

Clinical Practice Guidelines on the Use of Blood Components

**(red blood cells, platelets,
fresh frozen plasma, cryoprecipitate)**

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These guidelines are a joint initiative of the National Health and Medical Research Council and the Australasian Society of Blood Transfusion, in cooperation with the Commonwealth Department of Health and Ageing, the Royal Australasian College of Surgeons, the Australian and New Zealand College of Anaesthetists, and other relevant groups.

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Note: Unless otherwise indicated, figures were developed by the Working Party.

SUMMARY

These guidelines on the use of blood components (red blood cells, platelets, fresh frozen plasma and cryoprecipitate) are a joint initiative of the National Health and Medical Research Council (NHMRC) and the Australasian Society of Blood Transfusion (ASBT), in cooperation with the Commonwealth Department of Health and Ageing, the Royal Australasian College of Surgeons, the Australian and New Zealand College of Anaesthetists, and other relevant groups. The coalition of organisations involved in developing these guidelines demonstrates the degree of interest across the specialties in promoting the appropriate use of blood components.

In certain clinical circumstances, blood component therapy (the administration of components derived from human blood) can save lives, restore normal life expectancy and improve quality of life. However, it is increasingly clear that such therapy has limitations, and that the decision to transfuse must be made with great care. As well as the need to regularly review the evidence for the risks and benefits of any practice, there are several factors driving the move towards the most appropriate use of blood components:

- evidence that patterns of use are not necessarily based on current scientific evidence and may not result in the best outcomes for patients;
- continuing concern about the risk of adverse outcomes associated with blood component therapy, despite the increased viral safety of blood and continuing efforts to ensure the safety and quality of the blood supply; and
- increasing pressure on the blood supply worldwide, resulting in the need to optimise use of this precious resource.

These guidelines aim to support clinical decisions about the use of red blood cells, platelets, fresh frozen plasma and cryoprecipitate, by discussing the current evidence underpinning the indications for their use. Related topics such as the blood supply, technical aspects of the administration of blood components and the overall management of conditions for which blood components are given, are beyond the scope of the guidelines.

Evidence for inappropriate use of blood components

There are substantial differences in the clinical use of blood components across Australia and New Zealand as well as overseas. This reflects a lack of consensus among clinicians about specific criteria for appropriate use.

Several studies in Australia and New Zealand have found that the amount of blood used and the percentage of admissions involving the use of blood components vary across different types of hospitals, even for the same procedure or diagnosis, and that the rate of use that can be classed as inappropriate is

unacceptably high. These results are consistent with studies from Europe and the United States.

Various strategies have been developed to reduce the inappropriate use of blood, in Australia, New Zealand and overseas. These include guidelines and consensus conferences, as well as monitoring of transfusion practice (retrospective and prospective), education and self-audit by clinicians. Most evidence suggests that a 'complex' intervention is needed, combining clinical criteria for appropriate use, integration of quality improvement measures (including informed consent) into practice and ongoing monitoring and review.

Current evidence base for clinical practice

Sound evidence on which to base firm conclusions on important aspects of transfusion practice is lacking. While there are many articles and studies about blood component therapy, the number of randomised controlled clinical trials remains small. Many studies are further limited by small study populations.

Medical indications for the use of blood components are easier to define for some clinical circumstances than for others. In a number of situations where blood component therapy has a central role, the physiology is usually well understood, and the use of blood components is logical, can be monitored and has a direct relationship to the clinical outcome for the patient. In other clinical circumstances, the physiology is less well understood, the risks more difficult to quantify and clinical outcomes harder to define. There are a number of clinical situations in which the use of a specific blood component has been advocated and become common practice, but has not been shown to be of benefit.

In addition, for decades there has been general acceptance of laboratory results such as haemoglobin level or platelet count as the main indication for use of blood components. For example, a haemoglobin level of 100g/L has been generally recommended as a uniform transfusion threshold or 'trigger' for red blood cells. More recently, it has been acknowledged that a single automatic transfusion trigger should not be used, and that a range of clinical signs and symptoms also needs to be considered.

The current evidence base for each blood component can be summarised as follows:

- Many studies have investigated the implications of using a lower haemoglobin level as the transfusion threshold for red blood cells. There is level I evidence that use of red blood cells is inappropriate when $Hb > 100g/L$ in asymptomatic patients. There is level IV evidence that it can be regarded as appropriate when $Hb < 70g/L$ (depending on the severity of the disease). Comparative studies in adults with haemoglobin levels within the range 70–100g/L are limited in quality.
- Evidence on the use of platelets is largely based on observational studies in selected circumstances. However, there is level II evidence that the prophylactic use of platelets may be appropriate in bone marrow failure

when the platelet count is $<10 \times 10^9/L$ (in the absence of additional risk factors such as fever, antibiotics or new bleeding). Therapeutic use of platelets is likely to be appropriate when thrombocytopenia is a major contributory factor in the context of massive haemorrhage or transfusion. No benefit has been shown for the use of platelets in the treatment of immune-mediated platelet destruction, thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome or following uncomplicated cardiac bypass surgery.

- Well-documented indications for the use of fresh frozen plasma are limited to treatment of bleeding episodes or preparation for surgery in patients with factor deficiencies where specific factor concentrates are not available. There is no documented benefit from the use of fresh frozen plasma following uncomplicated cardiac bypass surgery, intravascular volume replacement in acute blood loss or treatment of immunodeficiency states.
- Studies suggest that use of cryoprecipitate may be justified in fibrinogen deficiency with bleeding.

While these guidelines present evidence-based recommendations to guide decisions on the use of blood component therapy, clinical judgement about the balance of risks and benefits should be central to any decision to transfuse. There may be significant variation in the situations in which use of blood components is appropriate, depending on the patient's age, signs and symptoms and other conditions. The decision should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.

Organisational practice

Changing organisational practice through quality improvement is as important as changing clinical practice. Quality in the clinical use of blood components implies administering the right quantity of the right component in the right way at the right time to the right patients, with adequate documentation of both process and outcomes.

In all situations where blood component therapy is given, a quality management system is needed which includes monitoring, assessment, action and evaluation to facilitate the most appropriate use of blood. This should include:

- collecting standardised data items, including the clinical and laboratory indications for transfusion;
- establishing a clinical/management group to monitor the use of blood components; and
- collecting consistent clinical indicators for accreditation purposes at State/Territory and national levels.

Community concern about blood issues and the safety of blood component therapy makes the consideration of consumer issues and processes for informed consent particularly important. Change at clinical and organisational levels within

hospitals will help to standardise the use of blood components. Consumers can also be important drivers of change to practice, if they are aware of the issues surrounding the use of blood components and know about the risks and benefits in their own situations.

Implementing the guidelines

Disseminating the guidelines alone will not change practice. To promote the most appropriate use of blood components, sustained change is needed at every level, from governments through to the institutions where blood component therapy is given.

In recognition of this, the NHMRC sought written submissions on the draft guidelines and held workshops in States and Territories of Australia to provide opportunities for interested parties across Australia and New Zealand to participate in refining the guidelines. Particular attention was paid to implementation and dissemination, to ensure that the guidelines involve and inform institutions, clinicians and other health professionals, consumers and the general community.

In addition to the quality management processes outlined above, a range of activities was identified through the workshops as appropriate for the implementation of these guidelines, including:

- developing summary materials for distribution to institutions where blood components are given;
- developing consumer materials to promote discussion of blood component therapy as part of the process of informed consent;
- establishing a website providing information on transfusion and links to other relevant sites;
- developing 'gate-keeping' software for ordering blood components and monitoring their use;
- developing educational materials for undergraduates and postgraduates; and
- including transfusion nurses in quality improvement processes in hospitals.

To maintain changes in practice, continuing resources will be required over a long time. The guidelines can be only part of an educational program for clinicians and other health professionals, that should start at undergraduate level and extend into the postgraduate period. It also needs the full support of hospital administrative staff through a clinical review process such as a transfusion committee, as well as widely publicised information about the true cost of blood components. These changes need to become a permanent part of hospital processes.

If these guidelines are implemented effectively there will be a number of positive implications in a range of areas. These include:

- improved consistency and appropriateness of transfusion practice;

- integration of transfusion practice into quality management systems in all institutions involved in blood component therapy;
- continuous monitoring and review of the appropriateness of blood component use at institution, State/Territory and national levels;
- increased community awareness of the issues surrounding blood component therapy; and
- reduced pressure on the blood supply.

SUMMARY OF RECOMMENDATIONS

A summary of the guideline recommendations follows. Clinical recommendations are given in Chapter 3 and recommendations for organisational practice are given in Chapter 4.

CLINICAL PRACTICE

It is important to note that the following clinical recommendations simply provide a list of circumstances under which the use of blood components could be accepted as appropriate therapy. The recommendations are not intended to serve as indications for their use, since not all patients who fulfil the criteria would actually benefit from blood component therapy, and in selected cases, such therapy may be appropriate for a patient who does not fulfil the criteria.

These recommendations are not applicable to most acute situations, or to specialty areas such as paediatrics and obstetrics. It is suggested that these recommendations be adapted to meet the needs of specialty groups while maintaining the general principles of the guidelines.

It must be the responsibility of all doctors to ensure that blood component therapy is given only when clearly indicated.

The transfusion decision

- 1** Blood component therapy should only be given when the expected benefits to the patient are likely to outweigh the potential hazards.

Red blood cells

- 2** The decision to transfuse red blood cells should be based on clinical assessment of the patient and his or her response to any previous transfusion as well as the haemoglobin level.
- 3** Use of red blood cells is likely to be inappropriate when Hb > 100g/L unless there are specific indications (level I evidence). If red blood cells are given at this haemoglobin level, reasons should be well documented.
- 4** Use of red blood cells may be appropriate when Hb is in the range 70–100g/L (level IV evidence). In such cases, the decision to transfuse should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.
- 5** Use of red blood cells is likely to be appropriate when Hb < 70g/L (level IV evidence). In some patients who are asymptomatic and/or where specific therapy is available, lower threshold levels may be acceptable.

Platelets

- 6** Use of platelets is likely to be appropriate as prophylaxis:
- in bone marrow failure when the platelet count is $<10 \times 10^9/L$ without risk factors or $<20 \times 10^9/L$ in the presence of additional risk factors (eg fever, antibiotics, evidence of systemic haemostatic failure) (level II evidence);
 - to maintain the platelet count at $>50 \times 10^9/L$ in patients undergoing surgery or invasive procedures (level IV evidence); and
 - in inherited or acquired qualitative platelet function disorders, depending on clinical features and setting (level IV evidence). In these situations the platelet count is not a reliable indicator for transfusion.
- 7** Use of platelets is likely to be appropriate as therapy (level IV evidence):
- in any patient who is bleeding in whom thrombocytopenia is considered a major contributory factor; and
 - when the platelet count is $<50 \times 10^9/L$ in the context of massive haemorrhage / transfusion and $<100 \times 10^9/L$ in the presence of diffuse microvascular bleeding.
- 8** Use of platelets is not generally considered appropriate in the treatment of immune-mediated platelet destruction, thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome or drug-induced or cardiac bypass thrombocytopenia without haemorrhage (level IV evidence).

Fresh frozen plasma

- 9** While few specific indications for fresh frozen plasma exist, its use may be appropriate (level IV evidence):
- for replacement of single factor deficiencies where a specific or combined factor concentrate is not available;
 - for immediate reversal of warfarin effect in the presence of potentially life-threatening bleeding when used in addition to vitamin K and possibly factor IX concentrate;
 - for treatment of the multiple coagulation deficiencies associated with acute disseminated intravascular coagulation;
 - for treatment of thrombotic thrombocytopenic purpura;
 - for treatment of inherited deficiencies of coagulation inhibitors in patients undergoing high-risk procedures where a specific factor concentrate is unavailable; or
 - in the presence of bleeding and abnormal coagulation parameters following massive transfusion or cardiac bypass surgery or in patients with liver disease.

- 10** The use of fresh frozen plasma is generally not considered appropriate in cases of hypovolaemia, plasma exchange procedures or treatment of immunodeficiency states (level IV evidence).

Cryoprecipitate

- 11** Use of cryoprecipitate may be considered appropriate in patients with fibrinogen deficiency where there is clinical bleeding, an invasive procedure, trauma or disseminated intravascular coagulation (level IV evidence).
- 12** The use of cryoprecipitate is not generally considered appropriate in the treatment of haemophilia, von Willebrand's disease, or deficiencies of factor XIII or fibronectin, unless alternative therapies are unavailable (level IV evidence).

ORGANISATIONAL PRACTICE

- 13** Documentation used in ordering or administering blood components (such as request forms or blood administration forms) should summarise the clinical recommendations of these guidelines and collect standardised data items. Clinical and laboratory indications for blood components should be accurately recorded in that documentation and in the patient's medical record.
- 14** In all situations where blood component therapy is given, a process for clinical review should be in place to monitor the appropriateness and safety of its use and to develop systems for the implementation of these guidelines.
- 15** Implementation of the recommendations in these guidelines should be adequately resourced by health systems.
- 16** As part of the informed consent process, a patient should be given clear explanation of the potential risks and benefits of blood component therapy in his or her particular case.

