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Guidelines for the clinical use of blood cell separators

A DOCUMENT PREPARED BY THE CLINICAL HAEMATOLOGY TASK FORCE OF THE BRITISH COMMITTEE FOR STANDARDS IN HAEMATOLOGY WITH THE ASSISTANCE OF THE ROYAL COLLEGE OF NURSING

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Introduction

These guidelines replace the DHSS Code of Practice for the Clinical Use of Blood Cell Separators (1977) and supplement the *Guidelines for the Use of Automated Plasma and Platelet Pheresis of Volunteer Donors within the UK Blood Transfusion Service* (1985).

The guidelines apply both to patients and donors. Patient procedures include: (i) plasma exchange with or without absorption columns or secondary membranes, and (ii) cytapheresis procedures which remove red cells, white cells or platelets. Donor procedures include: (i) white cell donation, (ii) platelet donation, and (iii) plasma donation in excess of 600 ml with plasma substitute replacement.

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The potential complications of therapeutic cell separator procedures are set out in Appendix I.

The clinical criteria that apply are inevitably not the same as those for volunteer donors set out in the document *Guidelines for the Use of Automated Machine Plasma and Platelet Apheresis of Volunteer Donors within the UK Blood Transfusion Service* (in preparation).

When considering the siting of a cell separator, it should be remembered that the equipment should be used regularly and frequently (i.e. on average at least twice a week), so that staff can maintain a high standard of proficiency in the operation and care of this equipment.

Clinical management of the cell separator service

A consultant, who will normally be a haematologist, must be in overall charge. The consultant is responsible for advice concerning cell separator procedures and for determining which patients and donors are suitable for these procedures, having regard to safety and to the general condition of the patient or donor. The consultant, or his deputy, is responsible for assessing patients and donors before the procedure and it follows that the patient should be referred to the consultant for determining which investigations are to be done. The consultant or a medical deputy appointed by him/her should normally be present at the start of a procedure and must remain nearby until it is complete. Patients and donors should never be left in a room without the attendance of a registered nurse or doctor.

Patients

INFORMED CONSENT

While it is not necessary to obtain written consent from patients (in normal circumstances the patient's attendance implies consent), it is important to ensure that whenever a patient's condition allows, a full explanation of the procedure is given by a doctor competent in cell separation procedures. In obtaining verbal consent, the doctor must explain the purpose of the separation, describe the procedure and explain the possible risks and discomfort involved. It is imperative that details of this consultation are recorded in the case notes and signed by the doctor in attendance.

EXAMINATION OF PATIENTS

The doctor in charge of the procedure must ensure that there are no medical contraindications to the performance of the procedure and in particular must see that the patient's pulse, blood pressure and cardiorespiratory status have been

recorded in the case notes. Where the patient is not under the continuing care of the doctor using the separator, a record of formal examination is required. If there are plans to use any material obtained from patients, agreement must first be obtained for hepatitis B antigen and HIV screening (see below).

FREQUENCY AND VOLUME OF APHERESIS

The consequences of multiple apheresis must be considered whenever recurrent procedures are required. Few medical conditions require more than 5 consecutive days' apheresis and usually fewer procedures are necessary during the first week of treatment. The volume of plasma removed should be related to the patient's estimated plasma volume. Each procedure normally involves a 1–1.5 times plasma volume exchange, which in an adult usually involves a 2–4 litre exchange per procedure. Very occasionally, apheresis is needed in children and it is essential that the volume of plasma removed is appropriately reduced to take account of the smaller plasma volume. A worksheet should be kept of the details of each procedure. Special note must be made of any adverse patient reactions.

See Appendix II for operational guidelines defining the standards of care required.

Donors

SELECTION AND CARE OF DONORS

Donors should be accepted according to the advice given in the National Blood Transfusion Service Memorandum on the Selection, Medical Examination and Care of Blood Donors (1984) with the exception that the higher age limit should normally be 55 years. First-time donors should not normally be accepted over the age of 50 years or under 50 kg in weight and they should preferably have given two routine blood donations without untoward effects. Occasionally, first-time donors may be accepted if they are specifically motivated, e.g. friend, relative, hospital volunteers, but they must fulfil the remaining criteria. Normally, unrelated donors should be recruited from the National Blood Transfusion Service donor panels, and requests for unrelated donors should be made to the regional transfusion director.

For platelet donations, the donor should not have taken any aspirin or other platelet-active drugs for an appropriate period. For aspirin this is about 7 days, but for other drugs it may be shorter.

