

**A GUIDELINE FOR TRANSFUSION
OF
RED BLOOD CELLS
IN SURGICAL PATIENTS**

Issued by the National Blood Users Group

The National Blood Users Group was established by the Minister for Health & Children in 1999 for the purpose of preparing and disseminating guidelines for the use of blood products in Ireland.

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POSITION STATEMENT

Use of red blood cell transfusion in surgical patients must be based on clear expectation of benefit, based on the best available evidence. Transfusing patients with allogeneic blood exposes them to risks such as infection, adverse immunological or other morbid events. The full extent of such risk cannot currently be defined. In particular the possibility that variant CJD (vCJD) may be spread by transfusion cannot be discounted at the present time. In addition recent and ongoing studies into transfusion in surgical patients indicate an association between transfusion of red cells and adverse immunomodulatory and cardiorespiratory outcomes that requires further investigation.

In this current state of knowledge, all orders for transfusion of red cells must be carefully assessed for appropriate indication and dose.

In general most haemodynamically stable adult patients will not require blood transfusion if the haemoglobin is above 9 g/dl. In surgical patients the lower limit for tolerance of anaemia is much more difficult to define from the available evidence: patients with ongoing blood loss, or with concurrent cardiovascular disease should probably be transfused when the haemoglobin level falls below 7 g/dl, and a higher threshold will be necessary for some patients.

Use of proven strategies that reduce exposure to allogeneic transfusion should be made widely available, and applied where appropriate. Such strategies include autologous transfusion techniques, and surgical, anaesthetic and pharmacological approaches that reduce blood loss.

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SUMMARY

1. Blood transfusion carries a real but unquantifiable risk of adverse outcome in surgical patients from infectious, immunological and cardiorespiratory morbid events. This risk may be reduced, but is not eliminated, by autologous transfusion techniques, which, in turn carry different risk profiles.
2. The only indication for red cell transfusion is to increase the oxygen carrying capacity so as to improve tissue oxygen delivery.
3. No single criterion can be identified as a “trigger for transfusion” because there is no readily available indicator of critical tissue oxygenation.
4. A transfusion is **rarely indicated** for Hb > 9g/dl. and is **almost always** indicated for Hb < 6g/dl, (particularly when the anaemia is acute).
5. Each patient should be considered on an individual basis with assessment of the clinical signs and symptoms, particularly those of haemodynamic instability, comorbidity and the risk of further blood loss.
6. Transfusion should be considered on a unit by unit basis. **For many patients, a transfusion of a single unit may suffice** to meet the clinical need of the patient and to reverse the clinical signs that led to the decision to transfuse.
7. The specific reasons for transfusion should be documented in the patient’s medical records. It may be important to be able to demonstrate that a definite indication existed for the transfusion.
8. Transfusions must only be **prescribed by appropriately trained medical practitioners**.
9. All patients undergoing elective surgery should be assessed pre-operatively in adequate time to identify and treat anaemia. Blood conservation strategies and alternatives to allogeneic transfusion should be considered at this time to reduce the need for allogeneic blood transfusion.
10. At operation blood loss can be reduced by good surgical and anaesthetic techniques, by minimising perioperative blood sampling, by maintaining normothermia and by the use of pharmacological agents where appropriate.
11. During and following surgery oxygen supply and demand will be improved by ensuring optimal volume status, providing adequate analgesia and supplemental oxygen and by maintaining normothermia.
12. Regular audit, education and review of guidelines should be performed in every hospital; hospital transfusion committees are the appropriate body to oversee these activities.

1. Introduction

There are wide variations between institutions and countries in transfusion practice. For patients undergoing the same surgical procedures with similar blood loss, the major predictor for transfusion is where the surgery is done, or who does it.¹ For example, the median number of units transfused in uncomplicated coronary artery bypass (CABG) surgery varies from one to five units. Similarly, the number of units transfused in primary total hip replacements varies between a median of two and five units in the different institutions. This large variation in acceptable practice clearly indicates the need for an improvement in the way blood is transfused in surgical patients. This is all the more important in the current state of understanding of the risks and benefits of red cell transfusion. Many individuals prescribing blood are unaware of recommended changes in published guidelines for transfusion practice²⁻³ and still adhere to outdated dogmas: for example the use of a 10 g/dl transfusion threshold, and the widespread practice of always transfusing a minimum of two units.

