Reference H
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# Notes on Transfusion

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# NOTES ON TRANSFUSION

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for the

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This edition of "Notes on Transfusion", like its predecessors, has been prepared by a Committee of the Regional Transfusion Directors.

The booklet is intended primarily for use by Medical staff of hospitals and its purpose is to describe briefly some of the principles of the practice of transfusion and to suggest procedures; it is not intended that recommendations in this booklet should supersede established local practices and procedures without the agreement of those concerned. The notes are not exhaustive or exclusive, for the subject is too large for all methods and procedures in use to be described.



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# NOTES ON TRANSFUSION

Transfusion therapy should be undertaken only after careful assessment of the patient's clinical condition to determine the nature and quantity of fluid to be transfused and the rate of administration. The patient may require whole blood, plasma reduced red cells, or other blood components or one of the plasma fractions. The nature and quantity of fluid transfused and the rate of administration are determined by initial clinical examination and subsequent response to therapy.

**A transfusion should never be given without a definite indication; not only is this in the patient's interest, since an element of risk is associated with every transfusion, but supplies of blood are limited and with the ever-growing demand for blood it is imperative that it should not be used unnecessarily.**

**The use of transfusion to correct moderate or slight degrees of anaemia that could be overcome as effectively, if more slowly, by other means, seems unjustifiable unless some cogent reason for speed of recovery exists. In some instances failure to institute simpler and safer but equally effective treatment earlier leads to the quite unnecessary use of blood transfusion.**

## I. CHOICE OF FLUID

1. WHOLE BLOOD is supplied in sealed plastic packs containing approximately 500 ml anticoagulated blood. This includes about 420-450 ml donor blood and 63 ml citrate phosphate dextrose (CPD), CPD-Adenine (CPD-A) or other B.P. or U.S.P. approved anticoagulant.

**Uses:** It is specifically indicated in situations of massive acute haemorrhage where all blood components are required in large amounts. It is not good transfusion practice to use whole blood where there are known deficiencies of single components such as red cells, platelets or plasma components, where concentrates of these elements are more appropriate and clinically more effective.

**Storage:** Whole blood should be stored only in a special blood bank refrigerator designed for the purpose, complying with British Standard Specification No. 4376 (1982) and under the constant supervision of a responsible doctor – normally the hospital Haematologist.

THE BLOOD BANK REFRIGERATOR SHOULD NOT BE USED FOR THE STORAGE OF FOOD OR PATHOLOGICAL SPECIMENS. DOMESTIC REFRIGERATORS IN WARDS MUST NOT BE USED FOR THE STORAGE OF BLOOD BECAUSE OF THE POSSIBLE VARIATION IN INTERNAL TEMPERATURE BEYOND THE ACCEPTED RANGE.

The correct temperature for the storage of blood is 4°C to 6°C. These limits must be rigidly observed to preserve the red cells and minimise the multiplication of chance bacterial contaminants. Blood must NEVER be allowed to freeze. Transfusion of blood which has been frozen and thawed may cause death.

The refrigerator should have an automatic temperature recording device and a battery-operated alarm system; exceptionally, where this is not possible, a maximum and minimum thermometer should be provided and the temperature recorded morning and evening in a book. Preferably the automatic temperature recording device should be driven by clockwork (so that it will continue to operate during a mains failure) and should record the temperature of water in a bottle within the refrigerator; the battery-operated alarm should be activated by the air temperature within the refrigerator, the level of activation chosen being such that the alarm will not ring when the refrigerator is opened in the course of normal use.

The time during which blood is out of the refrigerator or other cold storage (except in an insulated box) should be kept to a minimum and should not exceed 30 minutes on any one occasion, after which the blood should immediately be cooled again to between 4°C and 6°C. Blood which has been out of cold storage for longer periods should not be reserved for future use but should be appropriately labelled and set aside for return to the Regional Transfusion Centre. Containers of blood which have been partly used should NOT be re-used because of infection risk (See Section VI 7), but labelled appropriately and returned to the hospital blood bank.

Sometimes there is delay between the time at which blood is issued from the blood bank and the time when it is to be used, for example, in the operating theatre. On such occasions the blood should be kept in a refrigerator at 4°C to 6°C until it is used, or if there is no refrigerator, it should be issued in an insulated box.

It is advisable to reserve a clearly defined part of the refrigerator for containers of time-expired blood and blood which has become unfit for use for any other reason. These should not be discarded or allowed to accumulate but should be returned to the Regional Transfusion Centre at the earliest opportunity.

An accurate record of all blood issues and returns should be kept (See Section V).

**Suitability for use**

i. It is almost impossible to detect abnormal haemolysis in packs by simple visual inspection. A white layer on the surface of the plasma is usually fat and is not a contra-indication to use.



ii. All packs should have an expiry date clearly marked. Blood which has passed its expiry date should not normally be used.

iii. Any pack of blood in which cells have settled under gravity or following centrifugation should be carefully and thoroughly mixed to re-suspend the cells before use.

iv. All packs must be intact, showing no signs of damage or leakage.

2. PLASMA REDUCED BLOOD consists of packs of whole blood from which 180-220 ml plasma plus anticoagulant have been removed. The contents of each pack have a haematocrit of 60-65% and are less viscous than concentrated red cells (q.v. 4 below).

**Uses:** Plasma reduced red cells can be used for most transfusions where red cells are needed other than perhaps continuous massive transfusion where whole blood is preferable, with or without additional specific components.

**Storage and suitability for use:** as for whole blood.

3. RED CELLS IN OPTIMAL ADDITIVE SOLUTIONS are preparations of red cells from a pack of whole blood from which almost all the plasma has been removed, and replaced with about 100 ml of a solution such as saline/adenine/glucose/mannitol which is formulated to give optimal red cell preservation. The contents of such packs have a haematocrit of about 60-65% but a fiscosity approximating to that of whole blood.

**Uses:** as for plasma reduced blood.

**Storage and suitability for use:** as for whole blood.

4. CONCENTRATED RED CELLS are red cells in a pack from which plasma has been removed to the extent that the haematocrit is in excess of 70%. Availability varies from Region to Region.

**Uses:** They are valuable for treating some anaemias where it is essential solely to raise the haemoglobin level of a patient who is normovolaemic and will not tolerate a significant expansion of the blood volume.

**Storage and suitability for use:** as for whole blood.

5. WASHED RED BLOOD CELLS are red cells which have been centrifuged free of native plasma and re-suspended in saline.

**Uses:** They may rarely be indicated for those patients who react to the plasma of whole or plasma reduced blood (e.g. patients with strong anti-IgA antibodies).

**Suitability for use:** Because the packs have to be broached to replace the plasma, washed cells should be used IMMEDIATELY and certainly within 12 hours of preparation.

6. FROZEN RED BLOOD CELLS can be obtained from a few Regional Transfusion Centres and may be:

i. cells from normal healthy donors having exceedingly rare blood groups

or

ii. patients' own cells bled and stored previously in anticipation of later illness, e.g. transplant recipients or patients with atypical antibodies which react with almost the entire population.

Both the freezing process and the recovery of frozen cells take several hours and like washed cells (q.v. 5 above) require "open" processing. Frozen cells should therefore be used within 12 hours of thawing and recovery.

7. MICROAGGREGATE FREE RED CELLS. Citrated whole and plasma reduced blood shows a progressive tendency during storage for clumping or aggregation of effete cells, mainly leucocytes with platelets and some red cells. Only the bigger clumps (over 170 μ diam.) are retained by the standard giving set filters. Large numbers of microaggregates are reported to cause partial blockage of the recipient's pulmonary circulation.

**Uses:** Microaggregate filters are not normally necessary but may be desirable where transfusions of more than four units are anticipated, and older blood is used. They are *not* needed for blood under one week old.

NOTES: i. These filters do not retain white blood cells efficiently. If the patient has problems due to white cell antibodies then the use of leucocyte poor blood is more appropriate (see 8 below).

ii. Where microaggregate filters are used, blood flow rates are slow.

8. LEUCOCYTE POOR BLOOD. Some patients develop white blood cell antibodies as a result of previous pregnancies, transfusions or transplants, and may then react adversely to the leucocytes in transfused blood. These patients may uneventfully tolerate red cells from which most of the accompanying leucocytes have been removed. This is achieved either by use of an automated blood processor, leucocyte-removing filter, or in some Centres by inverted centrifugation, by



dextran sedimentation of the red cells or by use of frozen red cells (since washing to remove the cryo-protective agent eliminates most white cells also).

**Uses:** Patients as above who have already had more than one febrile reaction to whole or plasma reduced blood, should be investigated for the presence of white cell antibodies and be considered as candidates for leucocyte poor blood.

**Suitability for use:** Leucocyte poor blood should be used as soon as possible, and within 12 hours of preparation.

All eligible cases should be discussed with the hospital Haematologist.

9. WHITE CELLS. Concentrates of leucocytes, especially granulocytes, can be obtained by creaming off the buffy layers from packs of fresh blood, though many are needed: it requires up to 20 packs to provide one therapeutically effective dose for an average adult. More efficiently, granulocytes can be harvested by machine leucapheresis, though only in a few specialised Units.

All eligible cases should be discussed with the hospital Haematologist.

10. PLATELET PREPARATIONS are usually made from random units of freshly collected blood. A commonly used method of preparation is to centrifuge the blood slowly to make a supernatant of platelet rich plasma which is decanted into a second pack. Although this platelet rich plasma can be issued and used as such, in most Centres it is centrifuged again, rapidly, to sediment the platelets. The second supernatant is then decanted to leave a platelet concentrate which is resuspended in 40-60 ml plasma.

In some Regions, platelet concentrates are prepared from single donors who have been plateletpheresed on a cell separator.