Care must be taken to ensure that undue pressure is not put on persons to donate, particularly if they are related to the patient or are an HLA-matched donor. Donors must not be placed in a position where it is difficult for them to cease making further donations although they wish to stop.

Where a patient or a relative is acting as a donor and fails to meet the

standard criteria, their donor eligibility must be reviewed by the consultant in charge of the unit.

Before a volunteer is enrolled as a member of a cell separator donor panel, his general practitioner should preferably be consulted.

INFORMED CONSENT

A consent form must be signed by each donor before the donation (see Appendix III) and this must include consent for anti-HIV and HB_sAg screening. Before giving writen consent, the volunteer should be fully informed about the procedure he will undergo and the risks incurred by the doctor in charge of the procedure. In obtaining informed consent, the donor should be given the following information.

1. The purpose of the donation.
2. A description of the proposed procedure and the likely duration of the donation.
3. A description of the risks and discomfort involved which could include:
   (i) dizziness and/fainting,
   (ii) haematoma formation during the pumped blood return,
   (iii) citrate toxicity, related to the rate and volume of citrated blood returned,
   (iv) blood loss if the procedure has to be terminated and it is considered unsafe to return donor blood remaining in the cell separator,
   (v) chilling sensations on reinfusion,
   (vi) reactions to starch solutions used in white cell donation procedures.
4. General information with regard to the recipient's need for the donated product and the anticipated benefits.
5. An explanation that, as a voluntary donor, consent can be withdrawn at any stage of the procedure or of the apheresis programme.
6. Information on donor compensation. Health authorities will consider sympathetically and decide promptly any claim on a donor for compensation for any injury or loss attributed to having donated a blood product by means of a cell separator.

MEDICAL EXAMINATION OF DONORS

It is preferable to have an initial independnet assessment of the health status of the donor by consulting the donor's general practitioner. Further medical examination should be carried out by the medical officer who undertakes the consent, to ensure that the donor meets the required standard of health. Temperature, pulse rate and blood pressure observations should be recorded on the operator's worksheet.

If there is clinical suspicion of cardiorespiratory disease (as indicated by the patient's history and the clinical examination) a specialist opinion should be sought.

BLOOD TESTS

The following blood tests *must* be included as a predonation screen:

(i) blood grouping (ABO and Rh),
(ii) HB_sAg, HIV, TPHA,
(iii) haemoglobin, white cell and platelet count.

These additional tests *may* be indicated:

(i) HLA typing,
(ii) CMV antibody,
(iii) total plasma proteins and immunoglobulins,
(iv) liver function tests,
(v) urea and electrolytes,
(vi) coagulation screen,
(vii) screen for high-titre and anti-A/B (for group O platelet donors).

The results should be within the normal range for the age and sex of the donor.

Predonation white cell counts should exceed 4×10^9/l and predonation platelet counts should exceed 150×10^9/l.

Before white cell transfusions, a red cell crossmatch, an HLA antibody screen or a lymphocytotoxic crossmatch should normally be performed.

FREQUENCY, VOLUME AND DURATION OF THE PROCEDURE

Donors should not normally be expected to donate more often than once a fortnight. The peak extracorporeal volume including the donation should not exceed 15% of the total blood volume. A donor should not normally donate platelets or white cells more often than 12 times a year. The volume of plasma removed should not exceed 600 ml (excluding the anticoagulant) without replacement plasma substitutes being used.

No more than 15 litres of plasma should be taken in 1 year and not more than 2.4 litres in any 1-month period or more than 1 litre per week. The duration of a machine donation procedure should not exceed 3 h.

Donors who give the recommended maximum amount of plasma or cells annually should be given a full medical examination (including appropriate laboratory tests) once a year by an independent clinician.

DRUGS AND INFUSION FLUIDS

It is recommended that the choice of drugs and other substances given to donors should be restricted and that normally only the following should be used, and then only with the consent of the donor: acid citrate dextrose, heparin, steroids, dextran, hydroxyethyl starch, modified fluid gelatin, all albumin products.

Records of cumulative doses of corticosteroids should be kept for each donor. When complications develop during the procedure, any other drugs (e.g. protamine) may be used at the discretion of the consultant in charge of the cell separator or his deputy.

Facilities

ACCOMMODATION

When cell separators are used for therapeutic purposes, a cardiac arrest team must be readily available. Ideally, cell separators should be operated in an area reserved exclusively for this work. This area should be adequate to allow a cardiac arrest team to operate. In addition, the area should provide working surfaces and washing facilities.