This guideline has been written according to the principles of evidence-based medicine. Unfortunately there has been a lack of good clinical studies in blood transfusion that have attempted to measure relevant clinical outcomes of morbidity or mortality associated with transfusion. This picture has improved in the last few years, and it has become possible to identify some evidence on which to base rational practice. Where possible we have graded evidence in the standard form:

- *Evidence level A – randomised controlled trials of adequate design exist.*
- *Evidence level B –robust experimental or observational studies support the practice, though prospective randomised controlled trials have not been reported.*
- *Evidence level C – practice is based on expert opinion only.*

2. The Evidence Base

To help make an appropriate decision in clinical practice, the questions that need to be answered are:

- *What are the risks of acute anaemia?*
- *What are the benefits of transfusion?*
- *What are the risks of transfusion?*

The risks associated with severe acute anaemia have mainly been determined by observational studies in patients refusing transfusion, and in limited studies on volunteers – Level B evidence.

- Anaemia increases the risk of mortality when Hb falls below 5-6g/dl.⁴⁻⁵
- In the presence of cardiovascular disease blood loss of greater than 500mls increased the affect of anaemia on mortality *at any level of haemoglobin below 7g/dl.*⁵
- Acute reduction of Hb to 5g/dl while maintaining normovolaemia in 35 healthy resting adults did not produce evidence of inadequate oxygen delivery.⁶
- Acute isovolaemic anaemia in 8 young healthy humans to Hb levels of 7, 6, and 5g/dl resulted in decreased self-scored energy levels and an increase in heart rate but not hypotension⁷. Changes in energy and heart rate were reversible with the transfusion of autologous red blood cells.

The benefit from transfusion in patients with acute anaemia. The clinical benefit sought from blood transfusion is to reduce morbidity and mortality by improving tissue oxygen delivery and, as a consequence, tissue oxygen consumption. Recent published studies have attempted to define the ability of transfused blood to achieve such benefit.

Evidence Level A

- In a randomised, controlled trial in critically ill patients (n=838), the Canadian Critical Care Trials Group demonstrated that a restrictive transfusion strategy (transfusion trigger of 7g/dl; haemoglobin concentrations maintained between 7 and 9 g/dl), was associated with significantly lower mortality rates than a liberal transfusion strategy (haemoglobin concentrations maintained between 10–12g/dl).⁸ The restrictive strategy was associated with better overall clinical outcome. Blood transfusions were decreased by 54% in the restrictive transfusion group.

Evidence Level B

- An analysis of 8,787 patients who had surgery for hip fracture showed that 30 day mortality was not improved by transfusion when Hb \geq 8.0g/dl.⁹
- A study of 84 hip fracture patients showed no improvement in rehabilitation, morbidity or mortality when the indication for transfusion was based on symptoms or Hb<8g/dl versus a transfusion practice to maintain Hb>10g/dl.¹⁰
- In studies in septic patients, blood transfusion was associated with an increase in oxygen delivery but with no associated increase in oxygen consumption.¹¹⁻¹²
- In two animal studies, improvement in oxygen consumption, after extreme haemodilution, was only seen when the blood transfused was less than six days old.¹³⁻¹⁴

- These latter data suggest either an inability of the tissues to utilise the oxygen or an inefficiency in the release of oxygen by the red blood cells.

Evidence Level C

A consensus statement by the American Society of Anaesthesiologists stated that a transfusion is almost always indicated for Hb < 6g/dl, (particularly when the anaemia is acute) and that a transfusion is rarely indicated for Hb > 10g/dl.³ The patient's risk for complications of inadequate oxygenation should be considered. Each patient requires individual assessment of the clinical signs and symptoms and the risk of further blood loss.

Similar recommendations were made by a recent workshop of the European Union on the optimal use of blood.¹⁵

Risks of Blood Transfusion

The risks of blood transfusion are outlined in Appendix 2. Variant CJD is of particular concern at the moment in view of the fact that its transmission by blood transfusion is unknown and by the absence of a test to exclude potentially infectious donors.

