusion may be considered in an effort to control variceal bleeding.	Platelet count may show little increment following platelet transfusion in patients with splenomegaly.
• Normal (i.e. pre-bleed) systolic BP is often lower than in non-cirrhotic patients.		
• Deficiency of coagulation factors except fibrinogen and factor VIII is frequent.	Fresh frozen plasma is indicated only if there is documented coagulopathy. e.g. INR >2.0.	Keep INR <2.0 if possible. Complete correction is rarely possible with FFP due to the large volume.
• Giving red cells to try and raise Hb towards normal values may raise portal venous pressure, since blood volume is often increased. Over transfusion may contribute to rebleeding.		Coagulation factor concentrates may be indicated. Seek expert advice as some of the products have a risk of thrombogenicity, especially in patients with liver disease.
• Provided blood volume is replaced and cardio-respiratory function previously adequate, a haemoglobin of 9 g/dl appears to be adequate.	Transfuse red cells to approach but not exceed end point of 9 g/dl.	

1 Bleeding, especially if recurrent, is both intrinsically hazardous and is indicative of severe liver disease with a bad prognosis for the episode. A good outcome for the episode depends on overall management of infection, renal failure, ascites and encephalopathy.

Warfarin (coumarin) anticoagulant overdose.

Management should be guided by the principles in Table 15.

Table 15. MANAGEMENT OF WARFARIN OVERDOSE

A.	**Life threatening haemorrhage.**
	Give 5 mg vitamin K by slow intravenous infusion and a prothrombin complex concentrate (PCC) containing Factors II, IX, X together with Factor VII (if available). The dose should be based on 50 iu Factor IX or Factor VII per kg body weight.
	If no concentrate is available, fresh frozen plasma should be infused (about 1 litre for an adult), but this may be less effective.
B.	**Less severe haemorrhage such as haematuria and epistaxis.**
	Stop warfarin for 1 or more days. Vitamin K, 0.5 - 2.0 mg (iv slow infusion) can accelerate correction of abnormal clotting if this is clinically necessary.
C.	**International normalised Ratio (INR) of > 4.5 without haemorrhage.**
	Stop warfarin for one or two days: then review.
D.	**Unexpected bleeding at therapeutic levels of INR.**
	Investigate the possibility of another cause, guided by the apparent site of bleeding.

Thrombolytic therapy.

Although bleeding is not a common complication of fibrinolytic therapy at normal doses, the risk is not predicted or reduced by laboratory monitoring. If rapid reversal of the fibrinolytic state is necessary because of serious bleeding, fresh frozen plasma will reverse the acquired deficiencies of Factor V and VIII:C; cryoprecipitate will raise a very low fibrinogen level. Antifibrinolytic agents should be used only if there is life-threatening bleeding. They may cause large clots at the site of bleeding, with severe clinical problems. They should not be used in intracranial or renal tract bleeding.

Cardiopulmonary bypass.

Cardiopulmonary bypass usually impairs haemostasis due in part to its effect on platelet function. Especially in re-operations or in patients operated on for infective endocarditis, bleeding may be severe. Routine laboratory tests of coagulation do not accurately predict the clinical importance of the haemostatic defect. Platelet transfusion is indicated if there is microvascular bleeding or if the bleeding cannot be corrected surgically after the patient is off bypass and once heparinisation has been reversed with an adequate dose of protamine sulphate. Fresh frozen plasma helps to correct prolonged clotting times and may improve haemostasis, but the routine use of

fresh frozen plasma or platelets at the end of bypass does not reduce transfusion requirements.

Aprotinin (Trasylol) can reduce transfusion requirements in specific situations such as bypass surgery in patients with infective endocarditis but routine use is not advised for coronary artery or valve surgery in adults.

Congenital haemostatic disorders

Haemophilia.

In the UK patients with Haemophilia A, Haemophilia B (Christmas disease), and von Willebrand's disease should be registered with and cared for by a Regional Haemophilia Centre. The Haemophilia Centre should be contacted when a patient with Haemophilia presents to a clinical unit. Detailed guidance on the products recommended for management of these patients is published by the UK Haemophilia Directors and regularly updated. (Further reading)

When a patient with haemophilia is seen away from a specialist centre, it is important to get the best help available, quickly. (Table 16)

Table 16. POINTS TO NOTE IN INITIAL CARE OF A BLEEDING HAEMOPHILIA PATIENT.

Identification: If the patient is unconscious, check if there is information carried on a bracelet or medallion. Contact the Haemophilia Centre for advice and inform the local haematologist. (Phone numbers on page .)

Products for treatment: Coagulation factor concentrates VIII and IX respectively are needed for haemophilia A and B. The nearest supply may be in the patient's home provided for home therapy. In a real emergency and if clotting factor concentrates are unavailable, cryoprecipitate is the appropriate treatment for Haemophilia A and fresh frozen plasma is appropriate for Haemophilia B.

Dosage: Factor VIII in a dose of 1 iu/Kg should give an immediate 2% rise in plasma Factor VIII. Factor IX (1 iu/Kg) should give an immediate 1% rise in Factor IX level.

Monitoring: Clotting factor levels may be needed to assess response to treatment. Check with your local laboratory that these assays are available.

von Willebrand's Disease(vWD).

The assessment of treatment needs and response is not straightforward and needs measurement of both Factor VIII and von Willebrand Factor. Some patients can be managed with Desmopressin (DDAVP) without the need for any blood product. If clotting factor replacement is needed, a Factor VIII concentrate must be chosen that is

effective for vWD. Cryoprecipitate was formerly the chosen replacement therapy but should now be used only if a virus-inactivated concentrate is not available.

Every effort must be made to obtain immediate specialist assistance in the management of these patients.

Transfusion in chronic anaemia.

Nutritional replacement therapy with iron, vitamin B12 or folic acid or correction of the source of blood loss based on a correct diagnosis should be the treatment in most cases. Clinically anaemic patients are deficient in red cells, but have a normal or increased blood volume. A rapid rise in haemoglobin is rarely required. In rare cases when red cell transfusion is felt to be needed, red cell concentrate should be used to minimise the volume given. Patients who are elderly or who have cardiovascular disease or megaloblastic anaemia are most at risk of developing cardiac failure. Therefore red cells should be given slowly (4 hours per unit) at a time when the patient can be observed. A diuretic, such as frusemide should be given if there is felt to be a risk of circulatory overload.

Transfusion dependent anaemia.

Regular red cell transfusion may be required for patients with myelodysplastic syndromes, chronic lymphocytic leukaemia, aplastic anaemia, or malignant infiltration of the bone marrow.

Haemoglobinopathies.

Patients with beta thalassemia major or severe complications of sickle cell disease may need long term red cell support. These patients all require specialist investigation and management. Special precautions must be taken to reduce the risk of developing antibodies to red cells and white cells and the patient should be vaccinated against Hepatitis B and Hepatitis A. Accumulation of iron should be minimised by using a chelating agent (desferrioxamine).

In patients with haemoglobinopathy the aim of a regular red cell transfusion regime is to suppress endogenous red cell production and keep the haemoglobin between 10.5 and 15.5 g/dl. In the other conditions mentioned above, the need for transfusion is determined by the patient's clinical symptoms of anaemia.

If a patient is a potential candidate for bone marrow transplantation, it is important to obtain expert advice before starting transfusion as special selection of blood products will be needed.

Anaemia in chronic renal failure.

The treatment of choice is erythropoietin; to maintain an adequate haemoglobin without the need for regular transfusion. Erythropoietin and should be used according to the local hospital protocol.

Bone marrow failure and transplantation.

The treatment given to patients with malignant haematological disease or solid tumours often cause bone marrow suppression that requires transfusion support with platelets and/or red cells. In these patients, transfusion may be complicated by graft-versus-host-disease (GVHD), cytomegalovirus (CMV) infection, or the development of antibodies to HLA antigens. The latter can cause non haemolytic febrile transfusion reactions and may reduce the clinical effectiveness of platelet transfusions. Special precautions can help to minimise these problems.

Red cell transfusion.

The principles are given on page . Patients should be tested periodically to detect the appearance of antibodies to red cells. Check again for red cell antibodies if there is a pyrexial reaction to red cells, an unexplained fall in haemoglobin or if the clinical response to red cell transfusion is less good than expected.

Platelet transfusion.

A platelet transfusion regime should be set for the patient. The aim is to balance the risk of haemorrhage against the risks of repeated platelet transfusion (infection and alloimmunisation). Purpura and mucosal or retinal haemorrhage in a thrombocytopenic patient should always be treated promptly with platelet transfusion.