RESUSCITATION EQUIPMENT

Full resuscitation facilities (as agreed by the hospital cardiac arrest team) must be available.

Staff

TRAINING

Staff should be well trained and have regular instruction in resuscitation procedures and be familiar with the recommendations issued by the manufacturers of the cell separator in use. Written protocols should be available for each procedure undertaken and these should be strictly adhered to. The protocols should include a note of known complications of the procedure.

Normally, only doctors and qualified nurses should be trained to supervise the operation of cell separators. All members of staff operating the equipment must receive formal training either in their own or in another department. The consultant in charge must be responsible for arranging the training staff.

The consultant in charge, in consultation with the nurse manager, must be satisfied that the necessary training has been completed before allowing staff to carry out procedures and should sign a statement to this effect. The employing health authority should be made aware that nurses operating cell separators are undertaking duties outside their normal province and should be provided with a list of these duties.

The training should include consideration of the use and risks of anticoagulants and instruction in all aspects of the operations of the machine(s) in use. Training should also include consideration of the associated hazards and the action to be taken in the event of possible or actual harm occurring to the patient.

Machine safety

Numerous types of cell separators are now available, but all operate on either a continuous or an intermittent flow principle usually involving a two-arm venepuncture procedure allowing rapid return of citrated blood.

These systems consist of an instrumental device which will carry out whole blood separation, normally using a disposable apheresis set and a citrate and/or heparin anticoagulant solution. Such an integrated system withdraws blood from the donor, mixes it with anticoagulant in the required ratio, separates and collects the component selected, safely returning the remaining blood components to the donor/patient. For correct anticoagulant usage, refer to Appendix II.

1. The machine should comply with the relevant aspects of the Health and Safety at Work Act.
2. The machine shall comply with the requirements of British Standard BS 5724. Part I. Safety of Medical Electrical Equipment. Before supply, the purchaser should obtain a completed MLQ1 and MLQ2 form from the manufacturer, ensuring that the machine conforms with UK Health Departments Guidance notes, and should be purchased from a registered manufacture.
3. When a new machine is being used on loan for assessment, the health authority should seek written assurances that the machine conforms to appropriate safety standards. The Department of Health has advised that health authorities should use the standard form of indemnity for equipment on loan, an example of which was issued to health authorities on 20 November 1986. A copy of the standard form is available from regional supplies departments. The intention of the form is that it should be used in any equipment loan transaction in which there is no payment made by the health authority in order to establish a contractual relationship and more effectively protect the authority.
4. Sterile, single-use items and medical equipment should be purchased only from manufacturers who have been registered under the DHSS 'Manufacturers Registration Scheme'. A list of currently approved manufacturers can be obtained from the regional supplies department. The machine should be correctly installed and commissioned in accordance with the manufacturer's recommendations.
5. If cell separators are in use which are fitted with reusable separation devices, strict sterilization procedures should be followed in accordance with the original Code of Practice for the Clinical Use of Blood Cell Separators (DHSS 1977).

RECOMMENDED SAFETY FEATURES

Harness software

All tubing, separation bowls, collars, membranes and filters should preferably be single-use disposable items. When possible, they should normally be preconnected to ensure a sterile fluid pathway once venous access is achieved.

Manual override system

A manual override system is essential to enable the operator to override any automated procedure at any stage to allow intervention in the event of complications occurring.

Blood-flow monitor

Pressure sensors are required (i) to monitor blood flow during withdrawal, and (ii) to monitor venous pressure during reinfusion. If either of these situations occurs, a visual and audible alarm system should operate.

Anticoagulant flow indicator

A means of monitoring the rate of delivery of the anticoagulant throughout the procedure is essential.

Blood filter

The harness should incorporate blood filters to prevent aggregates formed during the procedure from entering the separator or from being returned to the patient/donor.

Air-in-line detector

The machine should include a protection system to ensure air infusion to the patient/donor cannot occur. The system should also incorporate a method of diverting accumulation of air from the patient reinfusion line should this occcur due to technical problems. The air detector must (i) activate an audible and visual alarm, (ii) activate line clamps to prevent further reinfusion, and (iii) stop blood withdrawal and anticoagulant pumps.

Operative pressure monitors

Plasma filtration machines must be provided with a monitoring device to record the transmembrane pressure and a protective system to ensure that the machine will only operate between recommended preset ranges. If the transmembrane pressure falls outside the preset ranges, an audible and visual alarm system should operate.