Evidence in studies specifically addressing patients with cardiovascular disease

In the myocardium, oxygen extraction is approximately 90%, and the tissue cannot compensate for reduced oxygen delivery (for example in anaemia) by an increase in extraction. This means that oxygen delivery to the myocardium is determined by the arterial oxygen content and the blood flow. In patients with stenotic vessels, there is little or no reserve to increase delivery by increasing flow. It would seem important in these patients to maintain oxygen content at a level where flow is optimal and to keep demand to a minimum.

Evidence Level A.

- The Canadian Critical Care Trials Group study did not demonstrate an increase in cardiac morbidity or mortality from the restrictive transfusion approach⁸. This study was powered for equivalence: it did not attempt to show that the restrictive approach was better. Instead it was designed to show that the restrictive approach was not worse. As a result while it does show that transfusion to 10g/dl does not improve cardiac outcome, it does not define the optimum transfusion protocol in patients with cardiovascular disease.
- In a randomised, controlled study of 428 consecutive patients undergoing elective primary coronary artery bypass grafting, study patients (n=212) received RBC transfusions in the postoperative period if the Hb level was < 8g/dl. Control patients (n=216) were treated according to individual physician's orders (Hb levels < 9g/dl as the institutional guideline). The lower threshold of <8g/dl did not adversely affect patient outcome but reduced red cell transfusion by 20%¹⁶.

Evidence Level B.

- In 1,316 high risk patients undergoing myocardial revascularisation, a minimum Hct \leq 17% (approx Hb 6g/dl) on bypass increased the likelihood of postoperative mortality.¹⁷
- In animal models with coronary artery stenoses, haemodilution was associated with myocardial ischaemia and dysfunction. With a critically stenotic left anterior descending artery, mild dysfunction occurred at a Hct of 24% (Hb 8g/dl) and severe dysfunction at a Hct of 14% (approx Hb 4.7g/dl).¹⁸ Cardiac failure developed earlier in animals with multivessel disease.¹⁹
- In a prospective trial in 99 patients undergoing major vascular surgery, in which patients were randomly assigned preoperatively to receive transfusions to maintain a haemoglobin level of either 9g/dl or 10g/dl, no difference was detected in morbidity or mortality.²⁰
- In an observational study in 27 patients at high risk for cardiovascular disease undergoing lower limb revascularization, an increased cardiac morbidity was associated with Hct <28% (Hb 9g/dl).²¹ However the small size of the study and the fact that transfusions were limited to lower Hct group makes observations difficult to interpret.
- Patients admitted to ICU after CABG with Hct >34% had a greater incidence of postoperative myocardial infarction and left ventricular dysfunction.²²

From the available evidence it can be concluded that patients with cardiovascular disease with a haemoglobin level of less than 8g/dl, may be at an increased risk of perioperative morbidity and mortality. However, in stable patients, there is no evidence that maintaining Hb > 9.0g/dl with blood transfusion reduces morbidity.

APPENDIX 1: STRATEGIES FOR MANAGEMENT OF TRANSFUSION REQUIREMENTS IN SURGICAL PATIENTS.

Patients in the perioperative period and particularly following operation can experience many problems associated with an increased oxygen demand e.g.increased catecholamines, shivering, pain etc. and reduced oxygen supply e.g.hypovolaemia and hypoxia. To reduce these to a minimum, the following are important:

- Ensuring optimal volume status
- Providing adequate analgesia
- Providing supplemental oxygen
- Maintaining normothermia
- Consideration of beta blockade in certain categories

PREOPERATIVE MANAGEMENT

Active management is required from the time the patient is first referred for surgery until discharge. This includes treatment of pre-existing anaemia, detection of subclinical iron deficiency, consideration of predeposit autologous donation and avoidance of drugs that increase surgical blood loss. **The routine use of preadmission clinics would facilitate this kind of assessment.**

Treatment of pre-existing anaemia, and reversal of sub-clinical iron deficiency.