INTRODUCTION

Blood components such as red blood cells, platelets and plasma derivatives are important in prophylaxis and treatment. Blood component therapy (the administration of components derived from human blood) is an established method for treating a range of conditions including blood loss and severe anaemia, and can both save lives and restore normal life expectancy. However, it is increasingly clear that blood component therapy has limitations, and that the decision to transfuse must be made with great care. As well as the need to regularly review the evidence for the risks and benefits of any practice, there are several factors driving the move towards the most appropriate use of blood components:

- evidence that patterns of use are not necessarily based on current scientific evidence and may not result in the best outcomes for patients;
- continuing concern about the risk of adverse outcomes associated with blood component therapy, despite the increased viral safety of blood and continuing efforts to ensure the safety and quality of the blood supply; and
- increasing pressure on the blood supply worldwide, resulting in the need to optimise use of this precious resource.

A lack of consensus on the most appropriate criteria for blood component therapy has led to wide variation in transfusion practice, and the inappropriate use of blood, in Australia and New Zealand as well as overseas. Existing guidelines for blood component therapy also vary, and strategies for changing transfusion practice have had mixed effectiveness. Overall, it has been found that it is difficult to change practice and even more difficult to maintain the change (McGrath et al 2001), especially if strategies are not sustained.

The development of national guidelines on the appropriate use of blood components in Australia and New Zealand was prompted by:

- a report by the Australian Health Ministers' Advisory Council (AHMAC) on alternatives to homologous blood donation (AHMAC 1999) which called for the establishment of clear guidelines on the use of blood and criteria for transfusion;
- a recommendation to Health Ministers from the Donor Deferral Working Group to introduce deferral of donations from some sources due to the theoretical risk of variant Creutzfeldt-Jakob Disease transmission through the blood supply; and
- increasing public awareness and concern about blood-related issues.

A recently published, wide-ranging review of the Australian blood banking sector (Blood Review Committee 2001), supported the development and implementation of these guidelines, and made similar recommendations for improving quality assurance processes in hospitals to improve transfusion outcomes.

These guidelines are a joint initiative of the National Health and Medical Research Council (NHMRC) and the Australasian Society of Blood Transfusion (ASBT), in cooperation with the Commonwealth Department of Health and Ageing, the Royal Australasian College of Surgeons, the Australian and New Zealand College of Anaesthetists, and other relevant groups.

Blood component therapy is relevant to many areas of medicine. The coalition of organisations involved in developing these guidelines demonstrates the degree of interest across the specialties in promoting the appropriate use of blood components.

Scope of the guidelines

The therapeutic use of blood components is the ultimate goal of the 'blood chain', a complex series of events that begins with the willingness of a donor to provide blood or plasma for the benefit of others, and ends with the follow-up of the person who has received components derived from the donation (EC 1999). In between are a sequence of processes, including:

- the collection, testing, banking and distribution of blood;
- the clinical decision to transfuse, followed by administration and monitoring; and
- broader issues such as the overall management of conditions for which blood component therapy is given, and whether alternatives to transfusion are appropriate in the particular situation.

Also relevant are quality processes throughout the sequence to ensure the safety and quality of the blood supply and promote appropriate use of this limited resource.

These guidelines focus on the clinical decision to transfuse and the supporting quality processes. Other aspects of the sequence are beyond the scope of the guidelines.

The guidelines are intended to apply irrespective of the source of blood components used in transfusion. As recommended in the AHMAC report on alternatives to homologous blood donation (AHMAC 1999), the first priority should be to ensure optimal clinical outcomes from the most appropriate use of blood, whether it is autologous blood which is deposited pre-operatively or donated homologous blood. Evidence for the use of alternatives such as pharmacological agents and blood substitutes is also discussed in the AHMAC report.

Aim of the guidelines

Clinical judgement, based on consideration of each individual patient, is central to the decision to transfuse any blood component. These guidelines aim to support clinical decisions about blood components, by discussing the current

evidence underpinning the indications for red blood cells, platelets, fresh frozen plasma and cryoprecipitate.

Overall, the guidelines aim to improve quality of care for patients by:

- improving the consistency and appropriateness of transfusion practice;
- promoting the integration of quality management systems into transfusion practice;
- reducing the overall number of transfusion-related complications;
- increasing consumer awareness of the benefits and risks of blood component therapy; and
- conserving a limited resource.

Development of the guidelines

The guidelines were developed by a Working Party appointed by the NHMRC. Working Party members were selected for their expertise in a range of relevant areas, including haematology, surgery, oncology, anaesthesia, nursing, epidemiology, consumer issues and health economics. The Working Party included representatives of an ASBT Scientific Subcommittee which developed draft guidelines for the appropriate use of blood components. The membership and terms of reference of the Working Party are at Appendix 1. It is recognised that the interests of specialty groups (such as obstetrics and paediatrics) were not represented, and that the specific requirements of these groups may not be covered by the guidelines.

At its first meeting, the Working Party agreed that the following principles should underpin development of the guidelines:

- actively seeking the involvement and input of key stakeholder groups in the development and implementation of the guidelines, so that the guidelines address the needs of both health professionals and consumers;
- addressing the identified need for science-based national guidelines that are easily applicable to individual patients; and
- guiding the best use of a scarce health resource based on evidence of clinical effectiveness and outcomes.

Assessing the evidence

The Working Party based its discussions and recommendations on available meta-analyses and reviews of blood component therapy, augmented by additional reviews of the literature, with expert advice sought where necessary.

The panel met to discuss and agree upon recommendations. The writing team then drafted recommendations and these were circulated to members for comment/agreement and resolution where necessary. There were no disagreements that could not be resolved.

The evidence supporting the recommendations was classified according to the NHMRC level of evidence ratings (NHMRC 1999), to enable readers to judge the strength of the evidence on which the recommendations are based.

Level of evidence ratings

- I: Evidence obtained from a systematic review of all relevant randomised controlled trials.
 - II: Evidence obtained from at least one properly designed randomised controlled trial.
 - III-1: Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
 - III-2: Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group.
 - III-3: Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.
 - IV: Evidence obtained from case series, either post-test or pre-test and post-test.
-

Source: NHMRC (1999).

Target audience

The guidelines were developed to meet the needs of the following target audiences:

- clinicians and other health professionals involved in blood component therapy, especially surgeons, physicians (haematologists, oncologists), anaesthetists, emergency and intensive care clinicians, junior medical officers and nurses;
- blood bank staff;
- patients/consumers;
- quality improvement and quality management personnel;
- transfusion committees in hospitals; and
- hospital and health service managers.

To address the varying needs of these groups, it is intended that the guidelines be published in a range of formats, to be developed with the specific target groups.

Consumers

Clinical practice guidelines are increasingly affecting the quality of health care and have the potential to affect the availability of health-care options for consumers. Deciding what guidelines will cover, how they will be developed and what they will say, are issues in which consumers have a considerable stake (Bastian 1996). For this reason, consumers have been actively involved in the development of these guidelines. Community concern about the safety of blood component therapy makes processes for informed consent particularly important (discussed in Chapter 4).

Consultation and implementation

Effective implementation of the guidelines will be integral to their success. The Working Party devised a comprehensive consultation strategy, in an attempt to involve and inform institutions, clinicians and other health professionals, consumers and the general community in revising the content of the guidelines and developing the implementation plan.

In addition to public advertisements and targeted mail-outs of the draft guidelines which sought written submissions, a series of workshops was held in States and Territories of Australia in February 2001. The workshops brought together stakeholders including professional colleges, the Consumers' Health Forum, State/Territory and national health departments and non-government organisations. They provided opportunities for interested parties across Australia and New Zealand to participate in refining the guidelines, particularly their implementation and dissemination. A list of those involved in the consultation process is included in Appendix 6.

From suggestions raised through the consultation submissions and workshops, a comprehensive implementation plan was developed (Chapter 5). Also raised during the consultation process was a wide range of issues that are beyond the scope of these guidelines but should be addressed. These include:

- screening requirements, specific types of blood components available, and other issues relevant to the blood supply;
- alternatives to minimise use of blood components;
- the administration of blood components, including dosage and timing;
- the overall management of conditions such as anaemia or acute blood loss, for which blood components may be given; and
- the use of blood components in specialised areas such as obstetrics, paediatrics and emergency medicine.

Structure of the guidelines

The guidelines are structured as follows:

- current practice in the use of blood components in Australia and New Zealand as well as overseas (Chapter 1);
- the evidence for appropriate use of blood components and strategies for improving transfusion practice (Chapter 2);
- specific recommendations for clinical practice (Chapter 3);
- recommendations for organisational practice and for raising consumer awareness of the issues surrounding blood component therapy (Chapter 4); and
- the dissemination and implementation strategy for the guidelines, and the proposed process for continuous evaluation and review of blood transfusion practice (Chapter 5).

1 CURRENT PRACTICE

Potential problems from inappropriate use of blood components include health risks associated with transfusion, unnecessary pressure on the supply of blood and greater likelihood of clinician exposure to medicolegal action. However, as noted in a 1997 editorial concerning transfusion practice, 'before optimal practice can be promoted, it must be defined' (Allain & Williamson 1997). Defining optimal practice involves examining current patterns of use, and assessing the evidence for the risks and benefits of blood component therapy for various groups of patients.

This chapter discusses current practice in the use of blood components in Australia and New Zealand as well as overseas, including evidence for inappropriate use and variation in practice that lead to both increased risks for patients and the waste of resources.

1.1 OVERVIEW OF BLOOD COMPONENTS

In Australia and New Zealand, as in most countries, voluntary donation of homologous blood is the major source of blood components used in clinical practice. The blood supply in Australia is organised through the Australian Red Cross Blood Service (ARCBS) in each State and Territory, and in New Zealand by the New Zealand Blood Service (NZBS). Local circumstances may determine availability in some areas.

Whole blood

Clinical use of whole blood, either stored or fresh, is now rare (except for autologous transfusion) as most donated blood is processed into components. There are no clear indications for the use of stored whole blood, as it is more likely to produce circulatory overload in some patients and the frequency of non-haemolytic transfusion reactions is increased. Unrefrigerated fresh whole blood, usually defined as being less than 24 hours old, still contains viable platelets and leucocytes and normal levels of labile coagulation factors. The availability of fresh whole blood is limited, as the logistics of blood accreditation make it difficult to have it released for clinical use within 24 hours of collection.

Red blood cells

Red blood cells are the carriers of haemoglobin and are necessary for the uptake, transport and transfer of oxygen from the lungs to tissues. Red blood cells are obtained from whole blood through centrifugation or sedimentation. To

minimise side effects directly associated with red blood cell transfusion, additional measures may be taken including leucocyte filtration, phenotyping, washing and irradiation. Pre-operative autologous deposits and directed donations, which are used in the same way as homologous donations, are alternative sources of red blood cells.

Red blood cells are given to increase the oxygen-carrying capacity of the blood, usually in cases of severe anaemia and severe blood loss. As it is difficult to directly measure intracellular oxygenation in the clinical setting, surrogate markers such as haemoglobin (Hb) level are used, together with a patient's signs and symptoms in relation to blood loss, volume depletion or anaemia, and consideration of other conditions. For decades, a haemoglobin level of 100g/L (or a haematocrit of 30 per cent) has been accepted as the transfusion threshold or 'trigger'—the point at which most patients with acute anaemia are given red blood cells, independent of other clinical factors. This threshold is believed to have originated in a discussion of pre-operative anaemia in 1941 (Hill et al 1999).

More recently, it has been acknowledged that a single automatic transfusion trigger should not be used. The Royal College of Physicians of Edinburgh consensus statement on red blood cell transfusion (1994) concluded '...there is no general agreement at which point transfusion should be given, or on the optimal target concentration to be achieved. There is no single haemoglobin or haematocrit value applicable to all patients'. It is also clear that clinically useful criteria are needed to assist clinicians in evaluating signs, symptoms, and coexisting conditions that put anaemic patients at higher risk of adverse outcomes.

Platelets

Platelets are one of the main cellular components of blood, and are central to haemostasis. The platelet products commonly available for transfusion are obtained either through apheresis or prepared from donated blood using the buffy-coat or platelet-rich plasma (PRP) methods. Modifications to reduce the risk of viral transmission and prevent graft-versus-host disease include leucocyte reduction, irradiation, plasma-depletion and the use of platelet additive solutions.

Platelets are transfused to prevent or treat haemorrhage in patients with thrombocytopenia or defects in platelet function (British Committee for Standards in Haematology 1992a). The role of platelet transfusion depends on the underlying disorder. Platelets may be transfused once or more to treat a single incident, or repeated transfusion may be required over a period of time. Refractoriness (repeated failure to obtain satisfactory response to platelet transfusion) may occur in a proportion of patients repeatedly receiving platelets (TRAP Study Group 1999).

The main use of platelets is to prevent bleeding in patients with haematological malignancies (particularly leukaemias) who have bone marrow failure caused by their disease or its treatment. The criteria on which to base the decision to transfuse vary widely. The clinical decision to transfuse platelets should be based on careful evaluation of the individual patient's condition, including

bleeding history and bleeding tendency, as well as the platelet count or any laboratory result reflecting platelet function (EC 1999).

Fresh frozen plasma

Fresh frozen plasma (FFP) is prepared from anticoagulated whole blood by separating the plasma from the blood cells (through centrifugation of whole blood or apheresis) and storing it frozen until it is transfused. FFP contains all of the blood coagulation proteins, including the labile factors V and VIII, as well as naturally occurring inhibitors.

Although well-defined indications exist for the use of FFP in certain situations, there are a number of other clinical situations in which the use of FFP has been advocated but has not been shown to be of benefit (British Committee for Standards in Haematology 1992b). As virally inactivated FFP is not currently available in Australia or New Zealand, the use of safer alternatives (eg heat-treated and virally inactivated specific clotting concentrate derivatives) should be considered before FFP is given.