Most platelet transfusions are given prophylactically and the policies of individual clinical teams differ. For stable afebrile patients, platelets are not usually given provided the count is above 10 x 10^9/l. If the patient has a fever and is suspected or known to have an infection, the threshold for platelet transfusion is usually 20 x 10^9/l. If the patient is stable platelet transfusion should be given to maintain platelet count: transfusion on alternative days is often sufficient. The adult "dose" of platelets is usually intended to contain at least 240 x 10^9 platelets. This can be provided either by pooling platelets prepared from 4-6 whole blood donations or by a single donor apheresis platelet unit.

Patients receiving intensive blood product support should be checked periodically for the development of antibodies to HLA Class I antigens especially if there are febrile reactions to platelet transfusions or if the increment in platelet count is less an expected. Poor increments are often seen if there is bleeding, infection, and splenomegaly. If a poor platelet increment occurs in the presence of HLA Class I antibodies, the patient may benefit from receiving HLA matched or crossmatch-

compatible platelets. However about a third of "refractory" patients continue to show a poor response even if HLA matched platelets are given.

"Refractoriness" to platelet transfusion.

Avoiding the development of antibodies to HLA antigens. About half of all intensively transfused patients develop HLA Class I antibodies. In some this leads to febrile transfusion reactions and it may accompany a poor response to platelet transfusion, often called "refractoriness" to platelets. A simple definition of "refractoriness" to platelet transfusion is that the patient's platelet count fails to rise by at least 10×10^9/litre the next morning after a platelet transfusion.

This simple measurement may help to predict the effectiveness of platelet transfusion in preventing clinically important bleeding.

Recently there has been much emphasis on avoiding the stimulaton of HLA antibodies by the use of leucocyte depleted blood components. While this may be important there is still very little evidence that avoiding HLA alloimmunisation improves the clinical effectiveness of platelet transfusion. This remains a controversial subject. The practice of individual clinicians may continue to differ until the results of further clinical trials have been assessed.

To avoid alloimmunisation the patient should consistently receive, from the start of treatment, blood products that have a white cell content below 0.5×10^6 per unit. These are made either by plateletpheresis or by filtration of platelets or red cells with special filters. These filters can be used at the time of transfusion but this is less reliable than filtering the blood component under controlled laboratory conditions.

Some units restrict the use of leucocyte depleted blood components to patients who experience repeated NHFTR.

All patients with aplastic anaemia who may later receive a bone marrow transplant should be given leucocyte depleted red cells and platelets. This is because HLA antibodies can reduce the chance of a successful 'take' of a bone marrow transplant.

Graft-versus-host-disease(GVHD): use of gamma-irradiated blood components. Engraftment of viable lymphocytes transfused with whole blood, red cells or platelets can cause fatal GvHD in patients with severely depressed T-cell immunity eg after progenitor cell grafting. *This **must** be prevented by irradiation of all cellular blood components (25-30 Gy). Leucocyte depletion by presently available methods **does not** reliably protect against GvHD.*

Cytomegalovirus(CMV) transmission. Since CMV infection is an important cause of mortality following transplantation, all bone marrow or peripheral stem cell allograft recipients should receive CMV antibody negative cellular blood products, regardless of the patient's CMV serological status or that of the donor. Fresh frozen plasma and cryoprecipitate have not been shown to transmit CMV. Other patients who should receive CMV negative cellular components include

- CMV negative autograft recipients,
- CMV negative acute leukaemia patients prior to transplant,
- all new patients with haematological malignancy until their CMV status is known,
- HIV positive patients who are CMV negative.

Since CMV is leucocyte-associated , an alternative is to use leucocyte filtered cellular components.

Selection of ABO groups for transfusion of bone marrow allograft recipients. If the ABO groups of donor and recipient are different the selection of the ABO group of cellular components to be transfused must be discussed with the hospital transfusion department.

Renal transplant patients.

In the past, 1-2 units of red cells were transfused to patients awaiting transplantation because this led to improved graft survival. Most specialists now consider that immunosuppression with cyclosporin makes this unnecessary. Anaemia is usually treated with recombinant human erythropoietin. If red cells are administered they should be leucocyte depleted to avoid development of HLA antibodies and reduce any risk of CMV infection.

Heart, heart/lung and liver transplantation.

Where both donor and recipient are CMV negative, CMV negative red cells and platelets should be used.

Liver transplant patients often have major abnormalities of coagulation and a low platelet count. Local protocols should define the pre-operative and intraoperative use of blood components. Steps often taken to minimise blood usage during surgery include the use of aprotinin, red cell salvage and continuous infusion of fresh frozen plasma during critical stages of the operation.

Intravenous immunoglobulin for immunological disorders.

Immune cytopenias.

Auto-immune thrombocytopenic purpura (AITP): IVIgG in high doses has a role in the management of some patients but it is not a substitute for standard treatment including steroids and splenectomy. IVIgG produces an increase in the platelet count of varying duration in about 70% of patients but it does not alter the natural course of the disease. IVIgG may be useful.

- To assist management of acute bleeding.
- To cover surgery or delivery in patients with AITP if the low platelet count causes risk of haemorrhage.

A total dose of 1-2 g/kg divided over 1-5 days is usual in patients with chronic AITP further occasional doses of 0.4 g/kg may help to maintain an adequate platelet count.

Neonatal alloimmune thrombocytopenia (NAITP).
Neonatal thrombocytopenia due to maternal ITP.
Post-transfusion purpura.

IVIgG has been used in all these conditions with variable results. In NAITP clinical trials of high dose IVIgG given to the mother have not confirmed earlier reports that this could prevent or reduce the severity of the disorder. IVIgG given to the neonate is effective in about 50% of NAITP cases and may be used with donor platelets which

lack the antigen against which the maternal antibody is directed. In neonatal thrombocytopenia associated with maternal ITP IV IgG is effective in some cases.

In all these conditions the initial dose should be about 1-2 g/kg. Specialist advice is essential.

Immunoglobulin treatment in antibody deficiency states.

Primary hypogammaglobulinaemia.

These patients have an inherited deficiency in antibody production. They need life-long replacement therapy to avoid or control the infectious complications of immune deficiency. Because intramuscular IgG is often poorly tolerated due to pain at the injection site (especially in children) it may be impossible to maintain levels of plasma IgG sufficient to prevent recurrent infection. The treatment of choice is regular administration of IVIgG. The standard dose is 0.2 g/kg body weight every 3 weeks but the dose may require to be increased or infusions given more frequently if recurrent infections persist. It is usual to aim to keep the plasma IgG level within the range of normal values. If IMIgG has to be used the conventional dose is 0.025-0.05 g/kg weekly.

Haematological malignancies.

Some patients with chronic lymphatic leukaemia or myeloma are unable to make effective antibodies and suffer from recurrent severe infections due to gram positive encapsulated bacteria (e.g. Strep. pneumoniae, H. Influenzae) that respond poorly to antibiotics. IVIgG at a dose of 0.2-0.4 g/kg every 3-4 weeks has been shown to reduce the frequency of episodes of these infections.

HIV.

Some children with HIV who suffer from recurrent bacterial infections benefit from IVIgG, 0.2 g/kg body weight every 3 weeks. Episodes of infection, antibiotic use and hospitalisation can all be reduced.

Other indications for intravenous immunoglobulin.

IVIgG is recommended for routine use in Kawasaki disease where a dose regime similar to that used in ITP is effective.

Treatment with IVIgG has been reported to be followed by clinical improvement in many other conditions including neuromuscular disorders that are thought to have an immunological basis. Treatment with IVIgG should generally be part of a clinical trial and may be justified as a last resort measure.

Intramuscular immunoglobulin for preventing infection.

Normal Human Immunoglobulin and so called "specific" immunoglobulin products (that contain higher levels of antibody against specific organisms) are used, often together with active immunisation, to protect against infection. A summary of the products and their use is given in Table 17.