**Uses:** Platelet concentrates may be indicated in patients with severe thrombocytopaenia using the following general guide:

a. Patients with platelet count less than $10 \times 10^9$/L should be treated.

b. Patients with platelet count $10\text{-}20 \times 10^9$/L with evidence of haemorrhage should be treated.

c. Patients with counts $20\text{-}50 \times 10^9$/L or on chemotherapy, may or may not need platelets.

Opinions vary on whether or not to give platelets prophylactically in the absence of haemorrhage.

Concentrates are issued either as packs derived from single blood donations, or in some Regions may be supplied as pools. The platelets from six standard donations (or equivalent) provides an adequate therapeutic dose for the average adult.

Platelets should be given through a recipient set with a filter. Do not use a microaggregate filter or inject the concentrates by syringe without a suitable filter. To ensure that the patient receives the full dose, a small volume of saline, say 100 ml, should be run through the recipient set after the infusion has been given.

**Storage:** Platelet concentrates should be stored at 22°C with continuous gentle agitation, preferably on a suitable rotator. Their "shelf life" is usually up to 3 days, though may be up to 5 days in new formulation plastic packs which allow improved gaseous exchange.

**Suitability for use:**

i. All platelets should be used *as soon as possible* on receipt because of their short life-span, and the risk of contamination in any packs which may have been pooled.

ii. Platelet packs have very variable numbers of red cells in them. For most patients this does not matter provided platelets of the same or compatible ABO group are given. The rhesus group may be immaterial in treating patients suffering from leukaemia. Compatibility tests are not usually necessary.

iii. Platelet packs should be intact showing no sign of damage or leakage.

11. PLASMA PROTECTION FRACTION (syn. Human Albumin Fraction (Saline), B.P.: P.P.F.: Stable Plasma Protein Solution, Ph. Eur.: S.P.P.S.) is supplied as 4.5 g/dl protein solution in bottles each containing 400 or 500 ml, or 100 ml for paediatric use. This solution exerts slightly less colloid osmotic pressure than an equal volume of plasma. Not less than 85% of the protein has the electrophoretic mobility of albumin, the remainder being globulins. The solution is stabilised with n-octoate and is heated to be free of hepatitis B virus. The solution contains 130-160 millimoles sodium per litre and not more than 2.0 millimoles potassium per litre. It does not contain clotting factors or pseudocholinesterase.

**Uses:**

i. Oligaemic shock following haemorrhage. P.P.F. may be used as a plasma expander following blood loss with trauma, surgical procedures or childbirth etc. It can be given either on its own, or while compatible blood is awaited.



ii. Burns and crush injury.

iii. Plasma exchange (see also Section XII). P.P.F. is used as a replacement fluid. Note, this form of treatment also reduces normal plasma components e.g. coagulation factors, unless replacement is supplemented with fresh frozen plasma (See 13 below), although the latter has to be used with caution.

iv. P.P.F. may be given without regard to the blood group of the recipient.

**Storage:** P.P.F. should be kept between 2° and 25°C in the dark.

**Suitability for use:**

i. The solution should be crystal clear and free from deposits.

ii. For non-N.H.S. commercial equivalent products, users are recommended to refer to manufacturers' guidance.

12. SALT POOR HUMAN ALBUMIN (B.P.); HUMAN ALBUMIN (Ph. Eur.) is provided as a 5% solution in bottles containing 20 g protein, of which not less than 95% has the electrophoretic mobility of albumin. The solution is stabilised with n-octoate and is heated to be free of hepatitis B virus. 100 ml human albumin solution is osmotically equivalent to 400 ml plasma. Compared with P.P.F. (see 11 above) it contains less sodium per gram of protein (not more than 0.65 m.mol/g q.v.3.1 m.mol/g) though about the same amount of potassium. It also contains neither coagulation factors nor pseudocholinesterase.

**Uses:**

i. In certain disorders of the liver with severe hypoalbuminaemia and generalised oedema. Although the value is uncertain, it has been claimed to be advantageous if given as a short and intensive course, particularly to patients undergoing major surgery, who have developed bacteraemia, or who are under intensive care for other reasons.

ii. In some nephrotic patients with the aim of inducing a diuresis. Its precise role in this situation is not clear.

iii. In the acute respiratory distress syndrome in adults where it may have a restricted use.

The use of 5% albumin solution, combined as necessary with diuretics enables relatively large amounts of protein to be given in a small volume of liquid. Haemodilution occurs rapidly after infusion and particular care must be exercised if any cardiac disorder is also present; if the patient is dehydrated, additional fluid should be given.

The dose to be given may be calculated as follows:

2 (D-A) x PV = Dose Albumin in g, where D and A are the desired and actual albumin levels in g/l (a minimum of 30 g/l should be aimed for) and PV is the plasma volume in litres, either known or estimated from 0.04 x body weight in Kg.

In practice, each bottle will raise the serum albumin level of the average adult by about 4 or 5 g/l.

It is recommended to give the required dose over about 12 hours to avoid gross fluid shift in the circulation, and to reassess progress before giving further doses.

**Storage:** Human albumin solution should be kept between 2° and 25°C in the dark.

**Suitability for use:** The solution should be crystal clear and free of deposits.

13. FRESH FROZEN PLASMA "F.F.P." is citrated plasma which has been separated from the red cells of single donor units immediately after collection and stored frozen when all coagulation factors are satisfactorily preserved for several months.

**Uses:**

i. In the management of certain specific disorders of clotting, particularly von Willebrand's disease and the milder form of Christmas disease (Factor IX deficiency).

ii. In more general haemostatic failures such as disseminated intravascular coagulation where all clotting factors may be deficient.

iii. In plasma exchange therapy (see also Section XII).

**Storage:**

i. Packs of F.F.P. should be stored at or below -30°C and protected from damage (the plastic is more brittle at this temperature).

ii. Maximum recommended shelf life under these conditions is six months.



**Suitability for use:**

i. All packs should be intact, showing no sign of leakage.

ii. Recipients should be given F.F.P. from a donor of the same or at least a compatible ABO group, and where available of the same Rhesus group.

iii. Each pack should be thawed by immersion in a water-bath at 37°C, then used IMMEDIATELY.

14. CRYOPRECIPITATES and DRIED ANTIHAEMOPHILIC GLOBULIN CONCENTRATES (intermediate and high purity). All these preparations have high concentrations of antihaemophilic globulin (factor VIII), are specifically indicated in the treatment of Haemophilia A, and are sometimes used in the management of von Willebrand's disease. Cryoprecipitates also have appreciable quantities of fibrinogen (see 17 below) and fibronectin (which may possibly be indicated for some cases of severe trauma). Cryoprecipitates are prepared from single donor plasma and therefore the amount of factor VIII in each pack varies widely. On the other hand, dried concentrates are prepared in a manner which allows the potency of a whole batch of ampoules to be assayed.

Both cryoprecipitates and the dried preparations are of limited availability and are generally used under the direction of specialised haemophilia treatment centres.

**Storage:**

i. Cryoprecipitates should be kept at or below −30°C, and protected from damage of the brittle plastic.

ii. Dried concentrates should be stored at +4°C.

**Suitability for use:**

i. Cryoprecipitates should be thawed in a water-bath at 37°C, then used immediately. 6-10 packs are generally used at a time, the contents of each thawed pack being infused through a filter, and each pack flushed with a small quantity of saline to obtain the maximum dose.

ii. Dried concentrates and the water used to reconstitute them should come to room temperature before solution is attempted. Reconstitution should be complete within two minutes and the contents of each ampoule then used immediately.

15. DRIED FACTOR IX CONCENTRATE. This preparation contains factor IX, prothombin and factor X, each usually concentrated to about the same degree. According to method of preparation, factor VII may or may not also be present. The potency varies with the method of preparation; the amount in each bottle will be stated on the label. Some preparations also contain heparin.

N.H.S. factor IX concentrate is available in England and Wales from the Blood Products Laboratory, Elstree and in Scotland and N. Ireland from all Regional Transfusion Centres.

The Oxford or other Haemophilia Reference Centres will advise on management of any cases needing it.

16. CRYOPRECIPITATE-POOR PLASMA. Replacement of large amounts of plasma proteins may be required in the management of hypoproteinaemia from liver or kidney disease and some bowel disorders, following extensive burns and in plasma exchange therapy. While P.P.F. and salt-poor human albumin solution are convenient and will help in many instances, the patients concerned may need other plasma proteins (such as immunoglobulins) present only in very small amounts in those products. Repeated use of F.F.P. in such situations can occasionally provoke reactions though the precise causes of these are usually unknown, and P.P.F. may be in short supply.

Most Regional Transfusion Centres prepare cryoprecipitates from fresh whole blood (see 14 above). As a by-product, cryoprecipitate-poor plasma is left over which contains almost all plasma constituents though with reduced amounts of coagulation factors I (fibrinogen), fibronectin, and of course antihaemophilic factor VIII. For use in the clinical circumstances outlined above, a few Centres have issued cryoprecipitate-poor plasma. Limited experience so far suggests that it may give rise to a lower incidence of reactions than is seen with F.F.P.

17. FIBRINOGEN. Concentrates of this clotting factor are now severely restricted to a few cases with afibrinogenaemia/dysfibrinogenaemia. In acute haemorrhage as part of disseminated intravascular coagulation, e.g. in some cases of obstetric accidental haemorrhage or following cardiac surgery, fibrinogen levels may fall to 100 mg/dl or lower. Because most such patients also need supplements of other coagulation factors, fresh frozen plasma is the treatment of choice – 4 units is a reasonable initial dose for an adult. Fibrinogen can also be given in the form of cryoprecipitates where 4 units have approximately the same amount of fibrinogen as 1 unit of F.F.P.

18. PLASMA SUBSTITUTES are solutions of macromolecular substances with minimal toxicity or antigenicity and which possess properties (e.g. viscosity and colloid osmotic pressure) resembling those of plasma. They do not contain haemoglobulin, protein (except gelatin solutions) antibodies or clotting factors and have only slight buffering



effects. They are not substitutes for whole blood nor do they completely replace plasma or plasma protein fraction. They should therefore be used with discretion.