Cryoprecipitate

Cryoprecipitated antihæmophilic factor, or cryoprecipitate, is the cold precipitable protein fraction derived from FFP. It contains factor VIII, fibrinogen, von Willebrand's factor and factor XIII and is used for the correction of inherited and acquired coagulation disorders such as hypofibrinogenaemia (marked fibrinogen deficiency).

As with FFP, newer and safer alternative therapies are often more appropriate for a range of indications commonly treated with cryoprecipitate.

1.2 SAFETY OF BLOOD COMPONENTS

Adverse outcomes

The risks of adverse events following blood component therapy include: incompatible blood transfused to patients; acute and delayed transfusion reactions; transfusion-related acute lung injury; graft-versus-host disease; post-transfusion purpura and infection transmitted by transfusion (EC 1999; Williamson et al 1999). While rare, these events can be life-threatening.

Rates of blood group incompatibility are not well documented but remain a concern in red blood cell transfusion. In the United Kingdom the Serious Hazards of Transfusion (SHOT) scheme collects information on serious adverse transfusion reactions. In the period from 1996 to 1998, reported reactions included 'wrong blood to patient' episodes (52 per cent), deaths from all causes

(6 per cent) of which 14 per cent were from the use of incompatible red blood cells, and infections (3 per cent) (Williamson et al 1999).

Viral safety

The ARCBS and NZBS carefully screen volunteer donors for infections that might be transmitted by transfusion. The risks of viral transmission are low and compare favourably with those reported overseas. While there are no national estimates of the risks of transmitting infectious agents through blood component therapy, a study in Victoria (Whyte & Savoia 1997) estimated the risk of viral infection from a repeat donation as 6.45 per million donations for hepatitis B, 4.27 per million donations for hepatitis C, and 0.79 per million donations for HIV. A study by the European Plasma Fractionation Association (EPFA 2000) confirmed the high degree of safety in blood components from donors in both Europe and Australia.

Nucleic acid amplification technology (NAT) screening, which was recently introduced in Australia and will soon be introduced in New Zealand, has the potential to further improve the detection of infected donors. Early estimates indicate that the risk of a repeat donation being infective may fall to 1.12 per million donations for hepatitis C and 0.11 per million donations for HIV (EPFA 2000).

The emergence of infectious agents for which there is no test available poses an additional threat to the safety of blood use. The recent appearance of variant Creutzfeldt-Jakob Disease in the United Kingdom and France, linked with the consumption of beef and beef products infected with bovine spongiform encephalopathy, raises the theoretical risk that diseases such as variant Creutzfeldt-Jakob Disease could be transmitted via blood components. Transmission by blood transfusion has been documented in sheep (Houston et al 2000). The lack of evidence about the actual risk of such events in humans further complicates the issue.

Assessing transfusion risk

National requirements for reporting and collating major transfusion hazards vary. Australia is developing a national system of haemovigilance, and there are currently mechanisms for voluntary reporting of adverse events in all States and Territories of Australia and in New Zealand. France has a haemovigilance system with mandatory reporting, while the United Kingdom SHOT scheme is voluntary and centralised. In the United States, there is no single haemovigilance system, rather a network of surveillance programs run by a variety of organisations, with mandatory reporting of fatal transfusion reactions.

While this data collection is critical for monitoring the risks of transfusion, there is no evidence that it has any effect in changing transfusion practice (Allain & Williamson 1997).

1.3 CURRENT USE OF BLOOD COMPONENTS

While there are national figures on the total amount of blood issued, there have been few studies on how blood components are used at hospital level in Australia or New Zealand. The following studies give some indication of current patterns in use:

- a study in a tertiary teaching hospital in Victoria which examined how hospital practice for the use of red blood cells, platelets and FFP conformed with published criteria (Metz et al 1995);
- a Western Australian review of the use of blood components from July 1994 to June 1995 (Finn et al 1998);
- a study to assess the appropriateness of the use of red blood cells in major urban hospitals in New South Wales (Rubin et al 2001);
- a retrospective study into the use of platelets, FFP and cryoprecipitate in a sample of New South Wales hospitals (Schofield et al 2001); and
- hospital-based studies in New Zealand examining appropriate use of blood components (Calder & Woodfield 1991; Hawkins et al 1994; Gilham & Mark 1997).

It should be noted that patterns of use are likely to vary markedly across States, Territories and countries and that proportions vary considerably from hospital to hospital because of the different patient mix.

Victoria

The study at the Royal Melbourne Hospital (Metz et al 1995) identified the use of red blood cells as 50 per cent of the overall use for chronic anaemia, 36 per cent for perioperative use, 11 per cent for bleeding and 3 per cent for exchange transfusions.

The same study found that medical oncology was the major user of platelets (78 per cent). Overall, 56 per cent of platelets were given prophylactically in bone marrow failure and 33 per cent were given to treat bleeding. For FFP, 41 per cent of use was to correct coagulopathy associated with surgery, 27 per cent to correct coagulopathy in bleeding, 16 per cent to reverse haemostatic disorders in patients having massive blood transfusion, 11.5 per cent for reversal of warfarin effect and the remaining 4.5 per cent for a number of miscellaneous conditions including liver disease and disseminated intravascular coagulation. The major users of FFP were general surgery, cardiac surgery and general medicine.

Western Australia

The Western Australian review (Finn et al 1998) found that major teaching hospitals used over two-thirds of all blood components, had the highest rates of use of blood components, and had the highest percentage of admissions

involving the transfusion of one or more units of blood components. These institutions accounted for 33 per cent of all adult admissions, and had a higher rate of emergency admissions than the smaller metropolitan, rural or private hospitals.

Red blood cells were the most commonly administered blood component, accounting for about 75 per cent of all blood components used in rural hospitals and about 55 per cent in metropolitan hospitals (Finn et al 1998).

Blood components associated with the coagulation process were more commonly administered in the general tertiary hospitals, possibly reflecting the higher prevalence of patients in these hospitals with the prerequisite clinical conditions.

New South Wales

The study into the use of red blood cells (Rubin et al 2001) found that they were most commonly given for anaemia (50 per cent), followed by pre- or peri-operative use (22 per cent) and abnormal, excessive or continued bleeding (13 per cent).

The study into the use of platelets, FFP and cryoprecipitate (Schofield et al 2001) found considerable variation in both surgical and medical specialties across the different hospital types included in the study. The surgical specialties using most blood products were cardiothoracic surgery at referral hospitals and general surgery at major metropolitan and major rural hospitals, with greater use for orthopaedic admissions than found at the referral hospitals.

More variation between specialties was found for medical than for surgical admissions. At referral hospitals, platelets were largely used for haematology admissions (53 per cent of patients), followed by oncology (13 per cent) and cardiology (9 per cent). Haematology and oncology were also major platelet users at major metropolitan and major rural hospitals, but general admissions also received a substantial proportion of the platelets given in these hospitals.

At referral hospitals, cardiology admissions accounted for 19 per cent of patients given FFP, followed by 14 per cent for haematology. FFP was also given across a wide range of admission specialties at major metropolitan hospitals, with the largest proportion for general medical (28 per cent). At major rural hospitals FFP was used for patients in the general medical category (90 per cent), cardiology (3 per cent) and oncology (1 per cent). The small number of patients given cryoprecipitate after a medical admission were spread across the major specialties.

1.4 INAPPROPRIATE USE OF BLOOD COMPONENTS

There are substantial differences in clinical use of blood components in Australia, New Zealand and overseas. A recent report from the European Community identifies three main problems (EC 1999):

- significant variability in the use of blood in the same clinical situations, implying that there is both overuse and potential under-use of blood;

- misuse of blood components (with the rate of transfusion errors being higher than that of transfusion-transmitted viral diseases); and
- lack of documentation about the process, rationale and outcomes of blood component therapy.

The variation in use reflects disparate views and lack of consensus among clinicians about appropriate criteria for blood component therapy, while the other two problems are related to organisational issues and the need for better quality management.

The rates of inappropriate use of blood components reported by most studies vary widely, and it is difficult to compare rates because of differences in the criteria used to define appropriate and inappropriate use.

Several Australian and New Zealand studies have identified variation in transfusion practice and areas in which blood use is inappropriate.

- The Western Australian review (Finn et al 1998) found that the rate of blood utilised and the percentage of admissions involving the use of blood components varied across different types of hospitals, even for the same procedure or diagnosis. The study concluded that the potential for rationalising the use of blood components is greater for elective surgical procedures than for admissions relating to emergency or chronic conditions.

Red blood cells

- The New South Wales study into red blood cell use (Rubin et al 2001) found that they were inappropriately administered in 30–50 per cent of cases (at the first audit). More red blood cells were used inappropriately for surgical than for other admissions. About 5 per cent of patients received a single unit of red blood cells, with 40 per cent of this use being classed as inappropriate.
- A study in a large teaching hospital in New Zealand found that red blood cells may have been administered unnecessarily in 29 per cent of procedures in which they were used (Calder & Woodfield 1991) and that the widespread introduction of guidelines for transfusion did not have a substantial immediate effect on use.
- A 1997 study in New Zealand (Gilham & Mark 1997) found that 24 per cent of red blood cells given to patients having primary hip joint replacement and 9 per cent of those given to people having complex hip replacement were used inappropriately, and that two units were commonly given when one would have been sufficient.
- The Victorian study (Metz et al 1995) found that the use of red blood cells could be classed as inappropriate in 16 per cent of procedures (one-third of all perioperative transfusion and 10 per cent of transfusion for anaemia) based on retrospective review of medical records. In a significant number of episodes, there was no documentation in the medical record of the specific indication for transfusion.

Platelets, FFP and cryoprecipitate

- The Victorian study (Metz et al 1995) found that platelets were inappropriately used in 27 per cent of cases. Inappropriate use of platelets was most commonly for bleeding, particularly in the perioperative period.
- This study (Metz et al 1995) also found that 31 per cent of FFP use could be considered inappropriate. Use for all indications had high inappropriateness rates, with the highest levels being for reversal of the warfarin effect.
- The New South Wales study into the use of platelets, FFP and cryoprecipitate (Schofield et al 2001) found that platelets were used inappropriately in 33 per cent of cases and FFP in 37 per cent of cases. Only a small amount of data were available for cryoprecipitate but these suggested that 49 per cent of cryoprecipitate use could be inappropriate.
- A New Zealand study (Hawkins et al 1994) found that 33 per cent of FFP and 30 per cent of cryoprecipitate transfused in a Wellington hospital was inappropriate.

These results are consistent with a wide range of studies from Europe and the United States. The largest of these is the Sanguis Study, a review of surgical transfusion practice in 43 hospitals in 10 countries of the European Community. It found wide differences between hospitals, both in the proportion of patients receiving blood component therapy and the amount of component used for the same patient category (Sanguis Study Group 1994).

1.5 ALTERNATIVES TO HOMOLOGOUS TRANSFUSION

The AHMAC review of the alternatives to homologous transfusion (AHMAC 1999) concluded that the use of interventions designed to minimise exposure to homologous blood has risen to a high level, but that these changes in practice are not well supported by evidence on their comparative effectiveness or cost-effectiveness. The review found that the first priority should be to ensure optimal clinical outcomes from the most appropriate use of blood, whether it is autologous blood which is deposited pre-operatively or donated homologous blood. In some cases alternatives may be clinically appropriate.

The findings of the review are supported by recent papers on transfusion medicine (Goodnough et al 1999a; 1999b) and on the use of transfusion in critically ill patients (Hébert et al 1999).

2 SUMMARY OF THE EVIDENCE

To improve the consistency and appropriateness of transfusion practice, guidelines need to reflect the evidence base rather than current practice. This chapter summarises the evidence for the appropriate use of blood component therapy, and for strategies to change transfusion practice. More detailed discussion of the clinical evidence can be found in Appendix 2. Appendix 3 provides details of the evidence on measures to reduce inappropriate use and includes a summary of existing guidelines.

Sources of evidence

There is a large number of articles and studies about blood component therapy, with wide variation in the strength of evidence cited. The number of randomised controlled clinical trials, which provide the highest level of evidence, remains small. Many studies are further limited by small study populations.

In its critical evaluation of evidence for the use of blood components in the clinical setting, the Working Party reviewed recent literature and made use of existing reviews including:

- recent review of the published literature by a working party appointed by the ASBT Scientific Subcommittee;
- an Australian systematic review of the literature on red blood cell use (Hill et al 1999);
- an overview of recent international studies and articles prepared to inform the European Community initiative for optimal use of blood (EC 1999);
- a literature review prepared to inform a report on the use of blood components in Western Australia from 1994 to 1995 (Finn et al 1998);
- a comprehensive (though not systematic) review of clinical practice literature on homologous red blood cell transfusion for the period January 1966 to December 1996 (Hébert et al 1997a); and
- a literature review undertaken by the American Society of Anesthesiologists to inform the development of evidence-based guidelines on the use of red blood cells, platelets, fresh frozen plasma and cryoprecipitate in the perioperative setting (American Society of Anesthesiologists 1996).

An overview of the reviews is given in Table 2.1. The material has been rated according to the six-point system outlined in the NHMRC's *A Guide to the Development, Implementation and Evaluation of Clinical Practice Guidelines* (1999) as given on page xx.

Table 2.1 Sources of evidence

Review	Period considered	Number of studies reviewed	Level of evidence
Hill et al (1999)	1997 to 1998	25	I
EC (1999)	not stated	18	II
AHMAC (1999)	1995 to 1998	209	II
Finn et al (1998)	not stated	16	II
Hébert et al (1997a)	1966 to 1996	189	II
American Society of Anesthesiologists (1996)	1966 to 1994	160	II

Note: There is considerable overlap of studies between reviews.