Practical clinical information about immunisation is given in the Handbook on Immunisation. *(Further reading)*

Table 17. THE USE OF IMMUNOGLOBULIN PREPARATIONS FOR PREVENTION OF INFECTION

Infection	Indications	Preparations, vial content	Dose
Hepatitis A	Contacts and travellers	**Normal Human Immunoglobulin (NHIg) 250 mg and 750 mg**	Under 10 yrs 250 mg, 10 years and over 500 mg
Measles	Immuno-compromised, contacts infant contacts with pre-existing severe illness	**NHIg 250 and 750 mg (unless Measles Immunoglobulin is available)**	
Immunoglobulin is not used with measles vaccine. An interval of at 3 months must elapse after an injection of immunoglobulin before measles vaccination is attempted.			
Rubella	Pregnant contact where termination is not an option	**NHIg 750 mg (unless Rubella Immunoglobulin is available)**	750 mg
Normal Immunoglobulin after exposure does not prevent infection and is not generally recommended for protection of pregnant women exposed to rubella. It may be used when termination of pregnancy would be unacceptable. In this case it should be given without awaiting reports on the woman's serological status. Serological follow-up is essential.			
Tetanus	High risk injuries to non-immune subjects	**Tetanus Immunoglobulin 250 iu**	250 or 500 iu
Use together with active (toxoid) immunisation in tetanus prone wounds in the following: (i) unimmunised subjects, (ii) immunisation history unknown, (iii) over 10 years since last tetanus vaccine. Dose 250 iu but use 500 iu if more than 24 hours have elapsed since injury or if there is heavy contamination of the wound.			
Tetanus	Clinical tetanus	**Tetanus Immunoglobulin; 3000 iu vials (if available or 250 iu vials)**	30-3000 iu/kg multiple IM sites or IV if suitable product available

Table 17 - Continued. The Use of Immunoglobulin Preparations for Prevention of Infection

Hepatitis B	Needle stab or mucosal exposure. Sexual exposure	**Hepatitis B Immunoglobulin (HBIg) 500 iu, 1000 iu**	1000 iu (or 2 x 500 iu: see note below)
Treat within 48 hours if possible and not ore than 10 days after exposure. If 500 iu given initially repeat dose at 28 days unless recipient has been shown to be immune or inoculum has come from a low risk (anti-HBc positive) individual or the recipient has received hepatitis B vaccine.			
Hepatitis B	New born babies of high risk mothers	**Hepatitis B Immunoglobulin 100 iu**	200 iu
As soon as possible and with 48 hours after birth. Combine with simultaneous active immunisation.			
Infection	**Indications**	**Preparations, vial content**	**Dose**
Varicella Zoster	Immuno-compromised contacts. Neonatal contact	**Varicella Zoster Immunoglobulin (SIG) 250 mg and 500 mg vials**	0-5 yrs 250 mg 6-10 yrs 500 mg 11-14 yrs 750 mg 15+ yrs 1000 mg. (Note these doses recommendations for BP. product: for other product see package insert)
Used in (1) chickenpox or Zoster contacts if they are immunosuppressed by reason of drugs, radiation, neoplasm or immunodeficiency disease; (2) neonates born 6 days or less after the onset of maternal chickenpox or whole mothers develop chickenpox (not zoster) after delivery; (3) other neonatal contacts of chickenpox or zoster if either the baby is very premature (less than 30 weeks gestation or under 1 kg birthweight) or the mother has no prior history of chickenpox; (4) if supplies permit it may be given to pregnant contacts to reduce the risk of severe infection.			
Other Immunoglobulin Preparations The following special preparations are available [from Regional Transfusion Centres in Scotland]. **Normal Immunoglobulin for intravenous use, Rubella Immunoglobulin, Measles Immunoglobulin, Tetanus Immunoglobulin 3000 iu pack for intravenous administration in treatment of established Tetanus, CMV Immunoglobulin.** All these products are supplied with package inserts and must be prescribed according to the manufacturer's instructions.			
Infection	**Indications**	**Preparations, vial content**	**Dose**
Rabies	Bite or mucous membrane exposure to potentially rabid animals	**Human Rabies Immunoglobulin (HBIg) 500 iu**	20 iu/kg
Rabies Immunoglobulin is used with rabies vaccine to provide rapid protection until the vaccine become effective. The recommended dose must not be exceeded and should be given at the same time as the vaccine. Half the dose should be infiltrated round the wound and the remainder given by deep intramuscular injection at a site separate from that used for rabies vaccine.			

Sources of Supply	
England and Wales	Normal Immunoglobulin: CDSC, Central Public Health Laboratory (CPHL) 0181 200 6868 and other Public Health Laboratories. Blood Products Laboratory 0181 953 6191 Tetanus Immunoglobulin: Regional Transfusion Centres. Hepatitis B Immunoglobulin: Hepatitis Epidemiology Unit, CPHL and other Public Health Laboratories. Rabies Immunoglobulin: Virus Reference Laboratory, CPHL. Varicella Zoster Immunoglobulin: CDSC at CPHL.
Scotland	All immunoglobulin products are supplied through the Regional Transfusion Centres
Immunoglobulin products from commercial suppliers may be available through hospital pharmacies.	

Transfusion of the new-born infant.

Normal values.

The blood volume is 80 ml/kg for full term infants and around 100 ml/kg for pre-term infants, depending on gestational age. The normal range of haemoglobin concentration in full-term infants is 14-20 g/dl. Platelet count ranges from 150 to 400 x 10^9/l. The prothrombin time and thrombin time can be slightly prolonged in full-term infants; more marked prolongation of coagulation times is seen in the pre-term. The level of vitamin K-dependent coagulation factors in the neonate is about 50% of the normal adult value. Fibrinogen and other coagulation factors are in the normal adult range at birth.

Table 18. NORMAL RANGES FOR TERM AND PRETERM INFANTS

	Term	Preterm (<37 weeks)	Adult (For comparison)
Haemoglobin, g/dl	14-20	12.6-20	13-18 (male)
Platelets x 10^9/l	150-400	150-400	150-400
PT (sec)	12-17	14-22	12-14
APTT (sec)	25-45	35-50	25-40
TT (sec)	12-16	14-18	12-14
Fibrinogen	1.5-3.0	1.5-3.0	1.75-4.5

Normal values for preterm infants depend on gestation.
*** These values are illustrative only: results from each laboratory must be related to the laboratory's own normal range.**

Thrombocytopenia in neonates.

There is an increased risk of haemorrhage in pre-term infants with moderate thrombocytopenia (50-100 x 10^9/l) and in full-term infants with platelet counts less than 20-30 x 10^9/l. The risk is increased if there is sepsis or coagulopathy. An appropriate dose of platelet concentrate is one single donor unit per 10 kg body weight or 10 ml per kg for the new-born. Neonates with thrombocytopenia associated with *maternal* autoimmune thombocytopenia (AITP) generally respond well to intravenous immunoglobulin (IVIgG) in a dose of 2 g/Kg body weight. Platelet transfusions have no value in prophylaxis of this condition but may be useful if there is bleeding.

Neonatal alloimmune thrombocytopenia (NAITP).

This is a rare, serious condition and specialist advice is required. NAITP is caused by maternal IgG alloantibodies against a fetal platelet specific alloantigen. High dose IVIgG (2 g/kg body weight) given to the neonate effective in about 50% of cases. However the treatment of choice is to give platelets, lacking the HPA 1a antigen. In the absence of suitable donor platelets, the mother's platelets may be used. They must be washed to remove the plasma which contains the platelet antibody and must be irradiated.

Haemolytic disease of the new-born (HDN).

What causes HDN.

Haemolytic disease of the new-born is caused by antibodies that are produced by the mother. These antibodies can cross the placenta and destroy the baby's red cells.

In the most severe cases of HDN the fetus may die *in utero* or be born with severe anaemia that requires replacement of red cells by exchange transfusion. There may

also be severe neurological damage as a result of a high bilirubin level. Effective care of the affected pregnancy and of the newborn requires the skills of a specialist team.

The antibodies that cause HDN are directed against antigens on the baby's red cells that are inherited from the father and are absent in the mother. The mother may develop these antibodies if fetal red blood cells cross the placenta (feto-maternal haemorrhage) during pregnancy or delivery. They may also result from a previous red cell transfusion.

Antibody to the Rh(D) antigen is the most important cause of HDN. It only occurs in pregnancies in Rh (D) negative women where the father is Rh (D) positive. The frequency of HDN due to anti Rh (D) has been greatly reduced by the prophylactic use of Rh(D) immunoglobulin and also because family sizes have become smaller.

Although ABO incompatibility between mother and fetus is common, severe HDN due to IgG anti-A and anti-B antibodies is very rare in caucasians in the UK. It is more common in some black populations. IgG antibodies against other blood group antigens (Rhe, RhC, RhE, Fy^a. K) occur in about 0.5% of pregnancies. These usually cause less severe morbidity than anti-Rh(D) because they result from a previous transfusion and because the father is often negative for the corresponding antigen. However if the fetus is positive for the antigen, the haemolysis can be as severe as in Rh(D) HDN.

Screening in pregnancy.

All pregnant women should have their ABO and Rh(D) group determined when they book for antenatal care at 12-16 weeks. This identifies Rh(D) negative mothers; the mother's blood is also tested for any IgG antibodies to red cells that could cause HDN. If these are found, the father's red cell type should also be determined. If he is homozygous for the antigen concerned the fetus will be positive also; if he is heterozygous, there is a 50% chance that the fetus will be positive. If an antibody is detected at booking, it should be monitored throughout the pregnancy in case the level of antibody increases.

If no antibodies are detected, Rh(D) negative mothers should generally have further antibody checks at 28-30 weeks gestation and at 34-36 weeks. Rh(D) positive mothers should be retested at 28-30 weeks if there is a history of red cell transfusion or hyperbilirubinaemia in a previous baby or if there are other risk factors for immunisation. Note that in some centres a simpler regime is used: this involves a check for red cell antibodies in all mothers at booking and again at 28-30 weeks.