All patients scheduled for surgery should have an assessment done to exclude the presence of anaemia. This should be performed in a timeframe that permits appropriate management. Assessment of iron status should be part of pre-operative management so that iron deficiency can be identified and treated. Correction of iron deficiency anaemia with oral iron supplements may take up to two months. Iron deficiency delays erythropoiesis in the postoperative period, and may increase the likelihood of receiving a blood transfusion²³. Therefore consideration may be given to assessing iron status even in non-anaemic patients particularly those on long-term aspirin or nonsteroidal anti-inflammatory (NSAID) medication.

Normovolaemic patients with asymptomatic anaemia presenting for surgery usually do not need transfusion before surgery. Transfusion may be considered later, taking into account intra and postoperative losses.

Erythropoietin. At present, it is not possible to recommend routine use of erythropoietin in preoperative patients. Its use should be considered for patients who refuse transfusion, where a contraindication to blood transfusion exists or in association with preoperative autologous donation.

Erythropoietin has been licensed for use in adult, **non-iron deficient patients**, with moderate anaemia (haemoglobin level 10-13gm/dl), to increase the yield of preoperative autologous donations prior to surgical procedures associated with substantial blood loss. Its use has to be

balanced against the reported increased risk of thromboembolic events and cost. It is not recommended in patients with a history of transient ischaemic attacks, peripheral vascular disease or myocardial infarction.

Pre-deposit autologous donation. Preoperative autologous blood donation is a facility where patients can donate their own blood, so that it is available for them, if needed, at the time of their surgery. Standards, guidelines and regulations exist for patient selection for pre-deposit autologous donation, as well as for the processing, handling and storage of the blood^{24,25,26,27}.

Avoidance of drugs that increase surgical blood loss. Where possible, aspirin, NSAIDs and other antiplatelet therapies should be discontinued in advance of surgery. Many patients with carotid and coronary artery disease are being treated medically with new, more potent, antiplatelet agents (ticlopidine and clopidogrel) that have a significant effect on operative bleeding. To reverse the effect of antiplatelet drugs, these need to be discontinued a minimum of seven days preoperatively. Alternative therapy needs to be considered where indicated. Recommendations exist for the perioperative management of anticoagulation in patients who are taking oral anticoagulants^{28,29}.

INTRAOPERATIVE MANAGEMENT

In the intraoperative period several factors require attention. These include management of blood loss, management of volume replacement, reduction of oxygen demands and the use of alternatives to allogeneic transfusion.

Management of blood loss: Attention to surgical technique can reduce the frequency of allogeneic transfusion. The use of different anaesthetic techniques has also been shown to reduce intraoperative blood loss³⁰.

It is important to maintain normothermia. Hypothermia contributes to the development of coagulopathies. Even moderate hypothermia (<35°C) is associated with increased perioperative blood loss.³¹ All patients having surgical procedures associated with significant blood loss should have their temperature monitored intra-operatively. Appropriate action should be taken to prevent and correct hypothermia using fluid warmers, thermal drapes, heated humidifiers and forced airwarming blankets where appropriate.

In major blood loss, and particularly if there is evidence of microvascular bleeding, coagulation studies should be performed. A basic screen includes pro-thrombin time (PT), partial thromboplastin time (PTT), fibrinogen level and platelet count. Appropriate component therapy should be administered as indicated by the clinical state and the coagulation tests³².

Blood loss should be monitored. Assessment of blood loss by weighing swabs and measuring suction loss usually results in an underestimation of the actual loss. When used in conjunction with serial haemoglobin measurements and haemodynamic parameters it helps to guide volume and transfusion therapy.

Management of volume replacement. Normovolaemia must be maintained in the presence of anaemia. In assessing volume replacement, consideration has to be given to preoperative deficits, which may be due to prolonged fasting, nausea, vomiting, diarrhoea, the use of osmotic bowel preparation regimens or a combination of these. Intraoperative losses will vary with the surface area of the patient exposed, third space interstitial loss and blood loss. Intraoperatively, initial volume replacement is usually with crystalloid and later with a combination of crystalloid and colloid.