**Uses:**

i. They are of most help in restoring an acutely depleted plasma volume when there are insufficient supplies of P.P.F. or F.F.P., or while compatible blood is awaited, and simple crystalloid solutions are no longer deemed appropriate.

ii. They may be given to recipients of any blood group, but a SAMPLE OF THE RECIPIENT'S BLOOD SHOULD BE TAKEN FOR GROUPING AND COMPATIBILITY TESTS BEFORE PLASMA SUBSTITUTES ARE GIVEN, since they may interfere with the correct interpretation of results.

iii. Recommended solutions include degraded gelatin in saline, and dextrans of the larger mean molecular weights (70,000, 110,000 and 150,000) which are available as 6% w/v solutions in isotonic saline or in 5% dextrose. Because these products remain in the circulation for some hours at least, they are valuable in acute haemorrhage, hypovolaemic shock, burns and prophylactically in surgery.

The low molecular weight dextrans (mean m.w. 40,000) have limited value as plasma expanders since they are rapidly excreted by the kidneys. Their main use is in the prevention and treatment of vascular sludging, thrombotic episodes and improving tissue circulation in crush injuries, threatened gangrene, skin grafting, etc.

iv. Doses of dextran solutions should NOT be given in excess of about 20 ml/kg body weight (1-1.5 litres for an adult) in 24 hours. Rather more gelatin may be given. Thus in hypovolaemic shock, the first 1.5 litres blood lost in an adult (proportionately less for a child) may be replaced by gelatin solution alone, between 1.5 and 4 litres lost, by equal volumes gelatin and blood; and for blood loss over 4 litres twice as much blood as gelatin should be given. In this way up to 10 litres gelatin may be infused in twenty four hours. NEITHER PLASMA SUBSTITUTES NOR PPF SHOULD BE GIVEN IN SUCH QUANTITIES THAT THE RECIPIENT'S HAEMATOCRIT FALLS BELOW 25%, blood and other blood products should be given as appropriate.

**Precautions.** Use of any plasma substitute results in dilution of the patient's clotting factors, and where these are already deficient (e.g. in disseminated intravascular coagulation or in thrombocytopaenia) they should be corrected at the same time. Where the clotting mechanism is already known to be abnormal, it may be better not to use plasma substitutes at all. Low molecular weight dextrans can promote oozing from wounds because of their direct action on the capillary circulation. Dextran solutions are incompletely homogenous; and the larger molecular weight dextrans (110, 150) give rise occasionally to febrile or antigenic reactions, and to anaphylactoid reactions especially in patients with a history of asthma or other allergies. Gelatin solutions contain calcium and should therefore NOT be mixed directly with citrated blood, and should be given with caution to patients on cardiac glycosides.

**Storage:** All plasma substitutes should be stored at room temperature below 25°C in a dark place. They should be crystal clear and free from deposits.

**Crystalloid Solutions:** At least in the initial management of acute blood loss situations, relatively simple electrolyte solutions have a valuable role. They are readily available, easy to administer, safe to use, relatively inexpensive and are free of some of the drawbacks of more sophisticated preparations. They are said to be of particular value also in the early treatment of major burns, protein replacement being instituted a day or two later.



## II VOLUME AND RATE OF TRANSFUSION

Dogmatic directions cannot be given concerning the volume and rate of transfusion. The following factors must be considered - the age of the patient, the general condition, the state of the circulatory system, and the indication for the transfusion. The young adult, with a normal myocardium, will tolerate the rapid infusion of relatively large quantities of protein fluid, even when the blood volume is normal. On the other hand, the chronically anaemic patient with an enfeebled myocardium, or patients with respiratory, cardiac or renal disorders, or infective and toxic conditions, must be transfused very cautiously.

i. In the presence of a severe injury accompanied by internal or external loss of blood, the rapid and adequate restoration of the blood volume is the immediate aim, and sufficient whole blood to raise the systolic blood pressure to at least 100 mg.Hg. should be given. Where sufficient blood is not available, plasma protein fraction and blood (in ratio 1 : 2) can be used.

In the previously healthy patient, a rate of 100ml/minute or even more will usually be tolerated until the BP reaches 100 mm.Hg. Thereafter the rate should be slowed and the transfusion continued slowly to maintain the systolic blood pressure at its normal level. The transfusion equipment should not be taken down, since further fluid may be needed during and after operation. For general purposes the patient's systolic blood pressure is a rough guide to the amount of fluid to transfuse. Therefore, the blood pressure sould be recorded regularly throughout the transfusion and at least after each unit transfused.

ii. In treating anaemia, it may be assumed that the red cells in one standard unit of whole or plasma reduced blood will raise the haemoglobin of an average adult by about 1.0g/dl. If in the absence of continuing blood loss the volume of blood required to raise the haemoglobin to the chosen level exceeds one third of the calculated blood volume (88ml/kg body weight) in spite of the judicious use of plasma reduced blood, the transfusion should be given in two parts separated by at least two days. The rate of administration of plasma reduced or concentrated red cells to a normovolaemic recipient should not exceed about 2 ml per minute (i.e. about 40 drops/min. depending on type of giving set). In severe anaemia with haemoglobin levels of under 4 g/dl, even this rate may be excessive especially if the patient is cachectic or suffers from cardiac or respiratory disease. Conversely, the infusion of any one unit of packed cells should not take more than about 4 hours because of the risk of infection developing in that unit. The chosen rate of flow should be constantly and accurately maintained, and the patient watched for signs of cardiac embarrassment. The venous pressure is a most valuable sign and

the state of filling of the jugular veins should be closely observed. The base of the lungs should be examined at frequent intervals for signs of pulmonary oedema. The careful use of diuretics prior to such a transfusion may be helpful.

iii. Similar caution must be used in transfusing patients with a septic condition or toxaemia. A large volume of fluid, even if administered slowly over a long period, should not be given as a single continuous transfusion to patients with such conditions; it should be divided and given slowly as a number of small transfusions.

Preferably, no major surgical procedure should be carried out where the haemoglobin is less than 10 g/dl. If the haemoglobin level cannot be restored by appropriate medical treatment, pre-operative transfusions may have to be given. Such transfusions should be given an adequate time before operation to allow their full benefit to develop and to avoid the possibility of a reaction occurrring at a time when it would be masked by anaesthesia.



## III BLOOD GROUPING AND COMPATIBILITY TESTING

Blood grouping and compatibility testing are laboratory procedures and should be performed only by persons, whether doctors or technical staff, who have had special instruction in modern techniques for such tests. For this reason no attempt is made to describe these techniques here. Instruction in the techniques of blood grouping and compatibility testing can, if necessary, be obtained at Regional Transfusion Centres.

Whatever form local arrangements may take, and whichever of the various recognised techniques of blood grouping and compatibility testing may be adopted, it is essential that a definite order of procedure be evolved and rigidly followed. The order of procedure, including details of techniques to be used, should be written out and be familiar to the laboratory staff. Exceptionally, if other members of hospital staff have to perform blood grouping tests they should be selected in agreement with the Haematologist and should be given instruction in the techniques they should use. The necessary pipettes, tubes, saline solutions etc. should always be kept in the same place. Antisera for use should:

i. be labelled properly

ii. be of adequate potency

iii. have been subjected regularly and frequently to control tests, and

iv. always be kept in the same place in the refrigerator

There is no laboratory procedure in which the results of erroneous techniques or interpretation are more disastrous than in the grouping and compatibility testing of blood. The result of a mistake may be fatal. The printed directions for carrying out these procedures are deceptively simple and may give a false sense of security. Special training and experience are essential if errors in grouping and compatibility testing are to be avoided. No patient, except in grave emergency, should be given a blood transfusion unless:

a. the ABO and Rh(D) groups of the patient's and donor's blood have been verified and are the same (see Section IX). Sometimes because of its rarity, blood for a group AB patient, especially group AB Rh(D) negative may be in short supply. The Haematologist will advise in this situation.

b. a compatibility test between the patient's serum and the donor's red cells has been done.

Indiscriminate use of Group O blood is undesirable and may be dangerous where, for instance, the patient already has one or more irregular blood group antibodies. Also, the plasma of some Group O donors contains potent anti-A or anti-B antibodies which will destroy the red cells of an A, B or AB recipient. Any group O blood issued for emergency should be free of high titre anti-A and anti-B haemolysins or agglutinins. (These will of course be partly eliminated from plasma reduced blood).

1. **BLOOD SAMPLES**

i. ADULTS AND CHILDREN: A suitable sample for blood grouping or compatability testing is 5 to 10 ml of blood collected with a dry, sterile, syringe and put into a dry, sterile tube, preferably of glass because plastic containers may cause delay in clotting. It is imperative that this sample should be clearly and accurately labelled immediately. The needle should be removed from the syringe before the blood is expelled into the test tube, since haemolysis may be caused by the ejection of blood under pressure through a fine bore needle. Additionally, an E.D.T.A. sample may be required in some Regions.

ii. INFANTS: In infants a stab wound may be made in the heel with a disposable lancet and 10 to 20 drops of blood should be collected in a dry, sterile tube.

iii. Great care must be observed when taking blood samples to avoid soiling the outside of the container or the request form with blood.

It is recommended that samples from 'high risk hepatitis' patients, for example jaundiced patients or patients in haemodialysis units, or those known to be positive for hepatitis B surface antigen (see Section VII 9) should be sent to the laboratory in containers protected by plastic bags, preferably heat sealed, and prominently labelled 'hepatitis risk'.