If anti-D or other antibodies are found during early pregnancy the level should be checked every 2-4 weeks throughout the rest of the pregnancy and specialist advice must be obtained about managing the pregnancy and childbirth.

Prevention of HDN - use of Rh (D) immunoglobulin ("Anti-D").

This blood product is administered to the Rh (D) negative mother when there is a risk that fetal Rh (D) positive red cells may enter her circulation, usually due to a feto-maternal bleed. Anti-D prevents the mother from being immunised and starting to produce anti Rh (D) antibodies.

Anti-D should be given as soon as possible after delivery in a dose of 500 iu to a Rh (D) negative mother who has no Rh (D) antibodies and who has an Rh (D) positive infant. The prevention is less effective if Anti-D is given later, especially after 72 hours, but even if the correct time for the dose is missed, Anti-D should still be given as it may give some protection.

A 500 iu dose gives protection for feto-maternal haemorrhage of up to 4 ml red cells.

A Kleihauer test (which determines the number of fetal red cells in the mother's circulation) should be done as soon as possible after the baby is delivered when the dose of Anti-D is being given. If this shows that the feto-maternal bleed is larger than 4 ml, extra Anti-D must be given in a dose of 125 iu/1.0 ml of red cells. These larger bleeds often occur with interventions such as caesarian section, manual removal of the placenta in twin pregnancy or after abdominal trauma.

The laboratory tests to determine the mother's Rh (D) type must be able to detect variants of the Rh (D) antigen because these variants may require special management of Anti-D prophylaxis.

Rh(D) immunoglobulin should also be given to the Rh (D) negative mother in other situations where she may be exposed to the red cells of her fetus. These situations are stillbirth, abortion (including therapeutic abortion), threatened abortion, ectopic pregnancy, amniocentesis, chorionic villus or fetal blood sampling, external cephalic version, abdominal trauma (eg seat belt injury) and antepartum haemorrhage.

Since mothers with some of these conditions may be seen in general practice or in hospital emergency departments rather than in the obstetric unit, it is important to be alert to the risk and to check the mother's Rh (D) type. In these situations Anti-D immunoglobulin should be given without waiting to determine the probable Rh (D) type of the father.

Before 12 weeks gestation anti-D is not required because there is no evidence for the presence of the RH(D) antigen in foetal tissue. Up to 20 weeks gestation 250 iu should be given. Later 500 iu should be given and a Kleihauer screening test is advised. If there is repeated APH in pregnancy, the 500 iu dose should be repeated every 4-6 weeks. The level of Anti-D in the mother's blood can be monitored and should be kept above 0.25 iu/ml.

Rh(D) immunoglobulin should also be used to prevent immunisation if for any reason blood components containing Rh(D) positive red cells (eg platelet concentrates), or organs from Rh(D) positive donors (eg bone, kidney) have to be given to a Rh(D) negative woman of child-bearing age or if Rh(D) positive blood is inadvertently transfused. The dose is calculated to remove the estimated amount of red cells transfused, as explained above.

Routine antenatal prophylaxis with anti-D. There is evidence that anti-D given in the 3rd trimester (500iu at 28 and 34 weeks) can further reduce the incidence of

CHAPTER V - ADVERSE AFFECTS OF TRANSFUSION

sensitisation from the present UK level of 1.5% to about 0.2%. This practice is being introduced in some units in the UK.

Failure to protect. It is important to note that some Rh (D) negative women still develop Anti-D because of failure to give Rh (D) immunoglobulin as above. Careful attention to the running of the preventive programme is the only way of avoiding a risk of damage to the mother's future infants.

Management of HDN.

Because severe HDN is now rare, women who are at risk of an affected pregnancy should have access to care in a unit that maintains specialist experience through regular management of these problems.

The condition of the foetus must be monitored throughout pregnancy as there may be a need for early delivery or intrauterine transfusion.

Affected neonates may be extremely ill and require specialist intensive therapy.

ADVERSE EFFECTS OF TRANSFUSION

Overview.

Blood products, like other treatments can benefit or do harm to the patient. Good clinical practice depends on understanding both the benefits that the treatment can provide for an each patient and the risks that the treatment may carry for that patient. An essential part of the equation is to take account of the potential benefits and risks for the patient of NOT using a blood product or of using an alternative.

Where does responsibility rest for the various processes and decisions ~~elements~~ that make up good transfusion therapy? Essentially, the *manufacturers* must ensure the safety of the product, and *clinicians* must prescribe and use it correctly. There are additional important tasks for which the *hospital transfusion department* usually carries the main responsibility. Table 19 gives a framework for understanding these tasks, and responsibilities, and summarises aspects of safety that are often of concern to patients, parents, or relatives. Tables 26 and 27 provide a summary of all the important adverse effects.

Acute Haemolytic or bacterial transfusion reactions.

The features are summarised in Table 20.

It is important to monitor the patient for at least the first 15 minutes of the infusion of each unit of blood to detect the earliest clinical evidence of acute reactions due to incompatibility or bacterial contamination.

Incompatible transfused red cells react with the patient's own Anti-A or Anti-B antibodies. This reaction can activate complement and cause disseminated intravascular coagulation (DIC). Infusion of ABO incompatible blood almost always arises from errors in labelling the sample tube or request form or from inadequate checks when a red cell transfusion is being given.

If red cells are by mistake administered to the "wrong" patient, (i.e. any patient other than the one for whom the red cells were supplied) the chances of ABO incompatibility are about 1 in 3. The reaction is usually most severe if Group A red cells are infused to a Group O patient. In a conscious patient, even a few mls of ABO incompatible blood may cause symptoms within 1 or 2 minutes (Table 20). The patient becomes restless or distressed and may experience pain at the infusion site, flushing, abdominal, flank or substernal pain and breathlessness.

Table 19. RISKS OF TRANSFUSION TREATMENT - AN OVERVIEW			
Risk?	**Impact on Patients or Prospective Patients**	**Who is Responsible?**	**Impact on Health Care Providers**
Virus infections.	• Fear of receiving blood. • Anxiety. • Need reassurance. • Want alternatives or no blood. • Actual risk is extremely small.	Manufacturer of blood products Prescribing clinician	Very Substantial: Pressure for autologous transfusion, use of expensive drugs such as EPO. Risk of legal claims. High cost of trying to achieve zero-risk in transfusion.
Accidents e.g. receiving the wrong blood.	• Some patients worry about this. • Actual risk small but .... • Possibly under recognised.	Clinical Team HTD*	Risk of legal claims. Medicolegal risk to individual clinicians.
Bacterial contamination of blood product.	• Patients assume there is no risk. • Very hazardous when it happens. • Actual risk small.	Manufacturer of blood products. Anyone involved in transport and storage of blood products.	Risk mainly to blood product manufacturer and HTD.
Complications due to red cell antibodies other than anti-A + anti-B.	• Patients have little knowledge. • Occasionally hazardous • Actual risks due to reactions are very small but .... • Over caution can contribute to delays when transfusion is needed urgently	HTD should detect the antibodies and supply safe blood. Clinical team should keep (and read!) good. patient records and warn the hospital transfusion department of possible problems.	
Over transfusion (circulatory overload).	• Patients have little knowledge. • No data about incidence. • Probably under diagnosed & under reported	Clinical team.	
Non Febrile Haemolytic Transfusion Reaction	• Regular recipients of red cell and platelets often very aware. • Distressing and unpleasant - not life-threatening. • In at least 2% of transfusions to regular recipients. • Probably under reported	Clinical team. HTD and sometimes blood products manufacture.	Cause of sub optimal patient care, delays for the patient, extra hospital costs.
Not transfusing when it is necessary	• Patients expect this would never happen (apart from Jehovah Witness). • If fear of viruses is rampant, reluctance to transfuse may put elderly and frail patients at risk - there is no good data.	Clinical Team	

* HTD - Hospital Transfusion Department

In an unconscious or anaesthetised patient, hypotension and uncontrollable bleeding due to DIC may be the only signs of an incompatible transfusion. Oliguria is common and is often followed by acute renal failure.

Table 20. ACUTE HAEMOLYTIC TRANSFUSION REACTION - RECOGNITION

Signs and symptoms may occur after only 5-10 ml transfusion of incompatible blood; so observe the patient carefully at the start of the transfusion of each blood unit.

If the patient has any of the following stop the transfusion and investigate.

Symptoms:
- **Feeling of apprehension or "something wrong".**
- **Agitation.**
- **Flushing.**
- **Pain at venepuncture site.**
- **Pain in abdomen, flank or chest.**

Signs:
- **Fever.**
- **Hypotension.**
- **Generalised oozing from wounds or puncture sites.**
- **Haemoglobinaemia.**
- **Haemoglobinuria.**

Fever is often due to a cause other than acute haemolysis. As an isolated finding, a rise of 1.5° above baseline temperature during transfusion should be investigated.