It is useful to have estimated how much blood loss can be tolerated, before the patient gets to a predetermined, minimally acceptable Hb. A 40kg patient with a preoperative haemoglobin of 12g/dl will reach a Hb of 8g/dl with a smaller blood loss than a 70kg with the same haemoglobin. Several formulae have been identified which help calculate an “acceptable” blood loss for an individual patient³³.

Reduction of oxygen demands. Anaemia is better tolerated when oxygen demands of the vital organs are minimised. Adequate depth of anaesthesia and appropriate analgesic techniques will reduce oxygen demands of the myocardium and brain tissue. A beneficial effect of beta-blockers in certain groups of patients has also been reported³⁴.

The use of alternatives to allogeneic transfusion: Intraoperative blood salvage (IBS) is a technique where the patient’s blood is collected, washed, concentrated and reinfused at the time of surgery. Its use has been documented in cardiac, orthopaedic, vascular, organ transplantation and trauma. It has been shown to reduce the requirements of allogeneic transfusion^{25,26,27}.

Postoperative blood salvage (PBS) is a technique where blood that is collected in the drains is returned to the patients. This has been well described after cardiac surgery and in orthopaedic surgery, particularly total knee arthroplasty. This technique is not without risk and should be carried out using specific standard operating procedures.

For their effective and safe use, all autologous transfusions techniques require active management by a lead clinician, adherence to standard operating procedures, and the use of appropriate algorithms to predict optimal transfusion support for the individual patient.

Antifibrinolytic agents. The use of antifibrinolytic agents has been investigated mainly in cardiac, orthopaedic, hepatic and urological surgery³⁵. These agents have been shown to be effective and safe in reducing blood usage particularly in redo cardiopulmonary bypass surgery, in redo valve grafts, and in liver transplantation.

POSTOPERATIVE MANAGEMENT

The issues that need to be considered are: management of volume replacement and ongoing blood loss, reduction of oxygen demands, management of anaemia and the use of alternatives to allogeneic transfusion.

Management of volume replacement and ongoing blood loss. The triggers for transfusion outlined above are appropriate guidelines in the postoperative period. It is important if these levels

of anaemia are to be tolerated by the patient that all other parameters are kept optimal. Postoperative patients in ICU or HDU have very close monitoring of their haemodynamic status, oxygenation, pain relief, biochemical and haematological indices and ongoing blood loss. Patients returning to areas that are less intensively monitored may need postoperative instructions based on the anticipated clinical picture that develops. In the postoperative period, where the patient is stable, there is no evidence that anaemia slows down recovery.

Clinical assessment of blood loss is known to underestimate actual loss. Many algorithms and computerised models are being evaluated to help predict loss more accurately. With improved point of care testing systems, serial estimations of haemoglobin and haematocrit are now possible. Regular checks of haemoglobin or haematocrit have been shown to reduce patient exposure to allogeneic transfusion¹⁰.

ROLE OF THE TRANSFUSION COMMITTEE

With modifications and development in surgical techniques and procedures, transfusion requirements will change. Ongoing audit and monitoring of practice should be part of the role of the transfusion surveillance officers and the hospital transfusion committees.

APPENDIX 2: ADVERSE EFFECTS OF TRANSFUSION

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Infections that can be transmitted by transfusion

Every donation is checked for:

- Hepatitis B virus antigen (HBsAg)
- Hepatitis C antibody (HCV Ab)
- HIV1 and 2 antibody (Anti HIV1, Anti HIV2)
- Treponema pallidum antibody
- HTLV I & II antibody

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

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

Because all donated units that test positive are discarded, any residual risk of transmitting infection is due to a person donating in the very early phase of infection before antibody is detectable in the donor's plasma – the so called window period of infection. The risk of this occurring has been calculated for the Republic of Ireland per component transfused as less than 1:3.3 million for HIV, 1:500,000 for HCV and 1:100,000 for HBV (Dr. J. O'Riordan, 1998).