*When blood samples are being taken from more than one patient for compatibility testing, it is essential that each patient is handled individually. The blood must be placed in the specimen bottle which is then labelled correctly after verification of the patient's name and other details, if possible from the patient directly, or from the wrist band or other personal identification. THE PRACTICE OF PRE-LABELLING SPECIMEN BOTTLES IS DANGEROUS AND MUST NOT BE DONE.*

2. **ABO BLOOD GROUPS (LANDSTEINER).** The Distribution of ABO groups in the UK is:



| *Blood Group* | *Approximate Frequency per cent in United Kingdom* | *Antigen Present On Cells* | *Isoantibodies Present in Serum* |
|---|---|---|---|
| 0 | 46.5 | Neither A nor B | Anti-A and Anti-B |
| A | 42.0 | A | Anti-B |
| B | 8.5 | B | Anti-A |
| AB | 3.0 | A and B | Neither Anti-A nor Anti-B |

Since Group A occurs almost as frequently as Group O, it is wasteful (as well as dangerous) to use Group O blood irrespective of the recipient's blood group.

3. Rh(D) BLOOD GROUPING: The Rh(D) group of every person who is to receive a transfusion should be determined and, with certain exceptions, blood of the appropriate Rh groups should always be given (see Section IX). These tests can take an hour or longer to perform properly and should only be carried out by suitably experienced workers. If there is any doubt of the procedure to be followed in a particular case, the hospital Haematologist should be consulted.

4. OTHER BLOOD GROUP SYSTEMS: Occasional patients have irregular serum antibodies which occur either naturally, or as a result of one or more previous blood transfusions or pregnancies, and which are directed to antigens in the many other blood group systems. These antibodies may be detected by pre-transfusion compatibility tests (see below) or preferably by preliminary screening tests performed as a routine at the time of Out Patients visit or an admission to hospital. This allows identification of those patients for whom specially selected blood may have to be obtained in advance from the Regional Transfusion Centre.

5. COMPATIBILITY TESTS: Every blood transfusion should be preceded by a compatibility test, the details of which must be recorded. The request for this test should be sent in writing to the laboratory as soon as possible after it has been decided to give a transfusion, in order to avoid unnecessary haste and to afford time for further tests, should the results prove doubtful. The onus of ensuring that this is done rests with the clinician who is to give the transfusion. A fresh sample of the patient's blood for compatibility testing is normally required before each transfusion if there has been an interval of more than two days since the last transfusion. However, compatibility tests for a series of transfusions, given within the course of a day or two, should all be performed with the

original pre-transfusion sample of the recipient's serum. It is thus generally necessary to send a fresh sample of blood for compatibility testing with each request for blood, but a particular effort should be made to ensure that the first sample is large enough to be used for a series of compatibility tests, if several transfusions are likely to be needed in the course of two or three days. When an application is made for a compatibility test the adequate identification of the patient should always be given, including full names, date of birth, ward, hospital number (and name of the hospital if the blood is being prepared by the Regional Blood Transfusion Centre or at another hospital). The previous transfusion and obstetric history (where appropriate) should also be given, especially when it is already known that the patient's serum contains irregular antibodies. For some laboratories, the full address of the patient is also required. The application form should then be signed and dated.

In an emergency, when delay may endanger life, transfusion of plasma substitute(s), plasma protein fraction or even saline should be started while blood is sought. It is stressed that although blood grouping and modified compatibility tests may be done in 20-30 minutes, the risk of errors is increased. Very rarely is the clinical urgency so great as to preclude even limited compatibility tests; such a situation might include a massive life-threatening haemorrhage, or haemorrhage occurring where laboratory facilities are too remote, e.g. during obstetric 'flying squad' calls. Under these circumstances selected group O Rh(D) negative blood should be used (unless the patient is known to have antibodies incompatible with that rhesus group). If the patient's own group has already been established beyond question, then blood of that group could also be used - if available.

For some exceptional reason it may be considered that it is undesirable to give plasma protein fraction or a plasma substitute while a compatibility test is done, and that blood must be transfused without such a test. Those in charge of blood banks should decide in advance, if necessary in consultation with the Regional Transfusion Director, the procedure to be followed in such exceptional circumstances. If a compatibility test is not performed, 10 ml of blood should be taken from the patient immediately before giving the transfusion, put into a dry, sterile glass tube and sent to the laboratory for blood grouping and compatibility testing with such containers of blood as may have to be given subsequently.

All samples from patients, which have been used for blood grouping or testing compatibility should be kept in the refrigerator at 4°C to 6°C or, if serum, frozen for not less than 2 days and preferably for at least 7 days after the transfusion since they may be needed for the investigation of reactions.



## IV ADMINISTRATION OF TRANSFUSIONS OF BLOOD AND OTHER FLUIDS

Practical instruction is essential. The following points are important:

i. Always check the group and compatibility label on the unit of blood with the group and identity of the patient before giving a transfusion to ensure that blood of the correct group will in fact be given. The majority of incompatible transfusion disasters occur through neglect of this simple rule. A double check procedure, as for other dangerous drugs, is wise. The patient's full name, hospital number and the name of the ward should be on the compatibility label of the blood to be given. Only in this way, can it be assured that blood of the correct group is given.

In the United Kingdom blood is labelled in the following colours:

| | |
|---|---|
| Group O . . . . . Blue | Group B . . . . . Pink |
| Group A . . . . . Yellow | Group AB . . . . . White |

Labels for rhesus negative as opposed to rhesus postitive blood are distinguished by different coloured printing superimposed on the ABO colours as above.

ii. It is usually safe to transfuse blood cold from the refrigerator. If it is medically necessary for blood to be warmed, it should be passed through a sterile plastic disposable heat-exchanging coil in a water bath or other appropriate blood warmer, controlled at 30°C to 37°C. If blood must be warmed, the doctor who is to give the transfusion, or Sister-in-charge, should supervise the process. Blood which has been haemolysed by overheating may cause death.

iii. Do not leave blood unused out of the refrigerator or insulated box for longer than 30 minutes.

iv. Do not reconstitute dried blood products until just before use.

v. Most transfusions can be given by simple venepuncture. Whenever possible select a vein in the forearm. The antecubital fossa should be avoided because of discomfort to the patient and the difficulty of immobilising the transfusion site in a restless patient.

vi. Cutting down on a vein is hardly ever justifiable. If, however, cannulation is unavoidable, a vein in the forearm (avoiding the antecubital fossa) is preferable to one in the lower limb, although the saphenous vein may have to be used in an infant or child in order to establish without delay a route for the rapid administration of fluids.

vii. Apply pressure (50-60 mm.Hg) with a tourniquet or a sphygmomanometer cuff round the upper part of the limb to distend the veins.

viii. Employ palpation as well as inspection in selecting a vein. After preparing the skin inject, if necessary, a little local anaesthetic intradermally over the selected vein and leave it for ½ - 1 minute to take effect.

ix. Disposable Plastic Giving Sets: Detailed instructions for using these sets are printed on the container. Connect the transfusion administration set with the plastic pack (or bottle) containing blood or other fluids and check that it is in working order before setting up the transfusion. When used with bottles, the piercing needles of the giving sets and a suitable airway needle should be inserted through the rubber closure. Note that plastic packs do not require an airway, also they are very easily punctured accidentally.

x. Introduce the needle (or cannula) into the vein, release the tourniquet and fix the needle and tubing securely in position with adhesive strapping in such a way that no pull is exerted on the needle.

xi. See that the patient is comfortable and that the arm or leg is suitably placed on a pillow if necessary, and is kept warm during transfusion. Splinting may be advisable and is usually necessary if the patient is to be moved, or is restless or unco-operative.

xii. The rate of infusion should be decided in advance and translated into number of drops per minute according to the type of giving set in use. Standard giving sets allow flow at about 15-20 drops per ml., burette type sets (e.g. 'minidrip', 'microdrip') at about 50-60 drops per ml. Further guidance may be found in the Manufacturer's Instructions issued with each set.

xiii. The patient should be watched closely especially during the first 30 minutes of a transfusion in order

a. to see that the desired rate of flow is in fact maintained and

b. to observe whether any untoward reaction occurs.



xiv. If the transfusion is not flowing satisfactorily or stops, inspect the set to see that the tubing is not kinked and examine the limb proximal to the needle to ensure that the vein is not being compressed, for example, by a rolled-up sleeve.

Adjust the regulating clamp. Inspect the position of the needle making certain that it is in fact in the vein, and manipulate it gently. If these simple manoeuvres do not re-establish the flow, close the regulating clamp and disconnect the set from the needle. Test the patency of the needle by gentle suction with a sterile syringe partly filled with sterile saline solution: do not try to inject saline through the needle. Test the patency of the set by releasing the regulating clamp. If either the needle or the set is blocked a fresh needle or set should be substituted. Do not try to clear the obstruction by applying positive pressure in the container.

xv. When resuscitating patients or casualties in severe oligaemic shock, very rapid rates of infusion may be required of fluid in rigid-walled containers (e.g. bottle). A roller pump applied to the tubing is recommended to achieve this RATHER THAN RAISING THE AIR PRESSURE WITHIN THE CONTAINER, BECAUSE OF THE DANGER OF AIR EMBOLISM (See Section VII 4).

Flow rates of fluid from a plastic pack can be increased by applying external pressure to the pack with a pressure infusor. Some giving sets also allow for increased flow rates achieved by intermittent compression of the drip chamber.

xvi. When the transfusion is completed, every container that has held blood or blood product used for that transfusion should be returned UNWASHED to the laboratory without delay. In the event of some complication, for example, haemoglobinuria or jaundice immediately following the transfusion, a sample of the fluid given will then be available for investigation. If no complication has occurred after 2 days, the used containers may be discarded as appropriate. There is difficulty in preserving plastic packs after transfusion because of leakage from the pierced pack. The procedure to be adopted locally should be decided by the Haematologist and clinician, in consultation if necessary with the Regional Transfusion Director.

xvii. Transfusions of blood or plasma or infusions of crystalloid solutions tend to be associated with thrombophlebitis if unduly prolonged. Furthermore, chance contamination of a giving set may lead to a heavy growth of organisms within the apparatus when its use is extended beyond 12 hours. THE INCIDENCE OF THESE COMPLICATIONS CAN BE REDUCED BY USING A NEW GIVING SET (AND POSSIBLY CHANGING THE SITE OF THE VENEPUNCTURE) AFTER AN INTERVAL OF 12 TO 24 HOURS.