In unconscious patients only the signs will be evident.

If an acute haemolytic transfusion reaction is suspected, the transfusion must be stopped and urgent steps taken to confirm or exclude this possibility. *The differential diagnosis must include infusion of bacterially contaminated blood.*

Treatment is described in Table 21.

Reactions due to red cell antibodies other than ABO.

Haemolytic reactions can be caused by other red cell antibodies in the recipient's blood, including anti-RhD, -RhE, Rhc and K (Kell). Reactions due to Anti RhD are rare since patients generally receive RhD compatible red cells. Reactions due to these antibodies are usually less severe than those caused by ABO incompatibility since they do not activate complement. Destruction of transfused red cells is mainly in the spleen or liver. The patient may experience fever, nausea and shivering. However,

Table 21. ACUTE HAEMOLYTIC TRANSFUSION REACTION - MANAGEMENT.	
Investigation	**Treatment**
1. Check again that the compatibility label of the blood unit corresponds with the patient's ID band, forms and casenotes. If a mistake is found tell the blood bank urgently since the unit of blood intended for your patient could be transfused to another patient. 2. Take 40 ml of blood for • Haematology: 5 ml in EDTA tube - FBC, platelet count, direct antiglobulin test (DAT), plasma haemoglobin. 5 ml in dry tube - Repeat compatibility testing. 10 ml in citrated tube - Coagulation screen prothrombin time, APTT, Fibrinogen. • Clinical chemistry: 10 ml for urea or creatinine and electrolytes. • Blood cultures: 3. Return blood pack(s) and giving set to the hospital transfusion department for bacteriology. 4. Check urinalysis. Start 24 hour urine function and haemolysis tests. 5. Run an ECG and check for evidence of hyperkalaemia. 6. Arrange for repeat coagulation screens and biochemistry 2-4 hourly.	1. Stop blood. Keep IV open with sodium chloride 0.9%. 2. Insert bladder catheter and monitor urine flow. 3. Give fluids to maintain urine output above 100 ml/h and if necessary give Frusemide 150 mg IV. 4. Insert a central venous pressure line and give fluid challenges of 100-200 ml sodium chloride 0.9% to help CVP between +5 and +10 cm water. 5. If no diuresis occurs after Frusemide, infuse 20% Mannitol 100 ml IV. 6. If urine flow 2 hours after 20% Mannitol and Frusemide is below 100 ml/h. *Seek expert advice - acute renal failure is likely.* 7. If bacterial contamination is suspected treat with broad spectrum intravenous antibiotics. e.g. *Seek expert advice.* 8. If patient has hyperkalaemia give 50 ml 50% glucose IV with 10 units of insulin IV. Follow with infusion of 10% dextrose containing 10 units of insulin over 4 hours. Resonium S by nasogastric tube, or rectally, may be needed to control potassium. 9. If Disseminated intravascular coagulation (DIC) develops give blood components guided by coagulation screen results. 10. If the patient needs further transfusion use rematched blood. There is no increased risk of a second haemolytic reaction.

the Jk (Kidd) and Fy (Duffy) antigens do activate complement and can cause severe intravascular haemolysis leading to renal and cardiac failure. Jk antibodies are often very difficult to detect in pretransfusion samples.

A falling Hb, or a rise in Hb that is less than expected, after transfusion together with a rise in bilirubin and a positive direct antiglobulin test indicates that the transfused red cells are being destroyed.

Delayed haemolytic transfusion reactions (DHTR).

In patients who have previously been immunised to a red cell antigen during pregnancy or by transfusion, the level of antibody to the blood group antigen may be so low that it cannot be detected in the pretransfusion sample. About 1% of parous women have red cell antibodies that are often undetectable by routine methods before transfusion. After transfusion of red cells bearing that antigen, a rapid, secondary immune response raises the antibody level so that after a few days, transfused red cells bearing the relevant antigen may be rapidly destroyed. The signs of this *delayed haemolytic transfusion reaction* appear 5-10 days after transfusion with fever, falling haemoglobin, jaundice and haemoglobinuria. Clinically significant delayed haemolytic transfusion reactions are rare. No DHTR was found in 530 patients who received almost 2,500 units of blood. Although DHTR is seldom fatal, it can cause further problems for a patient who is already seriously ill.

Non-haemolytic febrile transfusion reactions (NHFTR).

Fever or rigors during red cell or platelet transfusion affect 1-2% of recipients, mainly those who have been immunised to leucocyte antigens by pregnancy or previous transfusion. Antibodies in the patient's plasma react against transfused leucocytes in the blood component. The symptoms are shivering usually 30-60 minutes after the start of the transfusion, followed by fever. Most reactions can be managed by slowing or stopping the transfusion and giving an antipyretic e.g. paracetamol. (Table 22). It is important to remember that the symptoms could be due to an acute haemolytic transfusion reaction or bacterially contaminated blood. Recurrent, severe reactions in patients who require repeated transfusions of red cells or platelets may be prevented by the use of leucocyte depleted blood components. Initially microaggregate filters or buffy coat depleted red cells should be tried. Leucocyte removal filters which are much more expensive should be used if these other methods do not alleviate the reactions.

Allergic reactions.

The symptoms are urticaria and itch within minutes of the transfusion. Symptoms usually subside if the transfusion is slowed and antihistamine is given (e.g. chlorpheniramine 10 mg, by slow intravenous injection or intramuscular injection in patients who are not thrombocytopenic). The transfusion may be continued if there is no progression of symptoms after 30 minutes.

Chlorpheniramine (10 mg parenterally) should be given before transfusion when a patient has previously experienced repeated allergic reactions.

Table 22. PREVENTION OF ACUTE TRANSFUSION REACTIONS

- **Febrile non haemolytic transfusion reactions (FNHTR).**

  If the patient has had 2 or more FNHTR try:

  Paracetamol 1g orally 1 hour before transfusion.
  Paracetamol 1g orally 3 hours after start of red cell transfusion.
  Slow transfusion (RCC 4 hours, platelets up to 2 hours).
  Keep the patient warm.

  If the above measures fail, try:

  Apheresis platelets.
  Filtered red cells or platelets.
  Washed cells.

- **Allergic reactions.**

  If the patient has 1 severe or 2 minor allergic reactions:

  Chlorpheniramine (Piriton) 8 mg orally 30 minutes before transfusion.

- **Anaphylaxis.**

  Usually unpredictable.
  If the recipient is IgA deficient do not transfuse until you have obtained expert advice.

Anaphylaxis.

This is a rare but life-threatening complication. Treatment is summarised in Table 22. It may occasionally be associated with antibodies against IgA in patients who have extremely low levels of IgA in their plasma. If this is the suspected cause the patient should if possible not be transfused. Special products will be needed and the hospital transfusion department must be consulted.

Table 23. TREATMENT OF ANAPHYLACTIC REACTION DURING TRANSFUSION.

- **Stop the transfusion**
- **Maintain venous access with 0.9% saline**
- **Maintain airway and give oxygen**
- **Give adrenaline 0.5-1mg I.M., repeated every 10 minutes according to blood pressure and pulse until improvement occurs**
- **Give chlorpheniramine 10-20 mg by slow IV injection**
- **Give salbutamol by nebuliser**
- **Get expert advice. If in doubt get the duty anaesthetist.**

Transfusion related acute lung injury [TRALI].

This form of acute respiratory distress may be under-recognised. The cause is usually donor plasma that contains antibodies against the patient's leucocytes. Transfusion is followed by a severe reaction with chills, fever, non productive cough and breathlessness. The chest x-ray shows numerous mainly perihilar nodules with infiltration of the lower lung fields. The implicated donors are almost always multiparous women and are found to have antibodies to white cells.

Reporting to the Hospital Transfusion Department is important so that an implicated donor can be removed from the panel. Treat as for Adult Respiratory Distress Syndrome from other causes.

Fluid overload.

When too much fluid is transfused or the transfusion is too rapid, acute left ventricular failure (LVF) may occur with dyspnoea, hypotension and tachycardia. Standard medical treatment is a diuretic (e.g. frusemide 20mg IV initially) and oxygen. The transfusion should be stopped or slowed. Volume overload is a special risk with 20% Albumin solutions.

Patients with chronic anaemia are normovolaemic or hypervolaemic and may have signs of cardiac failure before any fluid is infused. If the patient must be transfused, give red cell concentrate, with diuretic therapy if required. Each unit should be given slowly and the patient closely observed. Restricting transfusion to one unit in each 12 hour period should reduce the risk of LVF.

Late complications of transfusion.

Iron Overload.