Variant Creutzfeld-Jakob Disease. Variant CJD is considered to be the human form of bovine spongiform encephalitis. At present it is not possible to be confident that it cannot be spread by blood transfusion. While this is not known ever to have occurred in humans, there are animal data that suggest it could happen. Considerably more understanding of the biology and epidemiology of this disease is needed to develop an accurate assessment of the risk of spread by blood or blood products. *In the current state of knowledge, doctors prescribing blood components for their patients must ensure that there are clear and cogent reasons for the transfusion that outweigh any potential risk of vCJD transmission.*

Other Hepatitis viruses. Hepatitis A may very occasionally be transmitted by blood products. Other transfusion-transmitted virus that may be associated with hepatitis have been reported; the clinical significance of these agents remains to be established.

HTLV (I and II) HTLVI can cause neurological disorders and a form of adult T-cell leukaemia. There is usually a delay of many years between infection and development of illness. It is likely that only a small proportion of those infected become ill. HTLVI is transmissible by the transfusion of cellular blood components. The prevalence of infection is high in some parts of the world, notably Japan and the Caribbean. The link between HTLV II infection and disease is less clear, but infection is found in some intravenous drug users.

Cytomegalovirus (CMV). Approximately 30% of Irish blood donors have antibody to CMV, but only a small proportion of antibody positive donations transmit the virus through transfusion. Transfusion transmitted CMV is of proven clinical importance in premature infants weighing less than 1200-1500g who are born to CMV antibody-negative mothers, and in CMV antibody-negative bone marrow allograft recipients who receive CMV sero-negative grafts. Although the risk of clinical CMV infection is much smaller in recipients of autografts, some centres recommend that these patients also should receive CMV negative products. For these patients, CMV safe blood components should be given. This is normally done by using donations that do not contain detectable antibody to CMV. An alternative is the use of leucocyte depleted blood components. Fresh frozen plasma and cryoprecipitate do not transmit CMV.

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

Treponemal infections. All donations are screened for serological evidence of *Treponema pallidum* infection. A further safeguard is that infectivity of *T. pallidum* declines as blood is stored at 2-6°C.

Chagas disease, caused by *Trypanozoma cruzii* is transmissible by transfusion. This is an important problem in some South and Central American countries where the infection is prevalent, and in donors returning from visits to endemic areas.

Bacterial contamination of blood components. Very rarely, bacterial contamination of red cell transfusions occurs. This is a cause of very severe and often lethal transfusion reactions. The estimated incidence is about 1 per million units transfused. Bacteria associated with severe septic reactions to red cell transfusion are usually cold-growing Gram negative species such as *Pseudomonas fluorescens*, an environmental contaminant or *Yersinia enterocolitica*, an organism that may enter a blood donor pack that is collected during an episode of asymptomatic bacteraemia. Skin contaminants such as staphylococci may proliferate in platelet concentrates stored at 20-22°C and this is a factor limiting the safe storage life of platelet concentrates. Bacterial contamination of platelet units may be considerably more common than contamination of red cell units; the severity of reactions to contaminated platelet units may be less severe, although fatal reactions can occur.

Malaria. Donor selection procedures are designed to exclude potentially infectious individuals from donating red cells for transfusion. Transfusion transmitted malaria occurs with a frequency of about 0.25/million units collected in the USA. This complication has not been reported to date in Ireland.

Acute transfusion reactions

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

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

In an unconscious or anaesthetised patient, hypotension and uncontrollable bleeding due to DIC may be the only signs of an incompatible transfusion. Oliguria is common and is often followed by acute renal failure. If an acute haemolytic transfusion reaction is suspected, the transfusion must be stopped and urgent steps taken to confirm or exclude this possibility. The differential diagnosis must include infusion of bacterially contaminated blood.

Reactions due to red cell antibodies other than ABO. Haemolytic reactions can be caused by other red cell antibodies in the recipient's blood, including anti-RhD, -RhE, Rhc and K (Kell). Reactions due to anti RhD are rare since patients generally receive RhD compatible red cells. Reactions due to these antibodies are usually less severe than those caused by ABO incompatibility since they do not activate complement. Destruction of transfused red cells is mainly in the spleen or liver. The patient may experience fever, nausea and shivering. However, the Jk (Kidd) and Fy (Duffy) antigens do activate complement and can cause severe intravascular haemolysis leading to renal and cardiac failure. Jk antibodies are often very difficult to detect in pretransfusion samples.