2.1 RED BLOOD CELLS

In an attempt to define the appropriate use of red blood cells, many studies have investigated the effectiveness of their use in reducing the risk of adverse events and the implications of reducing the transfusion threshold from the generally accepted haemoglobin level of <100g/L.

The role of perioperative use of red blood cells in reducing the risk of subsequent morbidity and mortality is unclear. In general, the published data indicate that red blood cells will usually be required when the haemoglobin level is <70g/L and will rarely be required when it is >100g/L. Comparative studies in adults with haemoglobin levels within the range 70–100g/L are limited in quality and cover a variety of interventions, patient populations and settings.

Despite the variation in the design and quality of the studies, the results are generally consistent (level I evidence):

- although there is clearly a threshold level at which it is appropriate to administer red blood cells to avoid adverse outcomes, it appears that this is considerably lower than the historical threshold of a haemoglobin level of 100g/L or a haematocrit of 30 per cent;
- there are no adverse outcomes in the majority of patients if restrictive transfusion thresholds are used rather than liberal strategies, and there is some evidence to suggest that restrictive strategies may reduce all-cause mortality and length of hospital stay as well as transfusion-related complications; and
- restrictive transfusion thresholds also significantly reduce the amount of red blood cells that are transfused.

In some patients, such as older people, the severely ill and people with coronary, cerebrovascular or respiratory disease, anaemia is less well tolerated. However, associations between anaemia and adverse outcomes, as well as modification in the degree of risk in these patients, have not been clearly established.

Table A2.1 in Appendix 2 (see page 53) summarises the results of randomised controlled trials into red blood cell use that reported on mortality, length of hospital stay and blood use.

2.2 PLATELETS

The use of platelets has developed without much clinical trial-based evidence of its effects and complications (Royal College of Physicians of Edinburgh 1998). There is considerable doubt about the precise indications for the use of platelets (Norfolk et al 1998).

Evidence for the prophylactic use of platelets can be summarised as follows:

- while platelets have generally been given in bone marrow failure when the platelet count drops below $20 \times 10^9/L$, studies comparing this to a $10 \times 10^9/L$ threshold have found no excess morbidity or mortality in the lower threshold group in the absence of additional risk factors (eg fever, antibiotics, evidence of systemic haemostatic failure) (level II evidence);
- although studies have suggested that spontaneous bleeding is uncommon with platelet counts $>20 \times 10^9/L$, the platelet count at which patients undergoing surgery or invasive procedures are likely to experience increased bleeding has not been investigated through controlled trials (level IV evidence); and
- there is evidence that the use of platelets is effective for surgical prophylaxis in hereditary platelet function defects but the evidence concerning acquired platelet function defects is less clear (level IV evidence).

Therapeutic use of platelets is confined to patients with thrombocytopenia and/or functional abnormalities who have significant bleeding from this cause. Massive transfusion often produces thrombocytopenia proportional to the amount of blood transfused, with clinically significant problems occurring after transfusion of 1.5–2.0 blood volumes. Consumption of platelets, as well as simple dilution, can also lead to microvascular bleeding.

The evidence does not show benefit from the use of platelets in the following circumstances (level IV evidence):

- in situations of immune-mediated platelet destruction, administering platelets rarely increases the platelet count but may provide a temporary improvement in bleeding;
- treatment of thrombotic thrombocytopenic purpura, which may be worsened by platelet transfusion, or haemolytic uraemic syndrome; and

2. SUMMARY OF THE EVIDENCE

- although platelet function defects and some degree of thrombocytopenia frequently occur even after uncomplicated cardiac bypass surgery, controlled trials of prophylactic platelet transfusion have not demonstrated benefit for these patients.

Table A2.2 (see page 54) outlines selected studies investigating different platelet transfusion triggers.

2.3 FRESH FROZEN PLASMA

While there have been clinical trials evaluating the use of FFP for a range of patients, most recommendations are based on clinical observations and the results of coagulation tests (level IV evidence):

- use of FFP in the treatment of bleeding episodes or preparation for surgery in patients with factor deficiencies where specific factor concentrates are not available is well-documented and universally accepted; and
- there is consensus that, in addition to administration of vitamin K, FFP alone or in combination with concentrates of vitamin-K-dependent factors is indicated for the immediate reversal of warfarin overdose associated with life-threatening haemorrhage.

It should be noted that this area is evolving rapidly.

There are a number of clinical situations in which the use of FFP has been advocated but has not been shown to be of benefit or where alternative therapies are equally satisfactory or considerably safer. These include prevention of coagulation disorders and severe bleeding following uncomplicated cardiac bypass surgery, intravascular volume replacement in acute blood loss or treatment of immunodeficiency states (level IV evidence).

Table A2.3 (see page 55) outlines selected studies evaluating the use of FFP.

2.4 CRYOPRECIPITATE

Use of cryoprecipitate may be justified in patients with fibrinogen deficiency where there is clinical bleeding, invasive procedures, trauma or disseminated intravascular coagulation (DIC) (level IV evidence).

Most patients with factor VIII deficiency are treated with factor VIII concentrates, and patients with some subtypes of von Willebrand's disease respond to administration of desmopressin.

It has not been conclusively shown that cryoprecipitate is of clinical use in patients with fibronectin deficiency (level IV evidence).

2.5 MEASURES TO REDUCE INAPPROPRIATE USE

Several approaches have been developed with the aim of reducing inappropriate use of blood components. Such measures have had varying results.

Guidelines

To guide clinical decisions and to create uniformity in transfusion practice, clinical practice guidelines have been implemented in many centres. Until the development of these guidelines, there has been minimal guidance in Australia and New Zealand on the most appropriate use of blood components, and many hospitals and blood centres have developed guidelines for their own use.

The Working Party reviewed guidelines on the use of red blood cells, platelets, FFP and cryoprecipitate endorsed by medical organisations overseas. Differences in existing clinical guidelines and their recommendations reflect the difficulty in defining clear evidence-based parameters as a uniform transfusion trigger. Further discussion of the guidelines and summaries of their recommendations are given in Appendix 3.

Review of existing guidelines identified nine clinical practice guidelines on the use of red blood cells. The issue of a transfusion trigger was addressed in the text or the recommendations of all the guidelines and the concept of an arbitrary transfusion trigger for the use of red blood cells was refuted by most. Instead most advocated that the decision to transfuse be made after review of the patient and the clinical situation and that, in addition, timely measurement of haemoglobin levels should be considered.

Four clinical practice guidelines addressing the use of platelets were considered. The guidelines found that platelets were indicated for the prevention and treatment of haemorrhage in patients with thrombocytopenia or platelet function defects. However, they considered that the need for platelets is dependent on multiple risk factors and not a single laboratory value (eg platelet count).

Of the nine clinical practice guidelines on the use of FFP that were reviewed, none advocated the routine use of FFP to treat coagulation disorders. Rather they recommended that the use of FFP be avoided when a safer and more effective product can be used to achieve the same therapeutic goal. The guidelines recommended that the administration of FFP should be guided by an assessment of coagulation factors and all but one of the guidelines recommended an assessment of the risk of ongoing bleeding as well as the elucidation of specific coagulation abnormalities.

Three guidelines were identified that make recommendations on the use of cryoprecipitate. The use of cryoprecipitate to correct low fibrinogen levels in bleeding patients was recommended by all of the guidelines.

Other strategies—review and audit

The degree to which guidelines have been effective in changing practice is unclear, but it is unlikely that the availability of clinical practice guidelines alone could significantly alter the use of blood components (Grimshaw & Russell 1993). In addition, it is necessary to better define both the efficacy and risks of transfusion, formulate the best transfusion practice, and then decide how best to promote and monitor it (Allain & Williamson 1997). Other strategies that have been developed in an attempt to reduce inappropriate use of blood components include:

- retrospective monitoring of medical records, which is often limited by inadequate documentation of the rationale for use;
- prospective monitoring of requests for blood components before they are issued, which is more successful;
- introduction of new transfusion policies or algorithms;
- education of health professionals; and
- peer review and self-audit.

The evidence suggests that a complex intervention that combines a number of these approaches is likely to be more effective. This is consistent with studies into changing clinicians' practice in other areas. For sustained change in practice, interventions need to be integrated into quality systems and it is likely that educational programs need to be repeated at regular intervals, if only to ensure that new hospital staff are aware of transfusion policies.

The evidence for the effectiveness of strategies in changing transfusion practice is discussed in more detail in Appendix 3.

2.6 GAPS IN KNOWLEDGE AND RESEARCH

Through its consideration of the available evidence to support transfusion practice, the Working Party was able to determine areas where research is lacking.

Red blood cells

The risks and benefits of the use of red blood cells in specific groups, such as patients with chronic conditions like respiratory and cerebrovascular disease and cancer, have not been clearly established and require further study.

Few studies have addressed optimal transfusion criteria for groups of patients with special considerations (eg older patients, and those with renal failure or haemoglobinopathies).

Few studies address the most common paediatric problems for which red blood cells are used (eg surgery, oncology and for critically ill patients), and most guideline recommendations are extrapolated from adult data (Hume et al 1997;

Bednarek et al 1998; Zimmermann et al 1998). There is clearly a need for additional carefully designed studies of red blood cell therapy in infants and children.

Platelets

Precise indications and optimal specifications for the use of platelets still need to be defined. There is a need for prospective randomised trials and clearly defined protocols (Royal College of Physicians of Edinburgh 1998).

Research is also needed into virally inactivated human or synthetic platelet preparations; the effects of platelet storage lesion on efficacy post transfusion; and the role of platelet substitutes.

Fresh frozen plasma

Research to develop safer FFP and alternative therapies is encouraged (NIH Consensus Conference 1985).

Cryoprecipitate

There is a need for further investigation of the use of cryoprecipitate in cardiac bypass surgery.

Transfusion management of massive haemorrhage

The management of massive blood loss and transfusion remains a controversial subject with minimal progress in recent years. The role of the transfusion of large volumes of stored blood in contributing to multi-organ failure and possibly to coagulation disorders indicate further research is needed. Further research into closer integration of haematological expertise and real-time haemostatic assessment and management is necessary.

Measures to change transfusion practice

There is a need for more high-quality studies into methods to change clinical practice (Grimshaw & Russell 1993; Tuckfield et al 1997; Bero et al 1998; Rubin et al 2000). There is also a paucity of evidence on strategies to maintain improvements in practices over time.

Restrictions on the use of blood components, whether based on the review of transfusion requests by haematology staff or on automated systems such as computerised audits may be effective (Allain & Williamson 1997; Tuckfield et al 1997) but require further evaluation (Tobin et al 2001).

Although there are numerous publications that describe the use of transfusion guidelines, very few studies evaluate whether the guidelines themselves are effective. There is clearly a need for studies that measure the impact of interventions designed to change practice. Such studies should also include a measure of cost of the intervention and any change in costs related to blood component use, as well as the impact on clinical outcomes (Hill et al 1999).

3 RECOMMENDATIONS FOR CLINICAL PRACTICE

Based on the evidence discussed in Chapter 2, recommendations can be made for clinical practice, giving criteria for blood component therapy in a range of clinical circumstances. These recommendations provide a list of clinical circumstances under which the use of blood components could be accepted as appropriate therapy. They are not intended to serve as indications for their use, since not all patients who fulfil the criteria would actually benefit from blood component therapy, and in selected cases, such therapy may be appropriate for a patient who does not fulfil the criteria.

The recommendations are not applicable to most acute situations, or to specialty areas such as paediatrics and obstetrics. It is suggested that the recommendations be adapted to meet the needs of specialty groups while maintaining the general principles of the guidelines. It should also be noted that these guidelines are not intended as a guide to the clinical management of conditions referred to in this chapter.

While the specifics of clinical assessment and administration of blood components relate to the individual patient and are beyond the scope of this guideline, general information on dosage and volume can be found in Appendix 4, and on tests for assessing haemostasis in Appendix 5.

3.1 THE TRANSFUSION DECISION

The clinical recommendations below reflect the World Health Organization (WHO) recommendations on developing guidelines on the clinical use of blood components (1998a). Table 3.1 outlines the principles highlighted by the WHO as important for consideration during the transfusion decision and in the event of a transfusion.

Table 3.1 WHO principles for the clinical use of blood components

1. Transfusion is only one element of the patient's management.
 2. Prescribing decisions should be based on the national guidelines on the clinical use of blood components, taking individual patient needs into account.
 3. Blood loss should be minimised to reduce the patient's need for transfusion.
 4. The patient with acute blood loss should receive effective resuscitation (intravenous replacement fluids, oxygen etc) while the need for transfusion is being assessed.
 5. The patient's haemoglobin level, although important, should not be the sole deciding factor in starting transfusion. The decision to transfuse should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.
 6. The clinician should be aware of the risks of transfusion-transmissible infection in the blood components that are available for the individual patient.*
 7. Transfusion should be prescribed only when the benefits to the patient are likely to outweigh the risks.
 8. The clinician should record the reason for transfusion clearly.
 9. A trained person should monitor the transfused patient and respond immediately if any adverse effects occur.
-

* It should be noted that the rates of non-infective complications are probably higher than those of infective complications.

Source: WHO (1998a).

Clinical judgement should be central to any decision to transfuse. The decision should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.

Medical indications for the use of blood components are easier to define for some clinical circumstances than for others. In a number of situations where blood component therapy has a central role, the physiology is usually well understood, and the use of blood components is logical, can be monitored and has a direct relationship to the clinical outcome for the patient. In other clinical circumstances, the physiology is less well understood, the risks more difficult to quantify and clinical outcomes harder to define. In all circumstances, the main clinical questions relate to balancing the risks and benefits, together with determining timing, dosage and administration frequency.