Transfusion dependant patients receiving red cells over a long period become overloaded with iron. Chelation therapy with desferrioxamine is used to minimise accumulation of iron.

Graft vs Host Disease (GvHD).

GvHD is a rare complication of transfusion caused by T-lymphocytes. Immunodeficient patients e.g. recipients of allogeneic bone marrow transplant recipients, and fetuses receiving intrauterine transfusions are at special risk for this disease.

GvHD has also occurred in immunologically normal patients after transfusion of a relative's blood (see page). Transfusion associated GvHD has a serious morbidity or mortality in 75-90% of affected patients. *Acute GvHD* begins 4-30 days after transfusion with high fever followed by a diffuse erythematous skin rash progressing to erythroderma and desquamation. Gastrointestinal and liver dysfunction occur and pancytopenia is common. *Chronic GvHD* occurs more than 3 months after transfusion and is manifested by thickening and atrophy of the skin. Bronchitis and interstitial pneumonitis may also be present.

GvHD is prevented by gamma irradiation of cellular blood components to a dose of 2500 cGy.

Immunosuppression.

Allogeneic blood transfusion alters the recipient's immune system in several ways. Two concerns are:

- Could tumour recurrence rates be increased? Prospective clinical trials have not shown a difference in the prognosis for transfused versus non transfused patients or for recipients of autologous, as opposed to allogeneic blood.

- Does transfusion increase the risk of postoperative infection? So far clinical trials have failed to prove that this occurs.

Post transfusion purpura (PTP).

PTP is a rare but potentially lethal complication of transfusion of red cells of platelets, most often seen in female patients. It is caused by platelet-specific alloantibodies. Typically 5-9 days after transfusion, the patient develops an extremely low platelet count with bleeding. Treatment is with high dose corticosteroids combined with high dose intravenous gammaglobulin. If platelet transfusion is unavoidable, platelets that

are compatible with the patient's antibody. should be used. Expert advice is needed in managing PTP.

Infections that can be transmitted by transfusion.

The perceptions of the risks of transfusion are greatly influenced by HIV transmission that occurred before today's safety testing procedures were available.

Blood donors, like anyone else, can occasionally carry an infectious agent, sometimes for a long period, without having any clinical signs or symptoms. For this reason, the laboratory tests shown in Table 24 are performed on *every* blood donation. No part of the donation can be released until all these tests are known to be clear. Computer systems are used to ensure that no blood with a positive test slips through the net.

There is very good evidence that with today's donor selection and testing procedures the risk is extremely small that a patient will acquire infection from blood products manufactured by the UK Transfusion Services. (Table 25) Blood products have become steadily safer over the year as previously unknown viruses have been identified and screening tests for them have been introduced. There has also been continuous improvement in the selection and testing of donors and in manufacturing processes. Inspection, regulation and licensing of the transfusion services by the Medicines Control Agency is an important contributing factor.

Table 24 . Infection Tests - Every donation is checked for:
• **Hepatitis B (HBsAg) virus antigen**
• **Hepatitis C (HCV Ab) antibody**
• **HIV1 and 2 (Anti HIV1, Anti HIV2) antibody**
• **Treponema pallidum antibody**

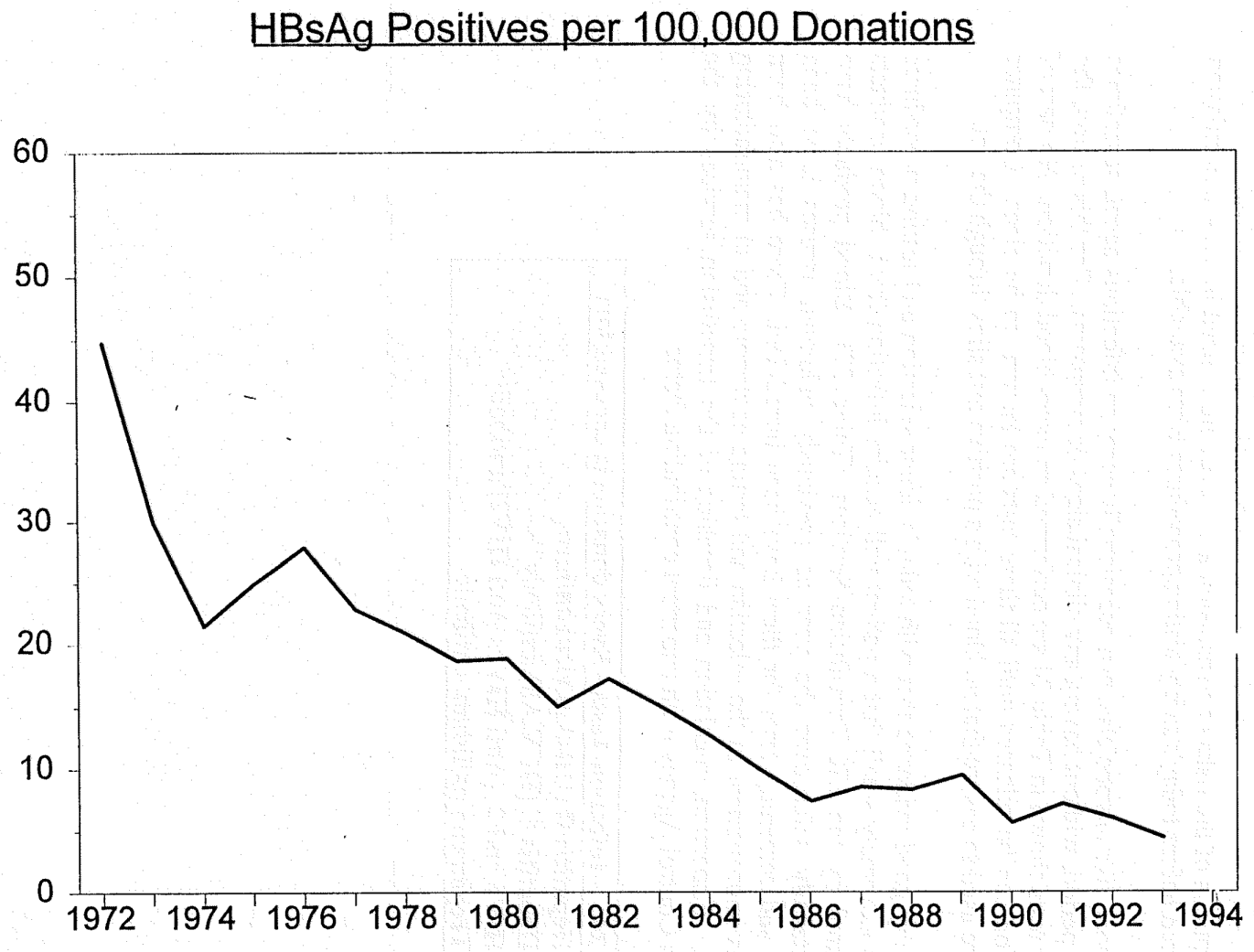


FIGURE 4. DECLINE IN HBsAg POSITIVE BLOOD DONATIONS IN THE UK 1972-1993.

We can see something of how effective the systems are from the results of check tests that are done on millions of donations before they are used to make Factor VIII and other plasma fractions. These show that the risk of a Hepatitis B or HIV positive donation slipping through the net is less than one per million.

The risk that a blood product may transmit an infectious agent depends on

- Prevalence in the community.
- Combined effectiveness of the processes used to exclude and detect infected donors.
- Viral inactivation.
- Immune status of the recipient.
- Number of individual donors contributing to each dose.

Table 25 gives estimates of the risks of virus transmission.

Table 25. RISKS OF TRANSFUSION-TRANSMITTED VIRUS INFECTIONS IN THE UK

- **Plasma fractions.**

  Minimal or zero risk of transmitting HIV, HTLV, HBV or HCV. Should protein enveloped viruses be present in donor plasma they may not be fully inactivated in all current products.

- **Blood components.**

  Not generally subjected to a viral inactivation step in production.

  HIV Current estimate 1 per million blood components transfused. Only one reported incident due to HIV-screened blood in the UK since late 1985 when screening commenced.

  HBV USA estimate: 1 per 200,000 components transfused in the USA. There is no UK estimate available.

  HCV Current estimates for UK and USA less than 1 per 30,000 components transfused.

  HTLV I/II UK Government Committee has estimated that a maximum of 3 recipients per year in the UK have any lifetime risk of developing HTLV associated disease.

Hepatitis B.

Figure 4 shows the steady reduction in the prevalence of Hepatitis B infection among blood in donors attending since the screening test first became available. Post transfusion Hepatitis B is exceedingly rare in the UK and no current figures for incidence are available.

Hepatitis C.