Fluid balance

If systems incorporate automatic fluid balance control to ensure balance between collected components and replacement fluids, there should be a visual display, to allow the operator to monitor (i) volume processed, (ii) cell/plasma removal rate, (iii) volume removed, and (iv) volume reinfused.

PROCEDURE PROGRAMMES

If a machine has more than one procedural programme available, there should be a visual display of the programme selected during the 'run' mode.

AUTOMATIC PRESSURE CUFF

If in use, there should be automatic inflation when the blood is being withdrawn and automatic deflation when blood withdrawal is stopped or during reinfusion if a single-arm technique is in use.

BLOOD WARMERS

Blood warmers should be operated in accordance with manufacturer's instructions and should incorporate a thermostatic control device which gives an audible alarm when a temperature deviation occurs.

MACHINE MAINTENANCE

Cell separator machines should be serviced in accordance with the manufacturer's instructions. A planned maintenance scheme should be followed.

If maintenance, repairs and modifications are undertaken by a hospital department, this should be done in accordance with the procedures outlined in Health Equipment Information HEI 98: Management of Equipment: DHSS EU 26, Electric Medical Equipment Guidance on Documentation required for maintenance. Cell separator machines should be cleaned after each procedure with a suitable decontaminating agent and a standard procedure for dealing with blood spillage should be adhered to (Howie Report 1978).

In the event of a mechanical failure of the machine, a service engineer should be contactable by telephone during normal working hours.

POWER FAILURE

To ensure donor/patient safety, the machine should automatically enter a standby mode once power returns after a temporary power failure. Also, a manual system for returning any remaining blood components to the patient/donor is desirable, particularly if the extracorporeal volume is in excess of 200 ml and the power failure continues.

References

BRITISH STANDARD BS 5724. Part I. Safety of Medical Electrical Equipment

DHSS (1977) *Code of Practice for the Clinical Use of Blood Cell Separators*

(HC (77) 22) Extended role of the nurse (1979 (GEN) 46) for Scotland

HOWIE REPORT (1978) DHSS code of practice for the prevention of infection in clinical laboratories

NATIONAL BLOOD TRANSFUSION SERVICE (1984) Memorandum on the Selection, Medical Examination and Care of Blood Donors

Appendix I. Potential complications of therapeutic cell separator procedures

Mortality in therapeutic haemapheresis is estimated at 3 per 10 000 procedures. Major hazards are related to:

(i) anticoagulants: citrate, heparin,
(ii) type of replacement fluid,
(iii) fluid and electrolyte balance.
(iv) vascular access,
(v) haemolysis,
(vi) air embolus,
(vii) infection,
(viii) paediatric usage.

ANTICOAGULANTS

Citrate toxicity

This has been recorded in up to 15% of procedures and can lead to cardiac arrhythmias and death. It is related to the concentration of citrate anticoagulant used, the concentration of citrate in the replacement fluid, the rate of citrate infusion, and to patient susceptibility. Citrate acts by chelating calcium ions; symptoms are due to hypocalcaemia and are as follows: circumoral parathesiae, muscle twitching, nausea and/or vomiting, chills, syncope and tetany (rare).

NB Severe hypocalcaemia can occur without any of the above warning symptoms.

Avoidance

1. Use the manufacturer's recommended anticoagulant at the correct ratio.
2. If different citrate formulations are to be used, it is essential to monitor the citrate levels in the return line to the patient/donor and to monitor ionized calcium levels in the patient/donor to ensure the maximum citrate dose rate is not exceeded.
3. If patient susceptibility is suspected, e.g. impaired liver function, reinfuse at a slow rate and monitor for signs of hypocalcaemia.

NB It is safer to correct by stopping or slowing the reinfusion rate than to infuse concentrated calcium solutions; hypercalcaemia induced in this way can be as dangerous as hypocalcaemia

Inadequate citration

If inadequate levels of citrate are achieved, this could lead to clotting in the extracorporeal cell separator circuit. This could either lead to the reinfusion of material with procoagulant activity and potentially precipitate disseminated intravascular coagulation (DIC), or cause haemolysis in the cell separator leading to reinfusion of haemolysed blood.

Avoidance

1. Use the manufacturer's recommended anticoagulant at the correct ratio.
2. Monitor the anticoagulant pump, the rate of delivery via the drip chamber and the volume of anticoagulant used throughout the procedure to ensure constant correct delivery of anticoagulant.
3. Visually observe and monitor the separation chamber or the return line filter for evidence of clotting.
4. Visually observe and monitor the colour of the separated plasma for evidence of haemolysis.

Adverse reactions to heparin

These include bleeding, allergy/anaphylaxis, dyspnoea and abdominal pain.