It must be the responsibility of all doctors to ensure that transfusions are given only when clearly indicated (McGrath et al 2001).

RECOMMENDATION

1. Blood component therapy should only be given when the expected benefits to the patient are likely to outweigh the potential hazards.
-

3.2 RED BLOOD CELLS

In deciding whether to transfuse red blood cells, the patient's haemoglobin level, although important, should not be the sole deciding factor. The various factors that should be used in deciding whether use of red blood cells is appropriate include patient factors, signs and symptoms of hypoxia, ongoing blood loss, the risk to the patient of anaemia in the setting of coexisting conditions and the risk of the transfusion. Some specific factors to consider are as follows.

- *Patient's cardiopulmonary reserve*—if pulmonary function is not normal it may be necessary to consider transfusing at a higher threshold. The pulmonary function should allow normal oxygen saturation of the patient's haemoglobin.
- *Volume of blood loss*—clinical assessment should attempt to quantify the volume of blood loss before, during and after surgery, to ensure the maintenance of normal blood volume.
- *Oxygen consumption*—this may be affected by a number of factors including fever, anaesthesia and shivering; if increased then the patient's need for red blood cell transfusion could be higher.
- *Atherosclerotic disease*—critical arterial stenosis to major organs, particularly the heart, may modify the indications for the use of red blood cells.

RECOMMENDATION

2. The decision to transfuse red blood cells should be based on clinical assessment of the patient and his or her response to any previous transfusion as well as the haemoglobin level.
-

Avoiding or minimising red blood cell use is advised when there is a borderline indication or evidence for benefit is weak. Figure 3.1 illustrates this risk/benefit analysis for the use of red blood cells in relation to anaemia.

3. RECOMMENDATIONS FOR CLINICAL PRACTICE

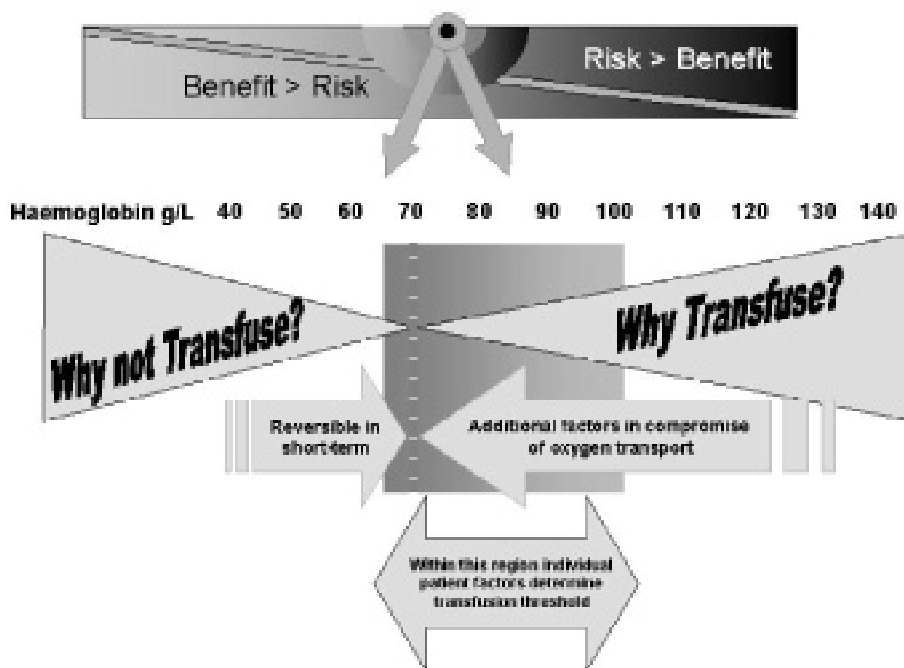


Figure 3.1: Risk/benefit analysis for the use of red blood cells

RECOMMENDATIONS

3. Use of red blood cells is likely to be inappropriate when Hb > 100g/L unless there are specific indications (level I evidence). If red blood cells are given at this haemoglobin level, reasons should be well documented.
4. Use of red blood cells may be appropriate when Hb is in the range 70–100g/L (level IV evidence). In such cases, the decision to transfuse should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality.
5. Use of red blood cells is likely to be appropriate when Hb < 70g/L (level IV evidence). In some patients who are asymptomatic and/or where specific therapy is available, lower threshold levels may be acceptable.

When the haemoglobin level is in the range 70–100g/L, clinical judgement about the risk of transfusion becomes paramount. On the basis of physiological principles, the following criteria may indicate that use of red blood cells is appropriate (level IV evidence):

- the patient is undergoing an operative procedure associated with major blood loss;

- there are clinical signs, symptoms or evidence that the patient has associated impairment in oxygen transport that may be exacerbated by anaemia; and
- to control anaemia-related symptoms in a patient on a chronic transfusion regimen or during marrow suppressive therapy and maintain haemoglobin >80g/L.

Rationale

Anaemia

At a haemoglobin level >70g/L, consideration should be based on why the patient *should* be transfused. However, at a haemoglobin level <70g/L the benefits of transfusion are more likely to outweigh the risks, and consideration should begin with why the patient *should not* be transfused.

Perioperative red blood cell transfusion may be required when anaemia cannot be corrected or time does not permit correction of a treatable anaemia. In the perioperative setting, specific attention must always be given to methods for minimising blood loss and minimising or avoiding red blood cell use.

Acute bleeding

With acute haemorrhage, in previously healthy patients who have suffered an acute blood loss of less than 25 per cent of their blood volume, restoring volume is more important than replacing oxygen carrying capacity. Plasma volume expanders may preclude the necessity for red blood cells, especially if bleeding can be controlled. Clear fluids also allow time for the preparation of compatibility tests. In the context of acute bleeding and hypovolaemic shock, the haemoglobin level is not the only consideration in determining the need for red blood cells. In a patient receiving colloids, the haemoglobin level or haematocrit is useful in indicating the need for red blood cells but is not an absolute measure of the degree of blood loss.

Red blood cells will be required if there is evidence of impaired oxygen transport, particularly when the loss of blood volume exceeds 25 per cent and the blood loss has not been adequately controlled. Loss of over 40 per cent of blood volume is life threatening. Where possible, it is preferable to avoid the transfusion of large quantities of blood more than 10 days old to minimise adverse effects from storage lesion, including multi-organ failure (Moore et al 1997; Zallen et al 1999; Flores et al 2001).

Section 3.6 contains an algorithm outlining steps in the management of acutely haemorrhaging patients.

Transfusion volume

The transfusion of red blood cells mostly involves the administration of between one and four units. The Western Australian review found that overall, 14 per cent of red blood cell use involved the administration of only one unit of red

blood cells; 16 per cent of these were related to renal dialysis; and 9 per cent to elective orthopaedic surgical procedures (Finn et al 1998).

Attitudes toward transfusion of a single unit of red blood cells are changing. In the past, the use of single units of red blood cells was seen as an index of inappropriate use but it now appears that there are situations where such use may be appropriate. Blood management practice guidelines have recommended that the following points be considered in determining the number of units of red blood cells to be transfused (Spence 1995):

- transfusion need should be assessed on a case-by-case basis;
- blood should be transfused one unit at a time, followed by an assessment of benefit and further need;
- exposure to blood components should be limited to appropriate need.

Appendix 4 outlines factors to be considered when determining the volume of blood components to be administered.

3.3 PLATELETS

The use of platelets is indicated for the prevention and treatment of haemorrhage in patients with thrombocytopenia or platelet function defects. The platelet count is the primary trigger for the use of platelets, with clinical risk factors for bleeding and the extent of bleeding also influencing the decision to transfuse. Figure 3.2 illustrates factors important in deciding whether or not to use platelets.

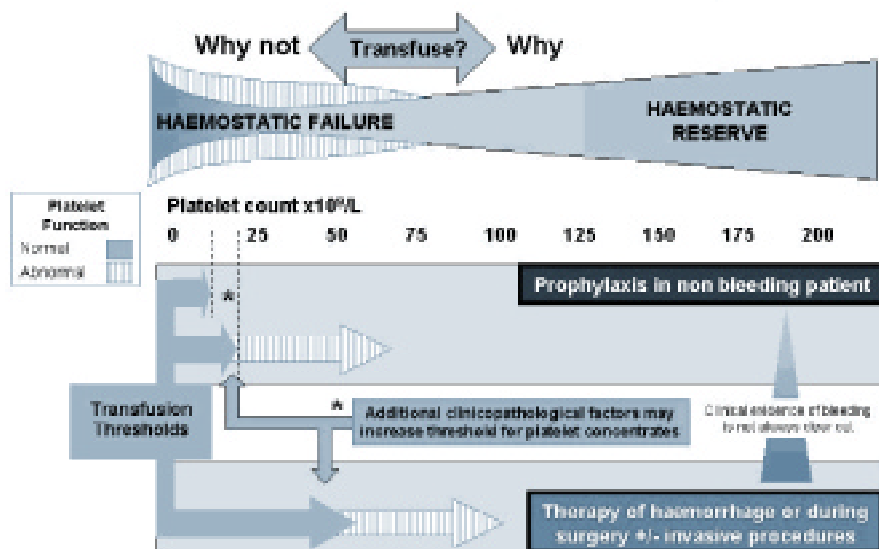


Figure 3.2: Platelet therapy

RECOMMENDATIONS

6. Use of platelets is likely to be appropriate as prophylaxis:
 - in bone marrow failure when the platelet count is $<10 \times 10^9/L$ without risk factors or $<20 \times 10^9/L$ in the presence of additional risk factors (eg fever, antibiotics, evidence of systemic haemostatic failure) (level II evidence);
 - to maintain the platelet count at $>50 \times 10^9/L$ in patients undergoing surgery or invasive procedures (level IV evidence); and
 - in inherited or acquired qualitative platelet function disorders, depending on clinical features and setting (level IV evidence). In these situations the platelet count is not a reliable indicator for transfusion.
 7. Use of platelets is likely to be appropriate as therapy (level IV evidence):
 - in any patient who is bleeding in whom thrombocytopenia is considered a major contributory factor; and
 - when the platelet count is $<50 \times 10^9/L$ in the context of massive haemorrhage/transfusion and $<100 \times 10^9/L$ in the presence of diffuse microvascular bleeding.
 8. Use of platelets is not generally considered appropriate in the treatment of immune-mediated platelet destruction, thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome or drug-induced or cardiac bypass thrombocytopenia without haemorrhage (level IV evidence).
-

Rationale

Bone marrow failure

Evidence from controlled studies has shown that in the absence of additional risk factors, prophylaxis at platelet counts $<10 \times 10^9/L$ is effective. However, if factors associated with bleeding in thrombocytopenic patients (fever, concurrent coagulation disorders, evidence of systemic haemostatic failure) are present or if there are potential bleeding sites as a result of surgery, the prophylactic use of platelets might be considered to keep the platelet count above $20 \times 10^9/L$.

Patients undergoing surgery or invasive procedures

In general, most guidelines recommend that platelet counts should be $>50 \times 10^9/L$ for surgical procedures, although no controlled trials examining this practice are available to provide guidance.

For patients undergoing surgical procedures with a high risk of bleeding (eg ocular or neurosurgical procedures) maintaining the platelet count at $100 \times 10^9/L$ may be appropriate.

Platelet function disorders

In hereditary platelet function defects there is evidence that platelet transfusion is effective in surgical prophylaxis and for treatment of bleeding episodes.

In acquired platelet function defects the evidence is less clear. For the platelet function defect associated with renal failure, correction of anaemia, desmopressin and cryoprecipitate are considered to be first-line therapy; there is no evidence to support the use of platelets.

Massive haemorrhage/transfusion

Therapeutic use of platelets should be confined to patients with thrombocytopenia and/or functional abnormalities who have significant bleeding from this cause. It has been documented that transfusion of greater than 10 units of red blood cells or one blood volume over 24 hours is often accompanied by a platelet count of less than $50 \times 10^9/L$, particularly when 20 or more units have been transfused. It has also been noted that diffuse microvascular bleeding is more frequent in patients who are massively transfused who have platelet counts between $50 \times 10^9/L$ and $100 \times 10^9/L$.

Contraindications

The use of platelets is contraindicated in the following situations.

- In situations of immune-mediated platelet destruction use of platelets rarely increases the platelet count. Such use is usually reserved for situations of potentially life-threatening haemorrhage.
- In thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome it has been reported that transfusion of platelets has been accompanied by acute deterioration. Platelets are generally considered to be contraindicated in this condition.
- Platelet function defects and some degree of thrombocytopenia frequently occur following cardiac bypass surgery. However, there is little or no evidence that prophylactic administration of platelets reverses the platelet function defect associated with the bypass, and platelet use should therefore be reserved for patients with bleeding not due to surgically correctable causes.

3.4 FRESH FROZEN PLASMA

FFP is frequently used inappropriately, either in respect of the particular indication or in excessive quantity for a given indication. There are also a number of clinical situations in which the use of FFP has been advocated but has not been shown to be of benefit or alternative therapies are equally satisfactory or considerably safer.