A change of giving set is sometimes specially indicated, for example, if a group AB patient has been transfused with group A blood following which, group AB blood becomes available. The giving set should be changed to avoid the anti-B in the plasma of the group A blood causing agglutinates of AB cells within the giving set. Similarly, when blood of any other ABO group is transfused following an emergency transfusion of group O blood, the giving set should be changed. This is also indicated when a change is made from blood to dextrose solutions and vice versa.



## V TRANSFUSION RECORDS

A record of every transfusion should be made in the patient's case notes in addition to the details recorded in the Transfusion Laboratory. It is not always appreciated that the main reason for accurate recording is protection of the patient.

1. THE PATIENT'S RECORDS must show:

i. The donation identification number of all blood and locally prepared blood products and batch number of manufactured products. The recording of these numbers must never be omitted since they may be the only means of tracing and checking a donor's blood if there is any question of incompatible transfusion, or of transmitted disease such as hepatitis. In the latter instance, it is important to be able to trace and withdraw other containers of the same icterogenic batches. Only by the careful and invariable recording of serial numbers on containers of transfusion fluid, can this be accomplished. In all cases of suspected post-transfusion hepatitis, tests of the recipient's serum for hepatitis B should be performed. This can normally be done by the Public Health Laboratory Service. THE REGIONAL TRANSFUSION DIRECTOR MUST ALSO BE INFORMED IMMEDIATELY SO THAT FURTHER TESTS CAN BE MADE OF THE BLOOD OF THE DONOR(S) CONCERNED.

ii. Details of the blood pressure (see Section II (i)) the pulse rate and temperature should also be recorded at the commencement of the transfusion and thereafter at frequent intervals dependent on the clinical condition of the patient.

iii. The time taken to give the transfusion.

iv. Results of urine analysis. Any urine voided during the transfusion and in the 24 hours afterwards should whenever possible be tested (colour, albumin test and examination of sediment). The reason for this is that the donor's blood may be abnormally rapidly destroyed and haemoglobinuria may occur, perhaps only once and may be the sole evidence of this destruction. It is therefore important to examine ALL urine voided during and after transfusion.

v. Particulars of any immediate reactions to transfusion (for classification see Section VI below, 'Complications and Dangers of Transfusion').

2. THE LABORATORY RECORDS are the responsibility of the Haematologist in charge of the hospital transfusion laboratory. Such records should show the following details of the use of all blood and blood products.

The blood bank register of records should show:

i. Date and time of removal of the blood from the blood bank

ii. Name of person fetching the blood from the blood bank

iii. Full name, ward and hospital number or home address of recipient

iv. ABO and Rh(D) blood groups of recipient.

v. Donation identification number, ABO and Rh(D) blood group and date of collection of each container of blood transfused

vi. Clinical condition necessitating transfusion

vii. Reactions, if any, stating -

a. their nature

b. whether patient has a history of miscarriage, stillbirth, hydropic, anaemic or jaundiced babies, or has had previous transfusions, or injections of blood or plasma

viii. The destination of each unit of blood or blood product (i.e. transfused, returned to stock, returned to Transfusion Centre etc).

3. The doctor in charge of the above records should at regular and frequent intervals, satisfy himself that unused units of blood or blood products issued to the wards and theatres have been returned to the hospital blood bank. He should thus be able to account for all units of blood or blood products received whether transfused or not.

4. The records should be preserved for not less than seven years.



## VI COMPLICATIONS AND DANGERS OF TRANSFUSION

### 1. FEBRILE REACTIONS

Febrile transfusion reactions have various causes including leucocyte antibody reactions, sensitivity reactions to foreign protein and unidentified pyrogens in the transfusion fluid. The most severe reactions are an indication for stopping the transfusion and arranging appropriate laboratory investigations. Fluctuations in temperature should be investigated to distinguish if possible those due to the patient's disease from those due to the transfusion.

Leucocyte antibodies may cause pyrexia, headache and rigor, but are not usually dangerous (see Section I 13).

### 2. OVERLOADING OF THE CIRCULATION AND PULMONARY OEDEMA

To treat patients with severe anaemia, concentrated or plasma reduced red cells should be used. With these, the danger of inducing circulatory overload is less than with whole blood, but the danger remains, especially in patients suffering from heart disease, chronic anaemia and cachectic states, severe sepsis, toxaemia etc. The risk is greatest if the transfusion is rapid or if the quantity of fluid given is too great for the particular case. Overload can be prevented by transfusing cautiously and with judicious use of diuretics given directly to the patient.

### 3. HAEMOLYSIS IN TRANSFUSION

The chances of haemolytic reaction due to incompatible transfusion are reduced by using only homologous blood, i.e. blood of the same ABO and Rh(D) groups as those of the recipient, and which has been shown by reputable techniques to be compatible with the blood of the recipient.

Caution should be exercised in the selection of Group O blood which should not be used indiscriminately, since the antibodies in the blood of certain group O donors are sufficiently potent to destroy the red cells of a group AB, A or B recipient and may thereby cause a dangerous haemolytic reaction. Very occasionally, a similar situation may arise when group A or group B blood is given to a group AB recipient.

A further danger with group O Rh negative blood is that an Rh positive recipient may have been immunised to one of the Rh antigens such as $\overline{C}$ or $\overline{e}$. There are, however, rare cases, especially some treated by 'flying squads' where the delay caused by any testing procedures would endanger life and here it is justifiable to use group O Rh negative (and usually also Kell negative) blood which has been shown to be free from dangerous anti-A and anti-B antibodies.

A haemolytic reaction, similar to that following the transfusion of incompatible blood, may follow the transfusion of out-dated blood, or blood which has been haemolysed by freezing, overheating or infection, or even of massive quantities of blood nearing the end of its statutory 'shelf' life.

While a haemolytic reaction may sometimes be asymptomatic, even after only a few mls. of blood have been given, there is usually a rapidly developing fever, perhaps accompanied by dyspnoea, intense headache, a feeling of constriction of the chest, and pain which may be intense in the lumbar region.

In severe cases, hypotension may develop and there may be a marked deterioration in the peripheral circulation. The reaction usually occurs during or immediately after transfusion but signs and symptoms may not appear for some hours. None may be apparent in the unconscious or anaesthetised patient. Haemoglobinuria and jaundice may occur. Several hours will usually elapse before the onset of jaundice and it may be delayed for a few days. Disseminated intravascular coagulation may occur during an episode of acute intravascular haemolysis, especially if this is a result of a large incompatible blood transfusion. This may lead to multiple haemorrhages of varying size in many different organs including the brain and can be fatal.

If such an episode occurs it presents as an acute medical emergency for which urgent advice and speedy diagnosis is essential.

Treatment of haemolysis following transfusion: when haemolysis following transfusion, due to incompatibility or any other cause, is suspected, the transfusion should be stopped immediately and expert advice should be obtained. Since renal failure is one of the most important complications, management should be directed towards the support and restoration of kidney function whenever this is impaired, as follows:-

i. If the patient shows signs of oligaemic shock, steps must be taken immediately to restore the general circulation by transfusion of compatible blood or plasma protein fraction. Delay increases the risk of renal damage. Low molecular weight dextrans are contraindicated.

ii. This infusion should be monitored by measurement of central venous pressure and should be discontinued when central venous pressure rises above normal levels.

iii. A fluid balance chart must be kept.

iv. All urine voided should be kept and the urinary urea and sodium concentration should be measured.



v. If the patient is oliguric, an initial dose of a diuretic such as frusemide is recommended pending further advice.

IN THE ABSENCE OF SATISFACTORY URINARY OUTPUT WHEN THE CENTRAL VENOUS PRESSURE IS NORMAL OR ELEVATED ABOVE NORMAL FURTHER ATTEMPTS SHOULD NOT BE MADE TO PROMOTE A DIURESIS AND ADVICE FROM A RENAL UNIT SHOULD BE SOUGHT.

The case should be regarded as one of acute intrinsic renal failure and this may be confirmed by finding a urinary sodium concentration of more than 20 mmol/l and a urinary urea concentration which approximates to that of blood. While the advice is awaited, the plasma potassium should be measured and and ECG performed. If the plasma potassium in greater than 6 mmol/l or there is evidence of hyperkalaemia on the ECG, prompt treatment is required and the investigations will allow emergency measures to be instituted as soon as the expert advice is available.

Once acute intrinsic renal failure is established, the patient should be moved whenever possible to a Renal Unit so that dialysis can be carried out until recovery from acute renal failure occurs.

The course of acute renal failure passes through three phases:

a. Oliguric phase - During this phase, the urine volume is less than 400 mls/24 hours. Treatment is aimed at maintaining fluid and electrolyte balance and limiting protein catabolism. Prophylactic dialysis is generally performed where necessary rather than waiting for the patient to develop symptoms or uraemia. The advantage of prophylactic dialysis is that an adequate protein and calorie intake can be maintained, minimising the risk of infection and encouraging recovery from the primary illness.

b. The early diuretic phase - This is heralded by a progressively increasing urine volume which may double on successive days, but the kidney is unable to concentrate and the management of renal failure must continue. This phase may last for two to five days.

c. Late diuretic phase - The kidney commences to concentrate and regains its normal capacity for controlling fluid, electrolyte and nitrogenous excretion.