NB If protamine is used to reverse heparin, the following adverse reactions can occur: chills and lightheadedness, allergy and/or anaphylaxis, dyspnoea and/or chest pain and flushing.

Because of these adverse reactions and the prolonged effect of heparin, citrate is recommended as the anticoagulant of choice for most cell separator procedures and the use of heparin in normal donors should be avoided.

REPLACEMENT FLUIDS

The following materials have been used alone or in combination for fluid replacement in therapeutic exchange procedures:

(i) plasma protein fraction (PPF),
(ii) human albumin solution 4.5% (HAS),
(iii) fresh frozen plasma (FFP),
(iv) whole blood and/or packed cells,
(v) volume expanders, e.g. modified fluid gelatin (MFG), hydroxyethyl starch (HES), haemaccel, dextran, crystalloids, e.g. saline hartmans, etc.

NB No therapeutic materials should be added to HAS, blood or other blood products.

For plasma exchange procedures the choice of replacement fluid depends on the frequency and volume of the exchange procedure and the underlying disorder. However, in all patients it is important to maintain adequate levels of protein during the procedure as inadequate protein replacement can rapidly lead to hypovolaemia and hypotension.

Total replacement with albumin-containing solutions avoids this problem. Note the maximum rate of removal should not exceed 20 ml/min. Procedures can be done safely with a mixture of 50% crystalloid + 50% albumin *but* if frequency of exchange is $> \times 1$/week and the volume of the exchange is $1.5 \times$ plasma volume and replacement fluid is part crystalloid part albumin, albumin levels as well as other plasma proteins progressively fall. If replacement fluid is PPF or HAS only, albumin levels will be maintained, but there will be a progressive fall in levels of (i) coagulation factors (including fibrinogen and antithrombin III), (ii) immunoglobulins, (iii) complement, and (iv) cholinesterase.

Reduction in coagulation factors can lead to bleeding episodes, particularly if there is a potential bleeding point, e.g. recent renal biopsy. This will be enhanced if heparin is used as the anticoagulant.

Reduction in antithrombin III levels (i) may predispose to thromboembolic episodes post-exchange, and (ii) reduce the effectiveness of heparin anticoagulation.

Reduction in cholinesterase levels can lead to prolonged periods of apnoea in response to the muscle relaxant suxamethonium used in general anaesthesia.

If volume expanders are used as part replacement, certain problems should be recognized, as follows.

1. Fluid overload precipitating congestive cardiac failure in the susceptible patient.
2. Allergic reactions particularly with dextrans.
3. Haemaccel has a high concentration of calcium which should *not* be mixed with citrated blood as this could produce clotting in the reinfusion blood line.

Complications of FFP

1. Allergy: can occur in up to 30% of cases.
2. Anaphylaxis/pulmonary oedema: can be fatal (strong association with the use of FFP replacement and the fatalities attributed to plasma exchange).
3. Citrate toxicity: the combination of citrated plasma and citrated red cells can lead to severe citrate toxicity if rapid reinfusion rates are used.
4. ABO incompatibility: if mismatched plasma is used.

5. Respiratory distress syndrome: plasma contains HLA and/or neutrophil-specific antibodies reactive with patient's leucocytes.
6. Hepatitis.
7. Acquired immune deficiency syndrome (AIDS).

NB similar complications can occur if blood is used as part of the replacement fluid.

Avoidance

1. Only use FFP if essential. Currently, the only situation where FFP is the replacement fluid of choice is thrombotic thrombocytopenic purpura.
2. Use PPF or albumin as the major replacement fluid. Although occasional hypotensive or idiosyncratic reactions can occur to albumin preparations, they are much less common. It should be remembered that if the infusion rate exceeds 10 ml/min, reactions are more likely to occur.
3. Single donor FFP units can be used at the end of an exchange procedure to maintain coagulation factors, immunoglobulin levels and cholinesterase levels if thought to be necessary.
4. Use of a 20 μ microaggregate filter reduces the incidence of allergic reactions. Microaggregates present in frozen/thawed plasma are probably responsible for the majority of allergic-anaphylactic reactions.
5. Ensure the patient is not IgA deficient. IgA-deficient individuals usually possess anti-IgA, and anaphylaxis is likely to occur in response to transfusion of any blood product containing IgA.

FLUID AND ELECTROLYTE BALANCE PROBLEMS

Hypervolaemia

Common in renal failure patients. It is controlled by decreasing the volume of the replacement fluids, maintaining the albumin level, monitoring the blood pressure and finishing the exchange in negative balance.