RECOMMENDATIONS

9. While few specific indications for fresh frozen plasma exist, its use may be appropriate (level IV evidence):
 - for replacement of single factor deficiencies where a specific or combined factor concentrate is not available;
 - for immediate reversal of warfarin effect in the presence of potentially life-threatening bleeding when used in addition to vitamin K and possibly factor IX concentrate;
 - for treatment of the multiple coagulation deficiencies associated with acute disseminated intravascular coagulation;
 - for treatment of thrombotic thrombocytopenic purpura;
 - for treatment of inherited deficiencies of coagulation inhibitors in patients undergoing high-risk procedures where a specific factor concentrate is unavailable; or
 - in the presence of bleeding and abnormal coagulation parameters following massive transfusion or cardiac bypass surgery or in patients with liver disease.
 - 10 The use of fresh frozen plasma is generally not considered appropriate in cases of hypovolaemia, plasma exchange procedures or treatment of immunodeficiency states (level IV evidence).
-

Rationale

Replacement of single factor deficiencies

FFP is only required when specific or combined factor concentrates are unavailable. In the Australasian setting, factor VIII (as plasma-derived or recombinant factor VIII preparations), von Willebrand factor (in plasma-derived factor VIII) and factor IX preparation are widely available as concentrates.

Immediate reversal of warfarin effect

Patients taking oral anticoagulant therapy have a deficiency of functionally active vitamin-K-dependent proteins, which can normally be reversed by the parenteral administration of vitamin K. In patients who are grossly overdosed and who have developed serious life-threatening bleeding episodes, the effects of anticoagulant therapy can be immediately reversed through the use of vitamin-K-dependent factor concentrates, alone or in combination with FFP. Vitamin-K-dependent factor concentrates alone may be indicated for less severe manifestations of warfarin overdosage where high volume FFP is relatively contraindicated (eg cardiomyopathy, severe left ventricular failure).

Acute disseminated intravascular coagulation

DIC, which can be associated with shock, trauma or sepsis, results in deficiencies of factors V and VIII, fibrinogen, fibronectin and platelets due to activation of the coagulation and fibrinolytic systems. Replacement therapy, including FFP, is indicated in acute DIC, where there is haemorrhage and abnormality of coagulation. In chronic DIC, or in the absence of haemorrhage, there is no indication for component therapy.

Thrombotic thrombocytopenic purpura

FFP is the accepted form of treatment for thrombotic thrombocytopenic purpura, often in conjunction with plasma exchange.

Inherited deficiencies of inhibitors of coagulation

FFP has been used as a source of antithrombin, protein C and protein S in patients with inherited deficiencies of these inhibitors who are undergoing surgery or who require heparin for treatment of spontaneous thrombosis. An antithrombin concentrate is generally available in Australia. Protein C and protein S are either not readily available across Australasia or are prohibitively expensive and the subject of special access schemes only. Availability of these specific preparations would obviate the need for FFP in the treatment of deficiencies of these inhibitors.

Conditional uses

In the following circumstances, FFP is only indicated in the presence of bleeding and abnormal coagulation:

- in patients with liver disease if bleeding has taken place or may be expected because surgery is proposed; or
- following uncomplicated cardiac bypass surgery in patients in whom bleeding is associated with proven abnormalities of coagulation other than residual heparin effect.

3.5 CRYOPRECIPITATE

As there is little scientific evidence regarding the effectiveness of cryoprecipitate in improving clinical outcomes, and specific factor concentrates are now widely available, its use should be limited to selected indications.

RECOMMENDATIONS

- 11 Use of cryoprecipitate may be considered appropriate in patients with fibrinogen deficiency where there is clinical bleeding, an invasive procedure, trauma or disseminated intravascular coagulation (level IV evidence).
 - 12 The use of cryoprecipitate is not generally considered appropriate in the treatment of haemophilia, von Willebrand's disease, or deficiencies of factor XIII or fibronectin, unless alternative therapies are unavailable (level IV evidence).
-

Rationale

Fibrinogen deficiency

Isolated fibrinogen deficiency is uncommon and is infrequently associated with bleeding in adults. Where there is clinical bleeding in such patients or there are invasive procedures or trauma, use of cryoprecipitate may be justified.

Fibrinogen deficiency is commonly encountered in DIC. In milder forms of DIC, fibrinogen is not indicated, particularly when fibrinogen levels exceed 1.0g/L. At lower levels of fibrinogen, and where there is clinical bleeding, use of cryoprecipitate to keep fibrinogen levels above 1.0g/L may be indicated.

Contraindications

In the treatment of many conditions, the use of cryoprecipitate has been replaced by treatment with specific factors.

- Virally inactivated, purified factor VIII concentrates of either human or recombinant origin, have superseded cryoprecipitate in the management of factor VIII deficiency in Australia and New Zealand. Where there is no alternative or in an emergency, cryoprecipitate may be utilised in the management of haemophilic bleeding. Large doses may be required to increase the factor VIII concentrations to therapeutic levels.
- Treatment of von Willebrand's disease is usually with desmopressin and a factor VIII concentrate shown to contain von Willebrand's factor. In cases of von Willebrand's disease non-responsive to desmopressin, cryoprecipitate remains a second-line alternative where the specific concentrate is not available.

3. RECOMMENDATIONS FOR CLINICAL PRACTICE

- Pasteurised factor XIII preparations are now available and should be used in preference to cryoprecipitate in the treatment of factor XIII deficiency. Where these are not available the use of cryoprecipitate may be justified.
- It has not been conclusively shown that cryoprecipitate is of clinical use in patients with shock and trauma and who have a relative deficiency of fibronectin.
- Cryoprecipitate is not uncommonly used in conjunction with human or bovine thrombin to prepare a fibrin adhesive layer during surgical procedures. Virally inactivated products, specifically designed to prepare a fibrin 'glue' are now available and should be used in preference to cryoprecipitate.

3.6 ACUTELY HAEMORRHAGING PATIENTS

In acutely haemorrhaging patients, early intervention can reduce later problems. This may involve the use of one or more blood components, depending on a range of factors. The first step is to differentiate between 'controlled' bleeding, usually during surgery, and established massive bleeding, usually associated with haemostatic failure, which is much more difficult to treat. The following algorithm outlines some steps in the management of acutely haemorrhaging patients.

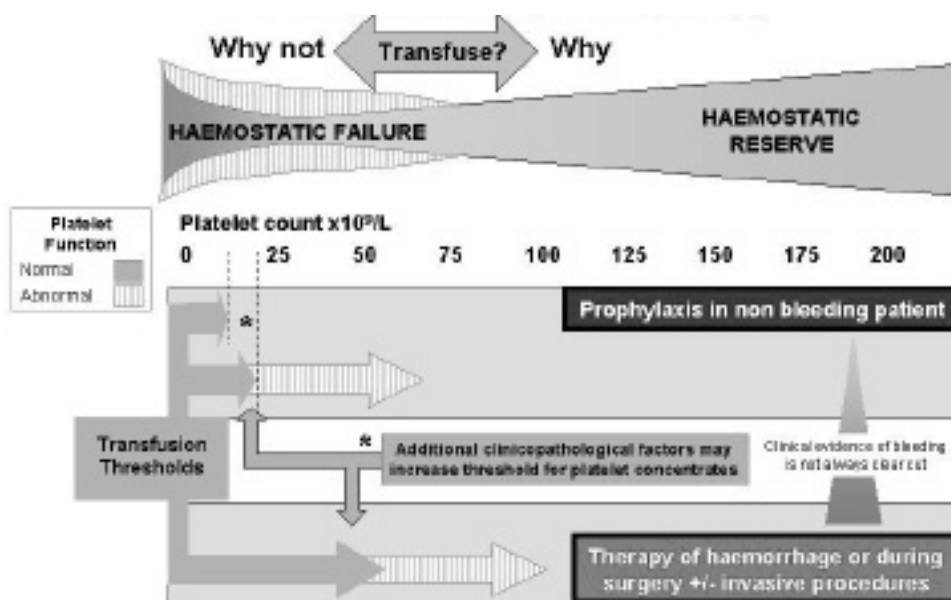


Figure 3.3: Use of blood component therapy in the acutely haemorrhaging patient

Notes: FBC = full blood count; PT = prothrombin time; APTT = activated partial thromboplastin time; TCT = thrombin clotting time

Tests for investigating for haemostatic defects are discussed in Appendix 5.

4 RECOMMENDATIONS FOR ORGANISATIONAL PRACTICE

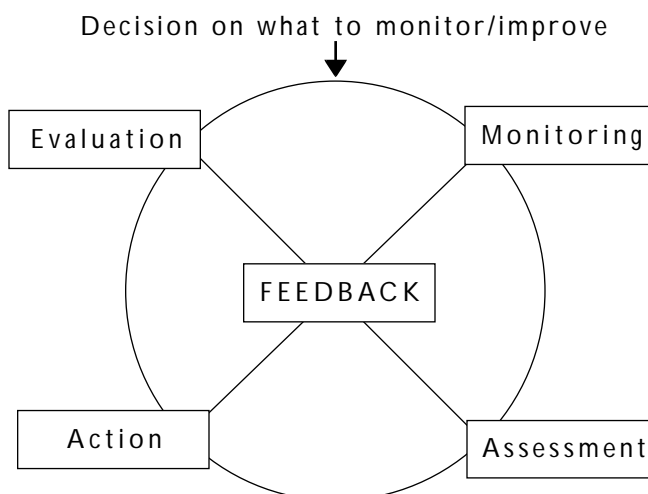
Formulating clinical recommendations only addresses part of the total quality management system for the use of blood components. This chapter includes recommendations for organisational practice, describing quality management systems that will facilitate the uptake of these guidelines at national, State/Territory and local levels. It also includes points for consideration for raising consumer awareness of the issues surrounding blood component therapy, and providing information to consumers about the risks and benefits of such therapy.

4.1 QUALITY MANAGEMENT

Quality in the clinical use of blood components implies administering the right quantity of the right component in the right way at the right time to the right patients, with appropriate documentation of both process and outcomes (EC 1999). Quality management systems are needed to facilitate monitoring of guidelines for appropriate use of blood components. There is evidence that incorporating evidence-based guidelines strengthens formal quality and clinical practice improvement efforts (Salem-Schatz et al 1990; Oxman et al 1995; Tuckfield et al 1997; EHCB 1999; Hill et al 1999).

The philosophy of continuing improvement is fundamental to EQUiP, (an accreditation tool utilised by many health-care agencies in Australia) as is accountability for the outcome of care and services (ACHS 1999). Accreditation tools such as EQUiP utilise components that include standards, clinical indicators, assessments and planning for quality (ACHS 1999).

The quality improvement cycle is similar to the Shewart Cycle introduced by Deming as early as 1950 (Walton 1989). The cycle aims to ensure that quality systems go beyond detecting and correcting errors, moving towards a continuous process of assessment, planning, implementation, evaluation and then reassessment.



Source: ACHS (1996).

Figure 4.1: The quality improvement cycle

Existing evidence on strategies to improve clinical use of blood components supports the following mechanisms at organisational level. It should be recognised that an investment of resources at all levels will be required to establish and implement quality management systems before any savings in the use of blood can be realised.

Monitoring

Monitoring comprises any systematic ongoing process of collecting information on clinical or non-clinical performance (ACHS 1996). A simple system of monitoring and evaluation is essential to assess patterns of blood use and the impact of national guidelines on the clinical use of blood at the local level (WHO 1998a). This will include transfusion documentation and collection of clinical indicators.

RECOMMENDATION

- 13 Documentation used in ordering or administering blood components (such as request forms or blood administration forms) should summarise the clinical recommendations of these guidelines and collect standardised data items. Clinical and laboratory indications for blood components should be accurately recorded in that documentation and in the patient's medical record.
-

Inclusion of criteria for appropriate use of blood components on request forms or other documentation used in ordering or administering blood components reminds clinicians of the criteria at the time that they are making the transfusion decision (Rehm et al 1998). Many institutions have developed transfusion request documentation for their own use. It is recommended that this documentation include a summary of the clinical recommendations of these guidelines (see page xiii).

A system should also be in place that allows audit at the local level through the collection of standardised data items including:

- blood component given;
- clinical or laboratory indications;
- reasons for giving blood component if not in accordance with guidelines;
- other relevant medical history of condition; and
- number of units required.

The clinical or laboratory indications for blood component therapy or for withholding such therapy should also be documented in the patient's medical record. For example, for patients with Hb<70g/L who are not given red blood cells, reasons for not transfusing should also be recorded in the patient's medical record.

Assessment

Monitored data should be assessed to determine the type and extent of any problems, opportunities for improvement or to demonstrate that the care provided is consistent with established guidelines (ACHS 1996).

Data collection systems measuring the impact of guidelines allow comparison between the evidence about outcomes gathered from clinical trials and real outcomes achieved in routine clinical practice (NHMRC 1999), and will also be useful in quality improvement and education programs.

Standardised information collected on request forms or blood administration forms should facilitate assessment of adherence to these guidelines and levels of appropriate transfusion practice. A process will be required for collecting, collating, reporting and acting on the data in hospitals.

Action

Action should be taken to rectify any identified problems, once the data have been assessed. Action to improve care may involve reallocation of resources, change in policy and procedures, and new equipment or administrative changes (ACHS 1996).

RECOMMENDATION

- 14 In all situations where blood component therapy is given, a process for clinical review should be in place to monitor the appropriateness and safety of its use and to develop systems for the implementation of these guidelines.
-

At the institution level, establishing and implementing a quality management system for the clinical use of blood components requires the commitment and cooperation of hospital and health service managers, quality improvement and quality management staff, clinicians, nurses and other health professionals.

In all situations where blood component therapy is given, it is recommended that a process for clinical review be in place. This may be through an existing committee or through establishment of a specific clinical/management group. The group should hold responsibility for education, monitoring and quality improvement (Soumerai et al 1993; Metz et al 1995; Tuckfield et al 1997). Clinical review groups or 'transfusion committees' should include senior representatives of clinical specialities involved in the use of blood components, nurses, blood bank, quality improvement and senior administration. In larger hospitals, this is likely to be a separate committee. However, this is not necessary and in smaller hospitals, the role could be undertaken by the medical advisory committee or through a local network (geographic or organisational).