Serological tests to detect Hepatitis C virus infection were introduced in 1985 and the tests have been progressively improved since then. The incidence of post transfusion hepatitis has reduced sharply: less than 1 in 3000 blood components result in Hepatitis C infection. The infection is usually asymptomatic and revealed only by disturbed live enzyme tests. About half the affected patients develop chronic hepatitis that can lead after some years to severe liver damage.

Other Hepatitis viruses.

Hepatitis A and Hepatitis E may very occasionally be transmitted by blood products. Further viral processes are being introduced to inactivate protein-enveloped viruses such as Hepatitis A in plasma fractions.

HTLV (I and II).

HTLV can cause neurological disorders and a rate form of adult T-cell leukaemia. There is a latent period usually of many years between infection and development of illness. It is likely that only a small proportion of those infected become ill. HTLVI is transmissible by the transfusion of cellular blood components. The prevalence of infection is high in some parts of the world, notably Japan and the Caribbean. The link between HTLV II infection and disease is less clear, but infection is found in some intravenous drug users. Surveys in the UK indicate that the risk of HTLV related-disease following transfusion of blood is exceedingly low. Blood donors in the UK are not currently screened for HTLV I/II infection.

CMV

Approximately 50% of UK blood donors have antibody to CMV, but only a small proportion of antibody positive donations transmit the virus through transfusion. Transfusion transmitted CMV is of proven clinical importance in premature infants weighing less than 1200-1500g who are born to CMV antibody-negative mothers, and in CMV antibody-negative bone marrow allograft recipients who receive CMV sero-negative grafts. Although the risk of clinical CMV infection is much smaller in recipient of autografts, some centres recommend that these patients also should receive CMV negative products, For these patients CMV safe blood components should be given. This is normally done by using donations that do not contain detectable antibody to CMV. An alternative is the use of leucocyte depleted blood components. Fresh frozen plasma and cryoprecipitate do not transmit CMV.

Human parvovirus B19.

This protein-enveloped virus may not be activated in all current plasma fractions. Processes are being introduced to do this. There is evidence that HPV B19 infection is associated with bone marrow suppression affecting red cell production in occasional patients.

Treponemal infections.

All donations are screened for serological evidence of Treponema pallidum infection. A further safeguard is that infectivity of pallidum declines as blood is stored at 2-6°C. Transfusion transmission is estimated to occur with a frequency of about 1/40,000 in the USA. There appear to be no reports of transfusion transmission in the UK in recent years.

Chagas disease, caused by T cruzii is transmissible by transfusion. This is an important problem in some South American countries where the infection is prevalent.

Other bacterial infections.

Very rarely, bacterial contamination of a blood component occurs. This is a cause of very severe and often lethal transfusion reactions. In the UK, 16 incident (9 fatalities) were identified during the 5 years to 1990, giving a rate of about 2/million units transfused. Bacteria associated with severe septic reactions to red cell transfusion are usually cold-growing strains: pseudomonas fluorescens, the type most often isolated is an environmental contaminant. Yersinia enterocolitica is an example of an organism that may enter a blood donor pack that is collected during an episode of asymptomatic bacteraemia. Skin contaminants such as staphylococci may proliferate in platelet concentrates stored at 20-22°C and this is a factor limiting the safe storage life of platelet concentrates.

Malaria.

Donor selection procedures are designed to exclude potentially infectious individuals from donating red cells for transfusion. Transfusion transmitted malaria occurs with a frequency of about 0.25/million units collected in the USA. Comparable data for the UK are not available.

Table 26. ACUTE COMPLICATIONS OF TRANSFUSION				
PROBLEMS	**CAUSE**	**WHEN? HOW OFTEN?**	**HOW DANGEROUS**	**TREATMENT AVOIDANCE**
Acute intravascular haemolysis of transfused red cells.	ABO incompatible transfusion. Group A donor into Group O recipient is worst.	Often during first few ml of infusion. About 1 in 500,000 red cell units transfused.	Mortality. 10% due to DIC and acute renal failure. Prevent: use safe documentation and checking systems or blood administration.	*Treat:* Table . *Avoid:* Page .
Infective shock.	Bacterial contamination of red cells or platelets with e.g. Pseudomonas, Yersinia, staphylococci.	Usually during infusion of first 100 mls of the contaminated pack. 2/million blood components transfused (UK)	Very high mortality Treat: manage septicaemia. Fluids and intravenous antibiotics e.g. gentamicin plus ceftazidime.	
Transfusion Related Acute Lung Injury. Non cardiogenic pulmonary oedema.	Donor plasma has antibody to patient leucocytes: aggregates trapped in lungs	During or soon after transfusion. *Rare:* Greater risk if large volumes of donor plasma given e.g. whole blood or plasma exchange with donor plasma.	Life-threatening.	*Treat:* Respiratory support, diuretics and high dose steroids. *Avoid:* • Don't transfuse, especially plasma • Donor selection.
Non-Haemolytic Febrile Reactions (NHFTR) to transfusion of platelets and red cells.	Antibodies to transfused white cells. Usually from previous pregnancies or transfusions.	Within hours. About 2% of all transfusion episodes. Mostly in patients who have had several previous transfusions.	Unpleasant, specially if the patient requires regular transfusions.	*Treat:* Paracetamol. *Avoid:* Use leucocyte reduced or depleted cellular components.
Urticaria (allergic reaction)	Patient has antibodies that react with proteins in transfused blood components.		Unpleasant.	*Treat:* Temporarily stop infusion and give chlor-pheniramine 10-20 mg iv. *Avoid:* Pre-medicate with chlorpheniramine 10-20mg iv before transfusion.

Table 27. **DELAYED COMPLICATIONS OF TRANSFUSION**

PROBLEMS	CAUSE	WHEN? HOW OFTEN?	HOW DANGEROUS	TREATMENT AVOIDANCE
Delayed haemolysis of transfused red cells.	Patient has IgG antibodies to red cell antigens usually Rh c, E. C Kidd - Jk^a Duffy - Fy^a Kell - K	5-10 days after red cell transfusion. Less than 1/500 episodes of red cell transfusion.	Reduced survival of transfused red cells so transfusion may be less clinically effective. Consequences of haemolysis can complicate other conditions.	*Treat:* • No treatment for antibodies per se. • Once present, they are a problem for future red cell transfusions so: *Avoid:* • Write prominently in case notes. • Inform the hospital transfusion department when you next request red cells to transfuse the patient. • Good practice in pre-transfusion testing.
Development of antibodies to red cells in the patient's plasma (allo-immunisation)	Transfusion of red cells of a different phenotype from the patient. Also caused by foetal to maternal bleeding during pregnancy and child birth.	Days to weeks after transfusion. Anti Rh (D) will develop in at least 75% of RH (D) negative patients transfused with a unit of Rh (D) positive cells. Other red cell antigens stimulate antibodies much less frequently. 1-5% of previously transfused or parous patients have red cell antibodies. Antibodies are much more common in female patients.	Only dangerous if the patient later receives a red cell transfusion!	*Treat:* • No treatment for antibodies per se. *Avoid:* • Write prominently in case notes. • Inform the hospital transfusion department when you next request red cells to transfuse the patient. • Good practice in pre-transfusion testing.

Table 27. **DELAYED COMPLICATIONS OF TRANSFUSION**				
PROBLEMS	**CAUSE**	**WHEN? HOW OFTEN?**	**HOW DANGEROUS**	**TREATMENT AVOIDANCE**
Development of antibodies that react with antigens of white cells or platelets.	Transfusion of blood cells of a different phenotype from the patient. Pregnancy.	About 40% of patients receiving platelet support for more than 2 weeks develop leucocyte and/or platelet antibodies. More likely if patient has a previous pregnancy.	Patient antibodies to HLA antigens may contribute to a poor clinical response to platelet transfusion. Page .	*Treat:* • No treatment for the antibodies per se. • If antibodies reduce clinical response to platelet transfusion, 'compatible' platelets may help (page). *Avoid:* • Use effectively leucocyte depleted red cells and platelets.
Iron overload.	One unit of red cells contains 250 mg of iron. It accumulates in the blood over a long course of red cell transfusion.	Clinical problems after several years of regular transfusion. Common in long term recipients of frequent red cell transfusion.	Liver damage and other problems are serious.	*Avoid:* • Planned transfusion regime. • Use chelating agent to increase iron excretion.

CHAPTER VI - INFORMATION FOR PATIENTS

INFORMATION FOR PATIENTS

An outline for a "patient's guide".

This leaflet explains why transfusion of blood is sometimes necessary. You may need transfusion as a planned part of your medical treatment or, if you are having an operation, it may be needed to replace blood loss. Although your consent to operation includes transfusion, it is important that you understand the reasons why Blood Transfusion might be advisable before you are asked to agree.