Hypovolaemia

Common in paediatric cases and small patients where the extracorporeal volume exceeds 10% of the patient's total blood volume. The initial signs are irritability, restlessness, yawning, drowsiness, cramps. Late signs are abdominal pain, vomiting, collapse.

Avoidance

1. Monitor blood pressure.
2. Maintain albumin levels.
3. Increase reinfusion rate if signs of hypovolaemia occur.

Hyperviscosity States

Patients with hyperviscosity are usually hypervolaemic. If this type of patient is made hypovalaemic with an increase in the haematocrit before a reduction in the plasmaviscosity has been achieved, a hyperviscosity crisis can be precipitated, i.e. do not raise the patient's Hb/haematocrit until at least half the plasma volume has been exchanged during the first exchange procedure.

Electrolyte imbalance

Problems that can occur include hypokalaemia, hyponatraemia, hypocalcaemia, hypomagnesia and aluminium toxicity (high levels of aluminium present in some PPF and HAS preparations).

Avoidance

Choice of replacement fluid must be tailored to individual patient requirements which must be assessed before commencing the exchange procedure. PPF and HAS have normal sodium levels but low levels of ionized calcium potassium and magnesium. Hence it may be necessary to normalize these levels by the addition of calcium and potassium to the replacement fluid.

In renal failure patients it may be advantageous to omit potassium in the replacement fluid, whereas patients on diuretics or steroids may be more prone to potassium depletion and may require supplements in the replacement fluid.

NB The combination of hypocalcaemia and hypokalaemia can increase the likelihood of cardiac arrhythmias.

Chilling

Rapid reinfusion without using a blood warmer can cause 'chilling' and rigors. Patients suffering from sickle cell disease are prone to haemolysis and a blood warmer should be used.

NB In paraproteinaemias, cold haemagglutinin disease and cryoglobulinaemias, the cryocomponent may be active at relatively high temperatures and gelling or agglutination may occur in the extracorporeal circuit unless precautions are taken.

1. Check for presence of a cryocomponent in all paraproteinaemias referred for plasma exchange.
2. Assess the thermal amplitude of the cryocomponent if possible.
3. Ensure the temperature of the cell separator circuit does not fall below the critical level by using blood warmers to:
   (i) warm the prime solutions,
   (ii) warm the replacement fluid,
   (iii) warm the reinfused blood.
4. Increase the temperature of the working environment.

COMPLICATIONS OF VASCULAR ACCESS

The safest venous access is by repeated use of the antecubital fossa veins. Where this is not possible, various types of vascular access have been used, none of which is without complications. Subclavian line/superior vena caval catheters have led to vessel perforation, haemothorax, pneumothorax and infection and thrombosis. Femoral vein catheters have led to haemorrhage, thrombosis and infection.

Arteriovenous shunts have led to shunt site infections, which have been associated with recrudescence of the disease. Arteriovenous fistulae have led to gangrene and subsequent limb amputation, thrombosis and a cerebro-vascular accident.

HAEMOLYSIS

Forcing blood by pump through a narrow orifice, particularly when blood is concentrated to a high haematocrit, may result in haemolysis.

Avoidance

1. All the software must be carefully examined before setting up the machine to ensure there are no kinks or twists in the tubing.
2. Constant observation of the colour of the plasma can detect the presence of haemolysis.
3. When using filtration machines, constant monitoring of the transmembrane pressure is essential and particular care must be taken if frequent episodes of low flow occur, as in this situation haemolysis is more likely to occur.

NB If haemolysis is suspected, the procedure must be terminated, as the return of damaged red cells to the patient/donor could precipitate DIC and mimic a haemolytic transfusion reaction.

AIR EMBOLUS

Most cell separators incorporate air detector devices in the reinfusion line. However, with the use of blood warmers and other software beyond the machine air detectors, there is a risk of air embolism if all the lines are not fully primed.

NB Never totally rely on 'fail/safe' alarm systems. Occasionally, they can fail and constant monitoring of all reinfusion lines is necessary to prevent air embolism from occurring.

INFECTION

Equipment contamination

Do not leave a machine primed for longer than 1 h before use.

Bacterial Infection

If bacterial contamination has occurred during the set-up and priming procedure, there is a risk of causing a severe bacteraemia, which could be fatal in an immunosuppressed patient. Plasma exchange depletes immunoglobulin if PPF or albumin is used as the replacement fluid. The combination of low immunoglobulins and immunosuppressive therapy predisposes the patient to infection. Prophylactic administration of immune serum globulin in patients particularly at risk should only be considered under special circumstances.