4. AIR EMBOLISM

If for some exceptional reason positive pressure can only be applied by raising the air pressure within a bottle (e.g. of plasma protein fraction etc.), the transfusion must be CONTINUOUSLY supervised by a doctor who understands the dangers, and the pressure must NEVER be

continued after the bottle is three-quarters empty. Positive pressure, however applied must never be used to overcome an obstruction in the giving set.

Air embolism may also result from leaks or faults in the apparatus or from faulty cannulation of a vein.

If air embolism is suspected, the patient should be placed on his left side and kept in this position for two hours. Only gradually should his position then be changed, the patient being observed closely for any untoward signs.

## 5. THE ADDITION OF MEDICAMENTS TO BLOOD

No medication should be added to the container and the practice of injecting substances through the set should be used with discrimination. If essential, they should only be injected according to instructions supplied with the giving set through the medication site with the flow 'clipped off'. As an alternative, a three-way or four-way disposable stop-cock can be interposed between the set and the needle in the patient's vein.

## 6. ALLERGIC REACTIONS

Skin rashes, urticarial weals and angioneurotic oedema may complicate transfusion. Treatment with antihistamine drugs is usually sufficient, but intravenous hydrocortisone may be necessary in severe reactions.

## 7. TRANSFUSION OF INFECTED BLOOD

Never leave blood out of cold storage longer than 30 minutes at a time, nor re-use a pack which has previously been part used. Interruption of refrigeration may allow chance contaminating bacteria to multiply and blood so infected may cause a severe or fatal reaction. The initial symptoms may be indistinguishable from those of a haemolytic reaction due to incompatible blood, but the characteristic feature is the onset of profound hypotension with warm extremities. Vomiting and diarrhoea may occur and there may be complaint of severe pain in the abdomen and extremities. The outcome appears to depend upon the degree of contamination of the transfused blood.

Therapy with antibiotics and infusion of such substances as plasma protein fraction, pressor agents and hydrocortisone form the basis of treatment. Investigation of a suspected case is dealt with under Section VII (v).



INCIDENTS IN WHICH TRANSFUSION OF INFECTED BLOOD OR BLOOD DERIVATIVE HAS OCCURRED OR IS SUSPECTED MUST BE REPORTED IMMEDIATELY TO THE REGIONAL TRANSFUSION DIRECTOR.

## 8. DONOR-TRANSMITTED INFECTION

Blood is collected by the Regional Transfusion Centres from donors in normal health and, as far as can be ascertained, free from diseases (e.g. hepatitis, malaria etc.) transmissible by transfusion. All such blood is subjected to tests for hepatitis B and syphilis. Although efforts are made by those concerned to ensure that donors are free from transmissible disease, when fresh blood is taken from a donor and transfused before appropriate tests have been completed an increased risk is present and must be accepted by the clinician.

## 9. POST TRANSFUSION HEPATITIS

Several causative viruses are known or suspected as being transmissible through transfusion of blood and some blood products. Hepatitis B is one of these and its existence in blood donations or products may be indicated by the presence of its surface antigen. Until suitable tests are available to identify other viruses concerned, there will continue to be a risk associated with the use of whole and plasma reduced blood, concentrated red cells, platelets, human antihaemophilic globulin, cryoprecipitates, factor IX concentrate, fibrinogen and thrombin. Hence donation identification numbers of all blood and blood products used should invariably be recorded in the case notes (see Section VI 1). Plasma protein fraction and salt-poor human albumin are rendered non-icterogenic by heating to 60°C for 10 hours; human immunoglobulin prepared by ethanol fractionation is also non-icterogenic.

Hepatitis B infection is usually (some claim exclusively) blood borne, hence its association not only with transfusion, but also with tattooing, acupuncture, ear piercing and illegal drug taking. Its incubation period is variable and ranges from about 50 - 180 days.

Infectious hepatitis due to the primarily enteric hepatitis A virus is clinically almost indistinguishable from hepatitis B especially in its milder form. However, it is hardly ever transfusion associated, can be epidemic, and has a shorter incubation period of about 28 days. These two viruses are clearly identifiable by sophisticated laboratory tests.

Very similar illnesses can also be caused by other viruses including the so-called 'non-A non-B' viruses. The latter are also transmissible by transfusion, but as yet no specific laboratory tests have been developed to identify them. The incubation period is also variable extending up to 70 days or more. The clinical course may be acute, or chronic leading to cirrhosis.

Post-transfusion hepatitis among other syndromes, can also be due to the Epstein Barr and cytomegaloviruses. Because these are endemic in the community most adult recipients of blood or blood products are already immune. However these viruses can cause acute and even fatal hepatitis following transfusion in small babies and other patients at particular risk, such as those who are immunosuppressed following transplantation or treatment for leukaemia.

CASES OF POST-TRANSFUSION JAUNDICE, TOGETHER WITH THE DONATION IDENTIFICATION NUMBER OF THE CONTAINERS OF BLOOD AND OTHER BLOOD PRODUCTS INVOLVED MUST, AS ALREADY RECOMMENDED, BE REPORTED IMMEDIATELY TO THE REGIONAL TRANSFUSION DIRECTOR SO THAT DONORS CAN BE INVESTIGATED AND ANY UNUSED MATERIALS FROM THE SAME SOURCE MAY BE WITHDRAWN.



## VII INVESTIGATION OF TRANSFUSION REACTIONS

In the event of a febrile reaction or untoward symptoms complicating a transfusion the hospital transfusion laboratory should be notified. All severe reactions should also be notified by the hospital transfusion laboratory to the Regional Transfusion Director. The following specimens are needed, initially, to make an investigation:

i. The blood samples used for the compatibility test before transfusions. Such samples should be kept in the refrigerator for not less than two days after every transfusion. (See Section III 4).

ii. The remains of blood or blood products in the containers used for transfusion. All containers of blood or blood products used for transfusion should be kept in the laboratory at $4^{o}C$ to $6^{o}C$ for 48 hours after use lest investigations prove necessary. (See Section IV (xv)).

iii. A 10-20 ml sample of blood from a vein other than the one used for the transfusion, collected with a dry, sterile syringe as soon as possible after the reaction. Put about 2 ml into a sequestrene bottle and the remainder into a dry sterile container.

iv. A clean sample of urine. All urine voided for two or three days should be measured and examined; abnormally coloured urine should be conserved for investigation.

v. In the case of a reaction suspected to be due to infected blood, a sample should be collected from the patient for blood culture; simple Gram stain and cultures should be made of the remnants in the containers concerned and any blood packs used should be returned to the Regional Transfusion Centre for scrutiny for mechanical defects.

Most haemolytic reactions are accompanied by haemoglobinaemia or hyper-bilirubinaemia, or both, but these phenomena will depend upon the rate of destruction and elimination of the transfused blood, upon the rate at which the blood is given, and upon when the sample is taken. Examination of a sample of blood for these features is often the quickest way to decide whether a reaction is or is not haemolytic. If the observed rise of haemoglobin concentration does not approximate to the expected rise and no obvious cause, for example, haemorrhage, can be found, the possibility of an inapparent haemolytic reaction should be considered.

## VIII THE RHESUS (Rh) SYSTEM

There are several antigenic components of this blood group system. The 'D' antigen is the most important since it is the most potent in provoking antibody responses in recipients who lack it. For practical purposes, when people are referred to as being 'rhesus positive' or 'rhesus negative', what is usually implied is that they are rhesus D positive or rhesus D negative.

A recipient's Rh-D group should always be determined since most D-negative recipients, irrespective of their sex, will develop antibodies to the D antigen if transfused with even small amounts of D positive blood.

Moreover, a single transfusion of D positive blood may so sensitise a D negative female that any subsequent D positive offspring she may carry may be affected by haemolytic disease of the newborn (see Section IX). Ideally, therefore, all patients should be transfused with blood of homologous Rh group, unless there are special circumstances.

An Rh immunized person, if transfused subsequently with Rh incompatible blood may respond by destroying the donor's red cells: a fatal haemolytic reaction may occur.

There are very few occasions on which there is not time to group the patient and do a direct compatibility test. In some grave emergencies there may not be time to do this and the tendency is then to use Group O Rh negative blood although only about one out of every six patients will, in fact, be Rh negative.

Rh negative blood is essential for the transfusion of Rh negative females before and during the child-bearing age, and for patients already sensitised to the D antigen. Rh negative blood of any ABO group is also relatively scarce and therefore its use for patients who are not Rh negative accentuates its scarcity for those patients who should only receive such blood.

The relative scarcity of Rh negative blood is clear from the table, which shows the approximate percentage of Rh negative individuals by ABO groups in a random sample of United Kingdom population.

| | O | A | B | AB | Totals |
|---|---|---|---|---|---|
| Rh positive | 38.6 | 34.9 | 7.0 | 2.5 | 83.0 |
| Rh negative | 7.9 | 7.1 | 1.5 | 0.5 | 17.0 |
| Totals: | 46.5 | 42.0 | 8.5 | 3.0 | 100.0 |



It may happen exceptionally that when a recipient is known to be Rh negative, no Rh negative blood is available. In many of these instances plasma protein fraction or a plasma substitute can be used satisfactorily while blood of the appropriate group is obtained and blood grouping and compatibility tests are being done. The value of these fluids for this purpose appears to be insufficiently appreciated. Nevertheless, there may be occasions when blood must be given at once and only Rh positive blood is available for an Rh negative unsensitised patient. In such circumstances, the clinician must be told of the position by the Haematologist and, if he agrees with the proposal to give Rh positive blood, the risk must be taken. At other times because of a local shortage of Rh negative blood for the foreseeable needs of Rh negative females before and during the child-bearing age, and of patients already sensitised to the D antigen, it may be necessary to use Rh positive blood for Rh negative nulliparous females past the menopause who have not been transfused before and for Rh negative males who have not been transfused before. Here again the risk may have to be taken (after consultation between Haematologist and clinician), but consideration should always be given to the use of plasma protein fraction, FFP or a plasma substitute, while it is confirmed with the Regional Transfusion Centre that there is no reasonable possibility of Rh negative blood becoming available in time. Obviously all hospital staff should regard it as a duty in their use of transfusion therapy to avoid the wasteful use of group O Rh negative blood, and so minimise the occurrence of this dilemma.