The clinical review group should have the authority within the hospital structure to determine hospital policy in relation to blood component therapy and resolve any problems that have been identified (WHO 1998a). It should be given enough administrative support to ensure that it can carry out its responsibilities.

Principal functions of the clinical review group or transfusion committee are to (WHO 1998a):

- monitor the safety, adequacy and reliability of the supply of blood, blood components and alternatives to transfusion;
- monitor the use of blood components in the hospital;
- review incidents of severe adverse effects or errors associated with transfusion;
- develop systems and procedures for the implementation of these guidelines within the hospital;
- promote the effective implementation of the guidelines through the education and training of all clinical and blood bank staff involved in the transfusion process; and
- monitor the implementation of these guidelines in the hospital and take appropriate action to overcome any factors hindering their effective implementation.

A suitable mechanism for consumer input into this process should be identified.

Evaluation

Evaluation ensures that once an action has been implemented, it has improved an aspect of care or service.

As discussed, the process for clinical review in hospitals should be responsible for adapting guidelines for local conditions, auditing compliance with the guidelines, evaluating effectiveness and safety, providing feedback to clinicians and clinical management through identified communication and reporting channels, and developing practice improvement projects. These actions should help to ensure that there is continuous improvement in the quality of transfusion practice which is incorporated into routine processes.

The appropriate use of blood components should be included in the hospital-wide clinical indicator monitoring required by:

- hospital quality improvement risk management / clinical governance monitoring;
- local and State/Territory or national health authorities;
- State/Territory or national blood transfusion services (ARCBS or NZBS); and
- hospital accreditation bodies.

It is recommended that a range of consistent clinical indicators be developed, which could be incorporated into accreditation tools such as EQuIP. It should be noted that there could be exceptions to any broadly applied indicator.

Examples of clinical indicators may include:

- units requested/units transfused by patient category;
- the proportion of blood components given in accordance with or outside these guidelines as indicated by:
 - the proportion of red blood cells given for non-acute situations where the haemoglobin is above 100g/L;
 - the proportion of red blood cells given for non-acute situations where the haemoglobin is 70–100 g/L;
 - the proportion of platelets given as prophylaxis where the platelet count is $>20 \times 10^9/L$;
 - the overall proportion of patients receiving platelets where the platelet count is $>50 \times 10^9/L$;
 - the proportion of FFP given where there is no evidence of bleeding or abnormal coagulation (eg PT or APPT $1.5 \times$ control); and
- outcome of transfusion (acute complications of transfusion, delayed complications of transfusion, mortality).

Maintaining change

Experience has demonstrated that major sustained changes in clinical ordering patterns are difficult to achieve (Calder et al 1997; Tobin et al 2001). Tobin et al conclude that there is a clear need for strategies to ensure long-term compliance with clinical practice guidelines so that early success in changing transfusion practice can be maintained. An editorial commenting on these findings adds that the onus must be on individual clinicians to be familiar with the practice guidelines in their field and openly account for their practice decisions (McGrath et al 2001).

Development of clinical guidelines for the use of blood are only one part of what needs to be a long-term educational program for clinicians and other health professionals, starting at undergraduate level and extending into the postgraduate period. The continuing support of hospital administrative staff is needed to sustain clinical review processes (eg transfusion committees). Widely publicised information about the true cost of blood components will also promote their better use. These changes need to become a permanent part of health professional education, health systems and hospital processes, requiring continuing resources over a long time, if changes in practice are to be sustained.

RECOMMENDATION

- 15 Implementation of the recommendations in these guidelines should be adequately resourced by health systems.
-

4.2 CONSUMERS

Change at clinical and organisational levels within hospitals will help to standardise the use of blood. Consumers can also be important drivers of change to transfusion practice, if they are aware of the issues surrounding blood component therapy and know about the risks and benefits of its use in their own situation.

Blood component therapy should be seen as a possible component of a patient's overall management. As such therapy may be associated with immunological reactions, technical errors and other complications, clear explanation of the potential risks and benefits should be part of the overall process for informed consent.

RECOMMENDATION

- 16 As part of the informed consent process, a patient should be given clear explanation of the potential risks and benefits of blood component therapy in his or her particular case.
-

Information on relevant issues should be provided to patients in an appropriate manner, taking into account the impact of the patient's condition (Silburn 1999a), and including sufficient detail of the risks and benefits of blood component therapy and any alternatives being used to minimise blood use. Ineffective communication, more often than technical incompetence, has been named as a source of dissatisfaction for consumers (Spriggs 1996). The NHMRC and the New Zealand Ministry of Health have both produced guidelines for medical practitioners on providing information to patients to enable them to give informed consent (NZ Department of Health 1991; NHMRC 1993).

Written information should not replace verbal communication but should be provided as back up (Silburn 1999b). A combination of increasing knowledge and understanding in the context of duty of care and personal engagement is required for fully informed consent, as outlined in Figure 4.2. The information should be given by a person with appropriate expertise in the area. In an emergency, when immediate intervention is necessary to preserve life or prevent serious harm, it may not be possible to provide information. In this situation, continuing explanation after the transfusion to patients and their relatives is required.

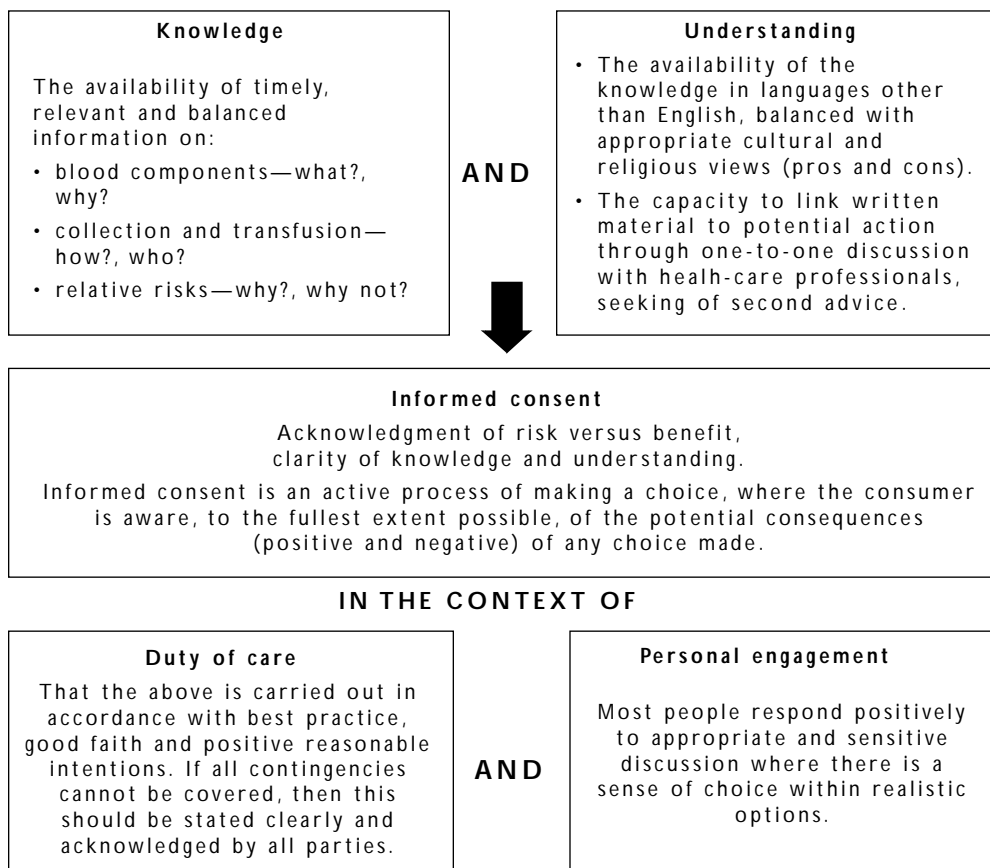


Figure 4.2: Process of informed consent

5 DISSEMINATION, IMPLEMENTATION AND EVALUATION

To promote and improve the quality of care at all levels, guidelines must become integrated into all levels of the health-care system and be informed by many different aspects of the system (NHMRC 1999). The consultation process used to inform the development of these guidelines therefore paid particular attention to implementation and dissemination.

5.1 DISSEMINATION

Dissemination involves making guidelines accessible, advertising their availability and distributing them widely. Multiple dissemination strategies ensure greater coverage than a single strategy (NHMRC 1999).

Submissions and workshop participants stressed the importance of addressing the varying needs of the target audiences of these guidelines and of education across the community. As a result, the guidelines will be available in a range of formats:

- the full version of the clinical practice guidelines (for use by health professionals);
- summaries of the recommendations for distribution to all institutions where blood is given;
- a guide for patients/consumers; and
- a brochure and poster for the general community.

These materials will be available on the internet with linkages to websites of professional and consumer groups connected with blood transfusion. As well, articles summarising the guidelines will be placed in local professional journals, association / college newsletters and magazines, in trade publications and in the national media.

5.2 IMPLEMENTATION

Although it is an essential feature of guidelines development, dissemination alone is not enough to change the behaviour of clinicians (Field & Lohr 1992; EHCB 1994; Oxman et al 1995; Bero et al 1998; EHCB 1999; Rubin et al 2000). For implementation of guidelines to be successful, they should be integrated with broader activities, such as continuing education and quality improvement, performance monitoring and accreditation (NHMRC 1999).

Strategies that have been shown to be effective in changing clinicians' behaviour or health outcomes, or both (Lomas & Haynes 1988; Lomas 1993; 1994; Oxman et al 1995) were considered by participants in the workshops. Table 5.1 summarises the activities identified through the workshops as appropriate for the implementation of these guidelines.

Table 5.1 Implementation activities

Governments	<ul style="list-style-type: none"> • Refining guidelines through consultation with stakeholders • Developing summary materials for distribution to institutions where blood component therapy is given • Developing consumer materials to promote discussion of blood component therapy as part of the process of informed consent • Establishing a website providing information on blood component therapy and links to other relevant sites • Developing, with standards organisations, appropriate clinical indicators for inclusion in accreditation processes (see Chapter 4) • Developing 'gate-keeping' software
Professional colleges, societies and organisations	<ul style="list-style-type: none"> • Participating in consultations to refine guidelines and inform implementation • Endorsing guidelines through policy statements • Linking professional websites to guidelines on internet • Developing educational materials for undergraduates and postgraduates • Continuing provision of technical support by blood banks to institutions where blood component therapy is given
Institutions	<ul style="list-style-type: none"> • Participating in consultations to refine guidelines and inform implementation • Supporting ongoing education of junior and senior clinical and administrative staff • Including discussion of blood component therapy in the process of informed consent (see Chapter 4) • Establishing a process for clinical review (see Chapter 4) • Monitoring quality improvement through collection of standardised data items (see Chapter 4) • When available, implementing gate-keeping software for ordering blood and monitoring use of blood • Including transfusion nurses in the quality improvement process

Education

Successful implementation of these guidelines will rely on education at all levels, from the community through to clinical and administrative staff in institutions where blood component therapy is given. While educational materials targeting

specific audiences will be derived from these guidelines at the government level, their uptake and reinforcement will need to be supported by professional colleges and organisations and by the institutions themselves.

Governments

Media publicity will include articles in the general press to inform the community about the issues raised in these guidelines and the importance of understanding the risks and benefits of blood component therapy.

With consumer organisations, the NHMRC and the ASBT will develop a consumer brochure to inform the general community and a guide for people likely to have blood component therapy. The consumer documents will focus on the risks and benefits of blood component therapy and explain that these should be placed in the context of individual patient needs. The development of the materials at a national level will support a consistent approach to including discussion of blood component therapy in the process of informed consent.

As the need for blood component therapy frequently arises in emergency situations where information cannot be given beforehand, more general dissemination of the consumer brochure (ie in doctors' waiting rooms) may be valuable. The distribution of a consumer poster highlighting the issues will promote the brochure and the guide.

Workshop participants also advocated that a summary of the guidelines for health professionals be made available in a handy format. Consequently, a pocket-sized card summarising the clinical recommendations included in these guidelines will be developed and widely distributed to clinicians. As well, summaries of the guideline recommendations will be developed for distribution to clinicians and to those involved in quality improvement.

Websites are a widely used educational tool. The inclusion of these guidelines, the summary documents and the consumer materials on the NHMRC website will allow wider dissemination. There is also potential for a broader educational initiative through a blood component therapy website that links to these materials and other relevant sites (ASBT, ARCBS, professional colleges, on-line journals etc) and includes up-to-date information on issues related to blood component therapy.

Professional colleges, societies and universities

The professional colleges and societies have been involved in the development of the guidelines and their refinement through submissions and workshops. The role of the colleges and societies in implementing the guidelines will be largely in supporting education of health professionals in transfusion medicine. Universities should develop material for undergraduate and postgraduate curricula to facilitate the teaching of effective transfusion practice. The relevant professional colleges and societies should ensure that such programs are in place, at undergraduate and postgraduate level.

The development of policy statements that reflect these guidelines would reinforce the uptake of the recommendations.

Institutions

Ongoing education in hospitals will also be important in changing clinicians' transfusion practices. Educational initiatives within institutions will be supported by transfusion committees and should:

- include education on transfusion medicine into orientation of new staff, including administrative staff;
- include ongoing education for clinicians; and
- be appropriately targeted to both junior and senior staff.