Viral infection

If FFP is used as the replacement fluid, hepatitis, particularly the non-A non-B variety, is a potential risk and can be lethal. FFP should only be used for TTP or when specific replacement of plasma deficient factors is required.

PAEDIATRIC USAGE

Protocols necessary for plasma exchange in children (from The Hospital for Sick Children, Great Osmond Street, London)

1. Record child's dry weight and resting blood pressure.
2. Crossmatch and prime machine with whole blood for the first exchange and subsequent exchanges if the pre Hb is <9 g/dl.
3. For children <30 kg, prime through to the return line with blood and/or plasma. If <20 kg, always prime with whole blood.
4. Use PPF as replacement fluid 80–120 ml/kg.
5. Use FFP with a 20 μ microaggregate filter at end of exchange from third day to replace depleted clotting factors.
6. Use a blood warmer on the return line.
7. The worst aspect for the child is insertion of lines. Great Ormond Street Hospital has found A–V shunts to be most successful and least traumatic to the child.

NB If possible, use a cell separator that has a small extracorporeal volume. Most continuous flow filtration (membrane) machines are suitable, but the disadvantage is that they require relatively high flow rates and usually require an invasive form of vascular access.

Contraindications to plasma exchange in children

1. Heart failure.
2. Uncontrollable hypertension.
3. Renal biopsy/major surgery 5 days before plasma exchange.

Appendix II. Guidelines for operators outlining standards of care for patients and donors undergoing blood cell separation

A consultant fully experienced in the operation of cell separators has overall responsibility for the health and welfare of patients/donors and for the observance of the codes of practice. Registered general nurses are responsible for nursing care aspects.

To provide optimal care, procedures should be carried out by a team of two personnel, one of whom should be a specifically trained registered nurse. The person who prepares the machine, ideally the registered nurse, will have the responsibility for its operation.

The nurse in charge has responsibility for:

(i) the physical and psychological needs of the patient/donor,
(ii) making sure that support facilities are available and functioning,
(iii) completing a comprehensive record/work-sheet,
(iv) making sure there is instruction on post-procedural care and subsequent follow-up of patient/donor.

STANDARDS AND MONITORING REQUIRED TO PREVENT COMPLICATIONS

The clinical hazards associated with procedures and the avoidance of such complications are clearly outlined in Appendix I.

In order to minimize operational error, the following should apply.

1. Information required with reference to specific patient/donor management.
   (i) The physical and psychological conditions of the patient/donor.
   (ii) Any associated nursing care required.
   (iii) The basic parameters required to establish the total blood and plasma volume: height, weight and haematocrit (relevant to the volume to be removed or exchanged and the anticoagulant ratio to be used).
   (iv) The details of current drug therapy, particularly anti-convulsants, anti-arrhythmics and steroids. It may be necessary to modify drug regimens or to give supplemental doses in order to maintain the desired drug concentration in the blood, especially when large quantities of plasma are to be removed.
   (v) If there is a history of cardiac valvular disease, specialist advice about antibiotic prophylaxis should be sought.
2. A written protocol for each procedure which must be specific for the machine in use must be available. It should include a detailed description of the entire procedure.
3. Maintenance of records and care plans, which include details of:
   (i) patient identification and diagnosis,
   (ii) the responsible medical officer and operator's signature,
   (iii) type of procedure and serial number of machine,
   (iv) batch number of solutions and software,
   (v) method of access,
   (vi) volume and rate of blood processed,
   (vii) nature and volume of anticoagulant and replacement fluids,
   (viii) duration of the procedure,
   (ix) details of any medication given,
   (x) adverse reactions and their treatment.

4. All nurses/operators must be aware of and be able to recognize the complications which may arise during the procedure and be fully conversant with the corrective or preventive action to be taken.
5. If the nurse/operator considers operating conditions unsafe or he/she does not feel competent to undertake the procedure, he/she should not proceed before seeking advice from the consultant in charge of the unit.
6. Results of appropriate laboratory tests itemized in the protocol for the procedure concerned should be available so that advice concerning the intervention or adjustment to treatment can be sought.
7. It is the nurse/operator's responsibility to ensure that the operating standards for the management of complications are complied with when undertaking procedures on patients or donors. These should include details of the following:
   (i) procedure in the event of a respiratory or cardiac arrest and application of the techniques involved and the equipment in use,
   (ii) procedure following accident or incident,
   (iii) action in the event of fire or bomb alert.
8. Any drug, anticoagulant or intravenous solution given to a patient/donor should be checked before administration, or introduction into the machine. This checking must be carried out by two people, one of whom must be a qualified medical officer or a registered general nurse. For example:
   (i) the appropriate method of anticoagulation must comply with prescribed policy for the particular procedure,
   (ii) the consultant responsible for cell separators or his deputy should prescribe the replacement regimen required for a particular procedure or patient treatment,
   (iii) the general guidelines for infusion or transfusion should be known and applied.