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

Delayed haemolytic transfusion reactions (DHTR) In patients who have previously been immunised to a red cell antigen during pregnancy or by transfusion, the level of antibody to the blood group antigen may be so low that it cannot be detected in the pretransfusion sample. About 1% of parous women have red cell antibodies that are often undetectable by routine methods before transfusion. After transfusion of red cells bearing that antigen, a rapid, secondary immune response raises the antibody level so that after a few days, transfused red cells bearing the relevant

antigen may be rapidly destroyed. The signs of this delayed haemolytic transfusion reaction appear 5-10 days after transfusion with fever, falling haemoglobin, jaundice and haemoglobinuria. Clinically significant delayed haemolytic transfusion reactions are rare. Although DHTR is seldom fatal, it can cause further problems for a patient who is already seriously ill.

Non-haemolytic febrile transfusion reactions (NHFTTR) Fever or rigors during red cell or platelet transfusion affect 1-2% of recipients, mainly those who have been immunised to leucocyte antigens by pregnancy or previous transfusion. Antibodies in the patient's plasma react against transfused leucocytes in the blood component. The symptoms are shivering usually 30-60 minutes after the start of the transfusion, followed by fever. Most reactions can be managed by slowing or stopping the transfusion and giving an antipyretic e.g. paracetamol. It is important to remember that the symptoms could be due to an acute haemolytic transfusion reaction or bacterially contaminated blood.

Allergic reactions. The symptoms are urticaria and itch within minutes of the transfusion. Symptoms usually subside if the transfusion is slowed and antihistamine is given (e.g. chlorpheniramine 10 mg, by slow intravenous injection or intramuscular injection in patients who are not thrombocytopenic). The transfusion may be continued if there is no progression of symptoms after 30 minutes. Chlorpheniramine (10 mg parenterally) should be given before transfusion when a patient has previously experienced repeated allergic reactions.

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

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

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

Fluid overload. When too much fluid is transfused or the transfusion is too rapid, fluid overload can lead to systemic and pulmonary venous engorgement. Pulmonary and acute respiratory failure may follow. Signs may include dyspnoea, tachycardia and hypotension. Standard medical treatment is a diuretic (e.g. frusemide 20mg IV initially) and oxygen. The transfusion should be stopped or slowed. Volume overload is a special risk with 20% Albumin solutions.

Patients with chronic anaemia are normovolaemic or hypervolaemic and may have signs of cardiac failure before any fluid is infused. If the patient must be transfused, give red cells rather than whole

blood, with diuretic therapy if required. Each unit should be given slowly and the patient closely observed. Restricting transfusion to one unit in each 12 hour period should reduce the risk of LVF.

Late complications of transfusion (excluding infectious causes).

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

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

GvHD has also occurred in immunologically normal patients after transfusion of a relative's blood. Transfusion associated GvHD is fatal in almost all cases. *Acute GvHD* begins 4-30 days after transfusion with high fever followed by a diffuse erythematous skin rash progressing to erythroderma and desquamation. Gastrointestinal and liver dysfunction occur and pancytopenia is common.

GvHD is prevented by gamma irradiation of cellular blood components to a dose of 25 Gy.

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

- Could tumour recurrence rates be increased? Prospective clinical trials have not shown a difference in the prognosis for transfused versus non transfused patients or for recipients of autologous, as opposed to allogeneic blood.
- Does transfusion increase the risk of postoperative infection? Current evidence suggests that transfusion does increase the incidence of postoperative infections in surgical patients, although this remains controversial; also controversial is the suggestion that leucocyte depletion of transfused red blood cells can attenuate this effect.

Post transfusion purpura (PTP) is a rare but potentially lethal complication of transfusion of red cells or platelets, most often seen in female patients. It is caused by platelet-specific alloantibodies. Typically 5-9 days after transfusion, the patient develops an extremely low platelet count with bleeding. Treatment is with high dose corticosteroids combined with high dose intravenous immunoglobulin. If platelet transfusion is unavoidable, platelets that are compatible with the patient's antibody should be used. Expert advice is needed in managing PTP.

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