Transfusion of blood or individual constituents of it are given to correct abnormalities in your own blood system. This treatment is only advised when these abnormalities cannot be corrected by any other means. Common reasons for giving transfusion include:

1. **Loss of blood.**

   An adult has about 10 pints of blood. Loss of small amounts, up to a pint of blood for example during blood donation causes no problems. Often loss of larger amounts does not need blood transfusion since other fluids, for example salt and water solution or synthetic substances such as dextrans or gelatin can replace the loss. The loss of a larger amount of blood can be extremely dangerous unless blood or a constituent of blood is given. For some operations, surgeons need to have blood available in case blood loss is more than expected.

2. **Anaemia.**

   Anaemia means that the amount of red cells in the blood is low. Anaemia often causes tiredness and breathlessness because the blood cannot carry enough oxygen to where it is needed in the body. There are many different causes for anaemia. Often treatment by drugs or vitamins is effective. If the anaemia does not respond or where rapid recovery is essential, blood transfusion may be the most effective form of treatment.

3. **Bleeding, blood clotting and other problems.**

   Sometimes blood loses the ability to clot properly so that bleeding after injuries continues for a long time. These problems can often be corrected either by giving transfusions of blood products made from blood. These are usually purified clotting substances (for example the substance that haemophiliacs lack) or cells known as platelets that can be extracted from blood donations.

How does your doctor decide what to advise?

Your doctor has to decide when transfusion is the best remedy for the problem you have. Alternative treatment may be available and your doctor will decide whether these can be used instead. Blood transfusion treatment like other forms of treatment including medicines carries a very small risk of harmful effects. Doctors weigh these potential risks very carefully against the benefits of transfusion.

What are the risks?

Millions of transfusions, saving many lives, are given every year in the United Kingdom. The vast majority of these cause no harmful effects. HIV infection (the virus that causes AIDS) is perhaps the best known risk but the chance of this in the United Kingdom is less than one in a million. This safety is the result of very stringent measures taken by the Blood Transfusion Service to ensure the safety of the blood supply. Hepatitis

SOURCES OF INFORMATION

(jaundice) is another possible complication. Every blood donation is tested for the viruses that cause hepatitis and AIDS.

Clotting factors and other blood protein products undergo virus killing processes that further reduce the risk of transmitted infection.

Other temporary side effects such as feverish reactions may occur. These are minimised by careful selection of blood in the hospital transfusion laboratory. They are usually insignificant compared with the expected benefit of your transfusion.

Can I use my own blood for transfusion instead?

In some circumstances this is possible and sometimes it may be recommended. Your doctor will advise you about whether this would be useful in your own individual circumstances.

The Blood Transfusion Service in Great Britain is fortunate in having the support of very large numbers of voluntary blood donors whose only reward is the knowledge that they are giving blood for the benefit of others. For this reason the safety of blood transfusion in the United Kingdom is recognised to be as good as the best in the World.

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Evidence - base for this handbook - availability.

The editorial team have agreed to assemble a floppy disk version of this book that will provide easy access to sources of evidence that underly the statements in this book.

Readers who are interested in helping us to develop this product or in using it once it is available may wish to contact the editor.

ADDRESSES

Table 28. TELEPHONE/FAX/E-MAIL NUMBERS OF REGIONAL TRANSFUSION CENTRES			
	Tel No.	**Fax No.**	**E-Mail.**
National Blood Authority (HQ)	01923-212121	01923-211031	
Newcastle Blood Transfusion Centre (Northern)	0191-261-1711	0191-232-4554	
Leeds Blood Transfusion Centre (Yorkshire)	01132-645091/2/3	01132-603925	
Sheffield Blood Transfusion Centre (Trent)	01142-424242	01142-435083	
Cambridge Blood Transfusion Centre (East Anglia)	01223-245921	01223-411618	
North London Blood Transfusion Centre (**Colindale**)	0181-200-7777	0181-200-3994	
Essex Blood Transfusion Centre (**Brentwood**)	01277-223545	01277-225662	
South Thames Blood Transfusion Centre (**Tooting**)	0181-672-8501/7	0181-767-4462	
Southampton Blood Transfusion Centre (Wessex)	01703-776441	01703-704067	
Oxford Blood Transfusion Centre	01865-741188	01865-741343	
Bristol Blood Transfusion Centre (South West)	01179-507777	01179-592552	
Birmingham Blood Transfusion Centre (West Midlands)	0121-414-1155	0121-414-1308	
Liverpool Blood Transfusion Centre (Mersey)	0151-709-7272	0151-709-0392	
Manchester Blood Transfusion Centre (North West)	0161-273-7181	0161-274-3941	
Lancaster Blood Transfusion Centre (North West)	01524-63456	01524-62602	
Cardiff Blood Transfusion Centre (Wales)	01222-890302	01222-890825	
Belfast Blood Transfusion Centre (Northern Ireland)	01232-321414	01232-439017	
Scottish National Blood Transfusion Centre (HQ)	0131-664-2317	0131-658-1639	
Aberdeen Blood Transfusion Centre (North East Scotland)	01224-685685	01224-662200	
Dundee Blood Transfusion Centre (East Scotland)	01382-645166	01382-641188	
Edinburgh Blood Transfusion Centre (North East Scotland)	0131-536-5300	0131-536-5352	
Glasgow & West of Scotland Blood Transfusion Centre	01698-373315/8	01698-356770	
North of Scotland Blood Transfusion Centre (**Inverness**)	01463-704212/3	01463-237020	
Dublin Blood Transfusion Board	00-353-1-603333	00-353-1-603419	
Cork Blood Transfusion Service Board	00-35-21-968799	00-353-21-313014	

REPLY CARD

HANDBOOK OF TRANSFUSION MEDICINE (2ND EDITION)

- I have the following comments

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  Name: _____ Position: _____

  Address: _____

  _____

  Postcode: _____ Tel/Fax No._____

Comment to HMSO:

*** Publisher - who should this be addressed to?!**

GLOSSARY OF TERMS, ABBREVIATIONS AND ACRONYMS

GLOSSARY OF TERMS, ABBREVIATIONS AND ACRONYMS

Apheresis (Single Donor) Platelet Concentrate	Platelets prepared by apheresis of the donor
Apheresis (Single Donor) Plasma	Plasma prepared by apheresis of the donor
Artificial Colloid Solutions	Gelatins, dextrans, hydroxyethyl starch
Anti-D Immunoglobulin	Human IgG preparation containing a high level of antibody to the Rh(D) antigen
Autologous Transfusion	General term for several techniques e.g. - preoperative blood donation - perioperative isovolaemic haemodilution - salvage from operation site (intraoperative) - salvage from operation site (postoperative)
BCSH	British Committee for Standards in Haematology
Blood Components	Whole blood, red cells, plasma, platelets, cryoprecipitate prepared in the Regional Transfusion Centre
Blood Products:	Any therapeutic product derived from human whole blood or plasma donations
CABG	Coronary artery bypass grafting
CMV	Cytomegalovirus
Crystalloid Solutions	Saline, Ringer's lactate etc.
DAGT	Direct antiglobulin test (Coomb's test) - sensitive method to detect red cell bound antibody
DIC	Disseminated intravascular coagulation
Epoietin	Approved name for recombinant human erythropoietin

FFP	Fresh frozen plasma. Plasma that is frozen within a specific time period after collection and stored in the frozen state until thawed for transfusion or crushed for fractionation.
GvHD	Graft versus host disease
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HEV	Hepatitis E virus
HTLV	Human T Cell Lymphotropic viruses
Human Parvovirus B19	A non-enveloped virus transmissible by blood products and potentially pathogenic in some groups of patients
Kleihauer Test	Acid elution of blood film to allow counting of foetal cells in maternal blood
Massive Transfusion	Transfusion in acute haemorrhage, defined variously as replacement of 1 blood volume within 24 hours, replacement of 1 blood volume *with whole blood* in 24 hours, etc.
NANB Hepatitis	Non A Non B hepatitis: former operational term for the most common class of post-transfusion hepatitis. Now known to be largely due to Hepatitis C virus, and >80% eliminated by HCV screening of donations.
PCC	Prothrombin complex concentrate
Plasma Fractions	Partially or highly purified human plasma proteins prepared under pharmaceutical manufacturing conditions and generally licensed by MCA
PTH	Post-transfusion hepatitis

Recovered Plasma	Plasma prepared from individual donations of whole blood
Recovered ('Random Donor') Platelet Concentrate	Platelets prepared from individual donations of whole blood
Red Cells	In the text of this report, the term is used for any red cell component unless otherwise stated
Rh(D)	The most immunogenic antigen of the Rhesus blood group system
TPH	Transplacental haemorrhage
TTP	Thrombotic thrombocytopenic purpura
Viral Inactivation	Additional manufacturing step in making blood products: validated to remove or substantially reduce infectivity for specified viruses. Some viruses may not be reliably inactivated by all the current methods.

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