TECHNICAL ASPECTS OF THE PROCEDURE

Harnessing and priming of the machine

1. Check that all disposable equipment, solutions and sterile packages available are in date, undamaged and that batch/lot numbers are recorded.
2. Recheck for harness faults during installation, priming and running of the machine.
3. The batch numbers of faulty harnesses should be reported to the manufacturer, so that the batch can be investigated and withdrawn if necessary.
4. Use aseptic techniques when connecting tubing and solutions.
5. Check that all alarm systems are functioning.

The above checks will assist in the prevention of the following:
   (i) bacterial infection caused by contamination during setting-up and priming,
   (ii) mechanical haemolysis caused by twisted or trapped tubes,
   (iii) the entry of air into the circuit caused by increased pressure in the extracorporeal circuit or loose connections.

The detection of faults in the automatic programming

Check that operation of the machine is correct for the given programme and that the programme is maintained throughout the procedure. The displayed function should be recorded at regular intervals.

Manual override

Manual override in automatic systems is necessary in the following circumstances.

1. Citrate toxicity. Stop or slow down reinfusion until symptoms subside.

2. Hypovolaemia. Stop withdrawal of blood and commence reinfusion until the patient/donor's condition is stable.
3. Major complications. Terminate the procedure without returning any machine contents. Examples of major complications include: haemolysis, under-anticoagulation, severe complications of vascular access, allergic reactions, haemorrhage, disease-related 'crisis' (e.g. myasthenic crisis), cardiac/respiratory arrest, serious faults in the equipment.

Minor complications include:

(i) venospasm or vasovagal reaction: slow down or stop the procedure until the patient recovers,
(ii) haematoma: apply pressure and resite the needle,
(iii) hypothermia: slow down or stop the procedure and check the function of blood warmer; take appropriate measures to warm the patient/donor.

Venous flow

1. Visually check that venous and anticoagulant flow rates are appropriate.
2. Ensure satisfactory maintenance of the pressure cuff, if in use.
3. Check for gelling or agglutination.

Reinfusion circuit

1. Check that no clotted or haemolysed blood or air emboli are delivered to the patient/donor.
2. Ensure that an adequate reinfusion rate is maintained.

Separation exit

1. Ensure that the appropriate undamaged blood components are removed at the required rate.
2. According to the machine in use, check that transmembrane pressure is maintained or that no excessive vibration or overheating occurs.
3. Observe for leaks in separator.

Pump function

1. Adjust the pump speeds as necessary to ensure smooth and efficient operation.
2. Check for any tubing occlusion, particularly in the pump heads.

Maintenance of fluid balance

1. Exclude deviation from machine readouts by measuring input and output of fluids.
2. Monitor reinfusion and draw flow rates.

COMPLETION OF PROCEDURE

On completion of the procedure, the patient/donor should be given appropriate post-procedural advice and care.

Provision for disposal of waste and used disposable equipment should be made in accordance with the Health and Safety Commission Report (1982) *The Safe Disposal of Clinical Waste.*

Cell separator machines should be cleaned after each procedure with a suitable decontaminating agent (The Howie Report, DHSS Code of Practice for the Prevention of Infection in Clinical Laboratories 1978). Staff should take care to protect themselves when using cleaning agents and solutions by wearing appropriate clothing incuding masks and gloves.

Appendix III. Donor consent form (cell separators)

1. I.....(Full name)
of .....(Full address)
hereby acknowledge that I have volunteered to donate blood by means of a cell separator. The nature and purpose of the donation of blood by those means and the risks involved to the donor have been explained to me by:
Dr..... *
I hereby consent to the donation of

by means of a cell separator and I agree to undergo medical assessment which will also involve giving a sample of my blood for tests including HIV. I consent to such further or alternative operative measures or treatment as may be found necessary during the course of the donation.
Signature of volunteer donor.....
Date.....

2. I confirm that I have explained the nature and purpose of this procedure to the person who signed the above form of consent.
Signature of doctor .....
Date.....

*The explanation must be given by a medical practitioner.