If for any reason blood has been given to a patient of unknown Rh group, the pre-transfusion sample should be submitted for Rh grouping without delay.

The Rh negative patient who has received Rh positive blood must thereafter be considered a 'dangerous recipient'. Reliance for detecting such patients must rest essentially upon obtaining a proper history especially of previous transfusions or injections of blood and following the correct procedure whenever a transfusion is to be given, i.e. using a request form and performing the blood grouping and compatibility tests by suitable techniques.

NOTE: In order to provide anti-D immunoglobulin for the prevention of Rh immunisation in Rh negative women (see Section IX), a small number of Rh negative men, and of women who are past child-bearing, have volunteered to receive immunising injections of Rh positive red cells. This fact must be taken into account should they ever require a transfusion and they must be considered as 'dangerous recipients'.

If an Rh negative female, before or during child-bearing years, inadvertently receives Rh positive blood, it may be possible to prevent the development of Rh antibodies by giving anti-D-immunoglobulin. In these circumstances the hospital Haematologist and Regional Transfusion Director should be consulted to determine the dose and timing of anti-D immunoglobulin to be given.

Further protection for such a patient against trouble from future transfusion may also be afforded by carrying out the following procedures:-

a. Entry, by the clinician in charge of the patient, of full details of transfusions in the case history notes which should be distinctively marked.

b. Examination of the patient's serum, if possible and preferably at the Regional Transfusion Centre, for the presence of atypical antibodies, bearing in mind that the appearance of antibodies may be delayed for up to six months. A negative result is, of course, not to be taken as removing the patient from the group of dangerous recipients.



## IX HAEMOLYTIC DISEASE OF THE NEWBORN (H.D.N.)

**Causes**

Occasionally, newborn infants are affected, sometimes fatally, by haemolytic disease due in each case to the mother having become sensitised to one or more blood group antigens which she does not herself possess. This sensitisation occurs most commonly as a natural feature of pregnancy, when a few foetal cells carrying incompatible antigens of paternal origin get into the maternal circulation, especially at the time of delivery. Rarely, similar sensitisation follows prior injections or transfusions of incompatible blood. Where such active immunisation of a mother has occurred from whatever cause, she produces strong antibodies which cross the placenta and lead to the destruction of the red cells of any subsequent baby also carrying those incompatible antigens.

Rhesus D is still the commonest antigen implicated in severe haemolytic disease of the newborn. Less often, similar sensitisation occurs in mothers who are Rhesus D positive or D negative, because of other rhesus antigens (c, E etc.) or antigens belonging to totally different blood group systems such as ABO, Kell, Duffy, etc. In each case, the resulting antibodies can cause H.D.N. as well as giving problems for the laboratory in finding compatible blood.

**Rhesus D prophylaxis**

Sensitisation to the Rh-D antigen is largely preventable, and its incidence has been greatly reduced since the introduction of passive prophylaxis of all Rh-D negative mothers (except those giving birth to a D negative baby). 500 i.u. anti-D immunoglobulin given to the mother within 72 hours of delivery leads to the rapid elimination of foetal D positive cells from her circulation and pre-empts active immunisation in all but 1-2% of eligible mothers. The rare failures may be due to the occurrence of a foeto-maternal haemorrhage earlier in the pregnancy, or to insufficient anti-D being given at delivery (including accidental failure to give it at all). Natural delivery is only one of many obstetric events which can predispose to sensitisation. All warrant passive prophylaxis as follows:

| | | | Anti-D to be given: |
|---|---|---|---|
| All Rh-D negative mothers | Threatened abortion<br>Abortion spontaneous<br>Abortion therapeutic<br>Ectopic pregnancy<br>Amniocentesis (e.g. for chromosome studies) | Before 20th week | 250 i.u. |

| | | | |
|---|---|---|---|
| | Antepartum haemorrhage<br>External cephalic version<br>Stillbirth | After 20th week | 500 i.u. or more if Kleihauer count indicates a larger foeto-maternal haemorrhage |
| Rh-D negative mothers with D positive babies | Caesarian Section<br>Forceps delivery<br>Normal delivery | | |

NOTE:- At time of going to Press, consideration is being given to the introduction of antenatal prophylaxis with anti-D at 28 and 34 weeks as well as delivery, to extend the protection for Rh-D negative mothers with no live baby.

**Affected Babies**

Babies suffering from H.D.N. frequently have to be delivered several weeks prematurely to reduce their exposure to damaging maternal antibodies. In addition to phototherapy and other forms of treatment, they may require one or more exchange transfusions in the first few days of life, as well as 'top up' transfusions somewhat later. (See also Section X). The most severely affected babies may also benefit from intra-uterine transfusions during the mid-trimester. Although babies with H.D.N. due to anti-D are Rh-D positive, they are given Rh-D negative blood either of the ABO group appropriate to the baby or of group O. This is because any D positive blood will be destroyed by the maternal antibody passed on to the baby before birth, while D negative red cells should survive normally.

Expert advice should be sought for any pregnancy complicated by irregular maternal antibody(ies), and for babies affected by H.D.N. Any blood given to such babies must be shown to be compatible with their mothers' serum.



## X TRANSFUSIONS IN NEONATES

**Newborn babies may require:**

a. 'Top up' transfusions of about 10-30 ml for anaemia following haemolytic disease (Section IX), or from prematurity with depressed red cell production, and sometimes to replace blood drawn for multiple laboratory tests.

b. 'Exchange' transfusions commonly in H.D.N. (Section IX) for the removal of sensitised foetal cells, damaging maternal antibody(ies) and of unconjugated bilirubin resulting from increased red cell breakdown. Less often, exchange transfusions may be needed for 'physiological' jaundice, especially in premature babies, where the normal mechanism for elimination of bilirubin is underdeveloped.

Newborn babies have more exacting blood requirements than adults. In addition to being of the correct group, and free of hepatitis B etc., donor blood for neonates should have a pH of about 7.2, a plasma potassium under 10 m.mol/l, a haematocrit of about 65%, and should not contain excessive anticoagulant. Some departments also exclude donations with evidence of past and thus potentially transmissible, cytomegalovirus (C.M.V.) infection.

In many Regions, blood for babies is collected into CPD or CPD-A anticoagulant using some form of multiple plastic pack system from which several small packs are prepared of part plasma reduced blood. Once prepared, such 'baby packs' can be stored up to 3 days for exchange and about 5 days for 'top up' transfusions. Fresh heparinised blood from 'walking' donors is not recommended since it is usually not tested prior to use. There is therefore a small, but increased risk of blood group errors being made, of transmission of both hepatitis and C.M.V., and the variable and sometimes excessive anti-coagulant used may potentiate any haemorrhagic tendency present.

Exchange transfusions are carried out through a catheter in an umbilical vessel; alternatively 5-10 ml baby blood is withdrawn and replaced with an equal volume of donor blood which is usually, though not always, pre-warmed (see Section IV ii). A 1-2 blood volume exchange taking up to two hours may remove up to about two thirds of the circulating bilirubin etc. This then usually rises again because of equilibration of plasma with extravascular fluid possibly supplemented by continued excess production. More than one exchange may thus be needed during the first few days of life.

c. Fresh Frozen Plasma: Occasional neonates, and especially premature babies and those with respiratory distress syndrome or sepsis have a haemorrhagic tendency from multiple coagulation factor deficiencies. While these often improve after vitamin K therapy, immediate replacement may be necessary and can be provided by fresh frozen plasma (Section I 13) of the appropriate or of a compatible blood group.

d. Platelets: Neonatal thrombocytopaenia is a rare consequence of maternal alloimmunisation to tissue or platelet specific antigens (Section XIII), or is idiopathic. Platelet transfusions may be needed for a few days, combined in severe cases with exchange transfusion(s) to help elimate damaging maternal antibody.

THE MANAGEMENT OF ALL NEONATAL TRANSFUSION PROBLEMS SHOULD BE UNDERTAKEN IN CLOSE COLLABORATION WITH THE HOSPITAL HAEMATOLOGIST.



## XI NORMAL AND SPECIFIC IMMUNOGLOBULINS

Preparations of normal immunoglobulins are used in the treatment of general immune deficiency states and also to provide passive prophylaxis against hepatitis A (since the normal donor population has quite a high level of antibody against this virus).

Besides anti-Rh (D), there is a clinical need for the following specific immunoglobulins:-

Tetanus, hepatitis B and rabies. Immunoglobulins which are used to help prevent those diseases respectively following accidental or suspected exposure. Requests are also received for cytomegalovirus, herpes simplex, measles, mumps, rubella, vaccinia and varicella or herpes zoster immunoglobulins. Vaccinia immunoglobulin may still be required (though rarely now) to treat complications of smallpox vaccination, or to give passive protection to unvaccinated smallpox contacts. The other specific immunoglobulins mentioned are used to give some protection to patients in whom an attack of the disease concerned would be dangerous, e.g. in immunosuppressed patients.

All the above immunoglobulins are for intramuscular administration ONLY. They MUST NOT be given intravenously. Preparations made for intravenous use are becoming available and may be more effective than the intramuscular products and with fewer side effects.

The specific immunoglobulins can be prepared only from the plasma of individuals who recently have been immunised or have suffered from one of these diseases. They are therefore scarce and should be used with discretion. All doctors, nursing and other members of hospital staff are asked always to keep the need for plasma from such individuals constantly in mind. Individuals over 18 years old, who have completed a course of immunisation against tetanus or received a booster injection of tetanus toxoid should be asked if they would be willing to give a donation of blood three to four weeks after completing the immunisation procedure. Those who have suffered an attack of chickenpox, herpes zoster, herpes simplex, mumps, rebella or measles in the previous three months should likewise be asked if they would be willing to give a donation of blood. The names and addresses of any who agree, together with a note of the disease or the immunisation procedure and relevant dates, should be sent to the Director of the appropriate Regional Transfusion Centre who will arrange direct with the volunteers to collect their donations.

## XII PLASMA COLLECTION AND PLASMA EXCHANGE

### 1. Plasma collection

Normal blood donations yield only limited amounts of factor VIII, specific immunoglobulins and other plasma components. To meet increasing demand for these products, collection of plasma (as distinct from whole blood is now widely practised using some form of 'plasmapheresis' of appropriate donors. This involves taking a normal blood donation, separating the cells from the plasma (retained for processing) and immediately returning the cells to the donor. The procedure is done either manually using a double plastic pack system, or automatically with one or other type of cell-separator machine. Because plasma constituents are quickly regenerated, normal healthy donors in this country are allowed to donate up to 600 ml plasma at a time at intervals of not less than 2 weeks, and up to a maximum of 15 litres in a year. They should be screened regularly to ensure there are no adverse effects.

### 2. Therapeutic Plasma Exchange

Similar procedures, suitably extended, can allow the removal of up to 2 or more plasma volumes at a time, with corresponding simultaneous replacement of fluid lost. Repeated 'plasma exchanges' of this magnitude are sometimes helpful as an adjunct to the treatment of diseases characterised by large amounts of circulating abnormal proteins or immune complexes. The rationale for this is that the damaging substances are removed from the blood and indirectly from the extravascular tissues. Patients considered eligible may include those with certain complications of paraproteinaemia, or with disorders having an immunopathological basis such as severe systemic lupus erythematosus, some forms of nephritis and life-threatening myasthenia gravis.

Plasma exchange may also help in the management of immunised rhesus negative pregnant patients who have very high levels of circulating anti-Rhesus-D antibodies. Here the aim is to reduce the amount of antibody reaching an Rh-D positive foetus and causing severe haemolytic disease. Selected cases of accidental poisoning and of liver failure also benefit from short-term intensive plasma exchange.

In all cases, replacement fluids given usually include plasma protein fraction, colloid fluids (such as gelatin solution) and simple electrolyte (saline); random donor plasma is less often used since it can sometimes provoke reactions.

All cases potentially suitable for plasma exchange should be discussed with the hospital Haematologist.



## XIII TISSUE TYPING

Transplantation provided the greatest impetus for the development of tissue-typing. The knowledge gained has also benefitted blood transfusion.

Patients whose primary clinical disorder (e.g. aplasia, leukaemia, thalassaemia, etc.) demands repeated transfusions, are quite likely to become immunised by histocompatibility (HLA), platelet-specific and other antigens carried on the transfused cells. The antibodies so produced make transfusion reactions more likely to occur and progressively more difficult to manage. (See Sections I 7, 8 and VII). Multiparous women are at a somewhat greater risk of such reactions as a consequence of sensitisation induced naturally through pregnancy. In both situations knowledge of the nature of the sensitisation may help in providing the most compatible blood and in reducing the incidence and severity of the reactions.

Aplastic or leukaemic patients, and particularly those who are considered candidates for bone marrow transplantation, should be screened for evidence of sensitisation. They and their immediate family (siblings, parents and children) should also be tissue-typed early in the course of the illness to try and identify the most suitable potential marrow donor(s).

All such requests for tissue-typing and HLA antibody screening should be discussed with the hospital Haematologist.

## REGIONAL TRANSFUSION CENTRES

ENGLAND

| | |
|---|---|
| NORTHERN REGION | Regional Transfusion Centre<br>Westgate Road<br>Newcastle upon Tyne NE4 6QB<br>Tel. 0632 737804/8 |
| YORKSHIRE REGION | Regional Transfusion Centre<br>Bridle Path<br>Leeds LS15 7TW<br>Tel. 0532 645091/3 |
| TRENT REGION | Regional Transfusion Centre<br>Longley Lane<br>Sheffield S5 7JN<br>Tel. 0742 387201 |
| EAST ANGLIAN REGION | Regional Transfusion and Immuno-haematology Centre<br>Long Road<br>Cambridge CB2 2PT<br>TEL. 0223 245921 |
| NORTH WEST THAMES REGION | North London Blood Transfusion Centre<br>Deansbrook Road<br>Edgware<br>Middlesex HA8 9BD<br>Tel. 01-952 5511 |
| NORTH EAST THAMES REGION | North East Thames Regional Transfusion Centre<br>Crescent Drive<br>Brentwood<br>Essex CM15 8DP<br>Tel. 0277 223545 |
| SOUTH EAST AND SOUTH WEST THAMES REGIONS | South London Transfusion Centre<br>75 Cranmer Terrace<br>London SW17 0RB<br>Tel. 01-672 8501/7<br><br>South London Transfusion Sub-Centre<br>David Salomon's House<br>Southborough<br>Nr. Tonbridge<br>Kent<br>Tel. 0892 28172 |



| | |
|---|---|
| WESSEX REGION | Wessex Regional Transfusion Centre<br>Coxford Road<br>Southampton SO9 5UP<br>Tel. 0703 776441 |
| OXFORD REGION | Regional Transfusion Centre<br>John Radcliffe Hospital<br>Headington<br>Oxford OX3 7LJ<br>Tel. 0865 65711 |
| SOUTH WESTERN REGION | South West Regional Transfusion Centre<br>Southmead Road<br>Bristol BS10 5ND<br>Tel. 0272 507777 |
| WEST MIDLANDS REGION | Regional Transfusion Centre<br>Vincent Drive<br>Edgbaston<br>Birmingham B15 2SG<br>Tel. 021-472 3111 |
| MERSEY REGION | Regional Blood Transfusion Centre<br>West Derby Street<br>Mount Vernon<br>Liverpool L7 8TW<br>Tel. 051-709 7272 |
| NORTH WESTERN REGION | Regional Transfusion Centre<br>Roby Street<br>Manchester M1 3BP<br>Tel. 061-236 8181<br><br>Transfusion Centre<br>Quernmore Road<br>Lancaster LA1 3JP<br>Tel. 0524 63456 |

*Central Laboratories*

Blood Group Reference Laboratory
Harkness Building
Radcliffe Infirmary
Woodstock Road
Oxford OX2 6HE
Tel. 0865 727212

Blood Products Laboratory
Dagger Lane
Elstree
Borehamwood
Hertfordshire WD3 6AX
Tel. 01-953 6191

Plasma Fractionation Laboratory
Churchill Hospital
Headington
Oxford OX3 7LJ
Tel. 0865 62002

*Central Blood Laboratories Authority*

The Crest
Blood Products Laboratory
Dagger Lane
Elstree
Borehamwood
Hertfordshire WD3 6AX
Tel. 01-953 6191

*Wales*

Regional Transfusion Centre
Rhyd-Lafar
St. Fagans
Cardiff CF5 6XF
Tel. 0222-890302

*Scotland*

*Regional Transfusion Centres*

North of Scotland Blood Transfusion Service
Raigmore Hospital
Inverness IV2 3UJ
Tel. 0463 34151



Aberdeen and North-East Scotland Blood Transfusion Service
Royal Infirmary
Foresterhill
Aberdeen AB9 2ZW
Tel. 0224 681818 Ext. 2086

East of Scotland Blood Transfusion Service
Ninewells Hospital
Dundee DD1 9SY
Tel. 0382 645166

Edinburgh and South-East Scotland Blood Transfusion Service
Royal Infirmary
Edinburgh EH3 9HB
Tel. 031-229 2585

Glasgow and West of Scotland Blood Transfusion Service
Law Hospital
Carluke
Lanarkshire ML8 5ES
Tel. 0698-373315

*Central Laboratory*

Protein Fractionation Centre
Ellen's Glen Road
Edinburgh EH17 7QT
Tel. 031-664 2317

*Scottish National Blood Transfusion Service*

Headquarters Office
Ellen's Glen Road
Edinburgh EH17 7QT
Tel. 031-664 2317

*Northern Ireland*

Blood Transfusion Service
89 Durham Street
Belfast BT12 4GE
Tel. 0232 46464

**HAEMOPHILIA REFERENCE CENTRES:**

| | | |
|---|---|---|
| Royal Free Hospital<br>Pond Street<br>London NW3 2QG<br>Tel. (01) 794 0500 | for | London, the South East and East Anglia |
| St. Thomas' Hospital<br>Lambeth Palace Road<br>London SE1 7EH<br>Tel. (01) 928 9292 | | |
| Oxford Haemophilia Centre<br>Churchill Hospital<br>Headington<br>Oxford OX3 7LJ<br>Tel. (0865) 64841 | | Oxford, Wessex the South West and the Midlands |
| Royal Infirmary<br>Oxford Road<br>Manchester M13 9WL<br>Tel. (061) 273 3300 | | The North West, Trent and Yorkshire |
| Royal Hallamshire Hospital<br>Glossop Road<br>Sheffield S10 2JF<br>Tel. (0742) 26484 | | |
| University Hospital of Wales<br>Heath<br>Cardiff<br>Tel. (0222) 755944 | | South and Mid Wales |
| Royal Victoria Hospital<br>Queen Victoria Road<br>Newcastle upon Tyne NE1 4LP<br>Tel. (0632) 325131 | | Northern England |
| Royal Victoria Hospital<br>Grosvenor Road<br>Belfast BT12 6BA<br>Tel. (0232) 40503 | | Northern Ireland |
| Royal Infirmary<br>Lauriston Place<br>Edinburgh EH3 9YW<br>Tel. (031) 229 2585 | | Eastern Scotland |
| Royal Infirmary<br>Castle Street<br>Glasgow<br>Tel. (041) 552 3535 | | Western Scotland |

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