Monitoring and audit

The recommendations on quality improvement discussed in Chapter 4 will be implemented through:

- the establishment of a process for clinical review in all institutions where blood component therapy is given;
- collection of standardised data items to facilitate assessment to capture information for quality improvement purposes;
- inclusion of discussion of the risks and benefits of blood component therapy in the process of informed consent;
- quality monitoring using the recommended clinical indicators; and
- development of practice improvement projects through the transfusion committee to ensure that there is continuous improvement in the quality of transfusion practice and to incorporate these into the routine processes of care.

Consideration should be given to the development of clinical audit tools, such as those developed in the United Kingdom in 1995 and available from the United Kingdom Royal College of Physicians (Royal College of Physicians of London 1995). Nine audit proformas were developed to encourage peer review in transfusion practice, including documentation of blood transfusion and monitoring acute blood transfusion reactions, as well as proformas for managing transfusion in specific conditions.

Development of clinical indicators

As discussed in Chapter 4, a range of clinical indicators should be developed and incorporated into accreditation tools.

A process will be required through States/Territories, networks involving the ARCBS or area health networks, for continuous review of the appropriateness of blood use and provision of technical help to hospital transfusion committees. Existing processes for benchmarking could perhaps be utilised for this, as they represent a continuous systematic process for evaluating clinical service outcomes and work processes of hospitals (Rasa 1999).

Continuous quality improvement

As discussed in Chapter 4, a process for clinical review (such as transfusion committees in hospitals) should be responsible for adapting these guidelines for local conditions, auditing compliance with the guidelines, evaluating effectiveness and safety, providing feedback to clinicians and clinical management through identified communication and reporting channels, and developing practice improvement projects. Submissions and workshop participants acknowledged the integral role of the transfusion committee in evaluation and monitoring and the need for the committee to be representative of the local institution.

The inclusion of transfusion nurses into the quality improvement process was advocated by some workshop participants. Transfusion nurses would be involved in the transfusion committee and could be linked in from other hospitals. The main roles of transfusion nurses would be to answer patients' questions about blood component therapy and to ensure that the system for collecting data is being adequately maintained. Transfusion nurses could also play a role in the education of ward staff.

Data collection

As discussed in Chapter 4, it is recommended that a summary of the clinical recommendations of these guidelines be included in the process of blood ordering and/or administration and that standardised data items be collected to allow assessment of compliance with the guidelines and of variations in practice, in hospitals and nationally.

Submissions and workshop participants were divided as to whether national standardised forms would be feasible as many institutions have developed their own forms appropriate to local needs. There was also discussion of the complexity of a request form that included the recommendations and collected data concerning all blood components. However, there was consensus that a minimum dataset should be collected.

It was acknowledged that the collection of standardised data would be simplified through the use of electronic data systems with clinical prompts. Computer-based software for ordering blood components and concurrently collecting transfusion data could be developed for use in Australian hospitals. Any such software should be made widely available at a minimal cost.

The software could link indications for blood component therapy with the decision-making process, with requests that fall outside the guidelines requiring further justification with either the blood bank, pathology or haematology staff. Data entry could use check boxes (no typing required), and detailed submenus of more exact indications could be referred to as required. This would keep the screens fairly simple, overcoming the likely complexity of paper request forms.

As well as reducing rates of inappropriate use of blood components, such software would make collecting data very simple and reduce the need for

surveillance of such activities by the transfusion committee. It could also be used to draw the clinician's attention to the need for informed consent.

5.3 EVALUATION AND REVIEW

Evaluation of guidelines aims to assess the validity of the guidelines and the effectiveness of their dissemination and implementation as indicated by their impact on professional behaviour, patient outcomes and health-care costs (Audet et al 1990). Areas that should be considered in evaluation of guidelines include (NHMRC 1999):

- assessment of the dissemination process;
- assessment of whether or not clinical practice is moving towards the guideline's recommendations;
- assessment of whether or not health outcomes have changed (where baseline data allow);
- assessment of impact on consumer knowledge and understanding; and
- economic evaluation of the guideline process.

These guidelines aim to improve transfusion practice by:

- reducing the proportion of blood components given without specific indications;
- ensuring adequate documentation of all use of blood components; and
- ensuring accountability processes are in place in all situations where blood components are used.

The lack of baseline data makes it difficult to make assessments about changes in clinical practice and health outcomes resulting from implementation of these guidelines. However, the collection of clinical indicators on blood components by all hospitals as part of the accreditation process (see Section 4.1) will allow future evaluation of the impact of the guidelines. This will be supported by evaluation of progress on the following over time:

- accreditation mechanisms linked to use of these guidelines in place; and
- blood components review mechanisms in place at all institutions using blood component therapy.

The effectiveness of the consumer booklet and poster in changing consumer knowledge could be assessed through focus groups.

5.4 ECONOMIC CONSIDERATIONS

Implementation of these guidelines will have economic implications, in terms of both savings and costs.

Savings should result as the inappropriate use of blood components decreases. A recent study (Rubin et al 2001) found that up to 30 per cent of current red blood cell use is inappropriate. Assuming a marginal cost of around \$33¹ per unit transfused (data from ARCBS), an average of 2 units per transfusion, and a halving of 30 per cent inappropriate use to 15 per cent, there is the potential for cost-offsets of up to \$3 million per year.

Data to show the inappropriate use of platelets, FFP and cryoprecipitate are not currently available, and it is therefore not possible to calculate the monetary impact of a reduction in inappropriate use.

The cost implications of these guidelines must also be considered, as the cost of implementation is likely to be substantial (eg infrastructure, ongoing education, monitoring systems, processes for clinical review). The main benefit is likely to be in the area of improved patient outcomes, although economic evaluation of the possible health impact of these guidelines is not possible currently. This is because the effect of reducing blood use on patient outcomes such as morbidity and length of hospital stay has not been quantified.

Adequate resourcing is essential if the benefits to patients and the health system are to be realised. To ensure that strategies have more than short-term effects in influencing transfusion practice, continuing funding will be required.

5.5 OTHER IMPLICATIONS OF THE GUIDELINES

These guidelines present the available current evidence on appropriate blood component therapy, and also consider diverse clinical experience and consumer concerns, in an attempt to promote more informed decision-making and improve patient care and outcomes. These guidelines go beyond recommendations for appropriate use of blood components. They are one of the first clinical practice guidelines to:

- define precise process measures for the quality of care;
- lay out mechanisms for continuous audit at the local, State/Territory and national levels; and
- point the way towards evaluation of changes in clinical behaviour which are motivated by their implementation.

¹ The national marginal cost of a unit of red blood cells from a whole blood donation is \$32.90. It should be noted that this is a minimum estimate, as the term 'marginal' means that overhead costs are excluded. This includes a component of fixed labour (ie departmental managers) which for ARCBS purposes is treated as an overhead.

If these guidelines are implemented effectively, there will be a number of positive implications in a range of areas:

- improved consistency and appropriateness of transfusion practice;
- integration of appropriate transfusion practice into quality management systems in all hospitals involved in blood component therapy;
- continuous monitoring and review of the appropriateness of blood component use at hospital, State/Territory and national levels;
- reduced number of transfusion-related complications;
- increased consumer awareness of the benefits and risks of blood component therapy and of their involvement in the decision-making process;
- increased community awareness of the issues surrounding blood component therapy; and
- reduced pressure on the blood supply.

Negative implications of the guidelines are also possible, if the intention of the guidelines is misinterpreted. Rigid application of the guideline recommendations could lead to some patients receiving unnecessary blood components. Undertransfusion could also occur, if it is not recognised that guidelines can never be completely comprehensive, and recommendations are applied in circumstances that are not specifically addressed in this report.

APPENDIX 1

MEMBERSHIP AND TERMS OF REFERENCE OF THE WORKING PARTY

Professor George Rubin (Chair)	Professor of Public Health and Community Medicine, University of Sydney at Westmead Director, Effective Healthcare Australia
Mr Christopher Carter	Consumer representative Perth Division of General Practice
Associate Professor Michael Davies	Director of Anaesthesia St Vincent's Hospital, Melbourne
Dr Mark Dean	Assistant Director, Australian Red Cross Blood Service
Dr Albert Farrugia	Therapeutic Goods Administration
Dr Richard Fordham	Director of Operations, The Lewin-Fordham Group
Professor Clifford Hughes AO	Cardiac surgeon, Royal Prince Alfred Hospital
Professor James Isbister	Clinical haematologist, Royal North Shore Hospital of Sydney
Professor Jack Metz	Formerly Head of Haematology, Royal Melbourne Hospital
Ms Fiona Stoker	Senior Nursing Adviser, Hobart
Associate Professor Graeme Woodfield	Transfusion Medicine Specialist University of Auckland, New Zealand

The terms of reference of the Working Party were to:

- critically evaluate existing research and clinical evidence for the use of blood components in the clinical setting;
- in accordance with the NHMRC *Guidelines for the Development and Implementation of Clinical Practice Guidelines* undertake the development of guidelines for the appropriate use of blood components in the clinical setting. The guidelines are to be developed in two stages: the first stage, dealing with the use of red blood cells, is to be available as a final draft to be considered by Council in December 2000; the second, will deal with platelets, fresh frozen plasma and cryoprecipitate;
- develop a protocol for the use of health-care workers in order to enable a reduction in the wastage of blood components utilised in the clinical setting;

- invite stakeholders to forward submissions to the group, to circulate for comment the draft report and to undertake other wide consultation as appropriate;
- develop an effective dissemination and implementation strategy;
- identify areas where evidence is lacking; and
- present a final report to the Health Advisory Committee and to Council.

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Mr Ken Davis	Senior scientist, Adelaide
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APPENDIX 2

REVIEW OF THE EVIDENCE

In its critical evaluation of evidence for the use of blood components in the clinical setting, the Working Party made use of existing reviews including the following:

The Newcastle Systematic Review Group

In 1998, the Australian Centre for Effective Healthcare agreed with NSW Health to conduct a project on the appropriateness of red blood cell transfusion in New South Wales hospitals. Objectives of the project included reviewing the available evidence, and a systematic review was subcontracted to the Newcastle Systematic Review Group (Hill et al 1999). This review was conducted using methods specified by the International Cochrane Collaboration.

EC review

The 1998 'Wildbad Kreuth Initiative' meeting aimed to address measures needed to introduce and implement quality management of blood components in the European Community. Participants were provided with a summary of the literature, which included discussion of evidence on medical indications for transfusion of red blood cells, platelets and plasma (EC 1999).

Western Australian review

A review of the literature concerning blood components was conducted as part of a project to examine aspects of blood component ordering and use in Western Australian hospitals (Finn et al 1998). The review investigated variations in use, levels of inappropriate use and measures to reduce inappropriate use. The impact of transfusion thresholds on clinical practice was not considered.

Hébert et al review

This review (Hébert et al 1997a) aimed to analyse the evidence describing practice variation in the transfusion of red blood cells as well as the risks, benefits, harms and costs associated with anaemia and transfusion. The review yielded 189 articles, of which 41 per cent were interventional and 59 per cent were observational.

The aims of the review were to identify all studies that investigated the impact of transfusion thresholds on the use of red blood cells and all studies that described methods of changing transfusion practice. The studies were reviewed in order to determine the best available evidence for adopting a particular transfusion threshold as a clinical guideline.

American Society of Anesthesiologists guidelines

In 1994, the American Society of Anesthesiologists established a Taskforce on Blood Component Therapy to develop evidence-based indications for transfusing red blood cells, platelets, fresh frozen plasma and cryoprecipitate in perioperative and peripartum settings (American Society of Anesthesiologists 1996). The Taskforce undertook a search of the literature and graded the evidence and the strength of individual recommendations in a systematic fashion.

Recent evidence

To ensure that the literature reviewed in these guidelines was complete and up to date, Medline searches were undertaken for the period 1999–2001 for red blood cells and 1994–2001 for the other blood components.

Searches were carried out using the following medical subject headings (MeSHs): erythrocyte transfusion, red blood cell transfusion, platelet transfusion, platelet concentrate, plasma transfusion, plasmapheresis, plasma exchange, plasma substitute, cryoprecipitate and cryoprecipitated antihemophilic factor. These searches were combined with other searches using the MeSHs blood component therapy, blood component transfusion, blood transfusion, adverse effects, postoperative complications, aged, immunosuppression and infection. The citation lists were reviewed to ensure that original data were used (ie primary studies); studies were in human adults; and clinical aspects of transfusion were examined.

Evidence on the use of red blood cells

International evidence indicates that adopting a restrictive transfusion policy for red blood cells can reduce post-operative morbidity and mortality. While few randomised controlled trials have considered appropriate indications for red blood cells, the results of these trials are generally consistent, and suggest that a restrictive transfusion threshold (haemoglobin level <70g/L) does not have any adverse affect on patient outcomes (Hill et al 1999). While even less is known about appropriate indications for the use of red blood cells in patients with compounding impairments in oxygen transport, there is some evidence that complications from anaemia are greater in patients with cardiac disease and that a higher threshold may be more appropriate for these patients (Carson et al 1996; Hébert et al 1997b). Lower short-term mortality has been associated with the use of red blood cells at haemoglobin levels of 90g/L in older patients with acute myocardial infarction and use of red blood cells may be appropriate in such patients with haemoglobin levels of 110g/L (Goodnough & Bach 2001; Wu et al 2001).

The Hébert review (1997a) identified six randomised controlled trials contrasting two transfusion strategies (Weisel et al 1984; Blair et al 1986; Fortune et al 1987; Johnson et al 1992; Hébert et al 1995; Vichinsky et al 1995). Only one study,

conducted in patients with sickle-cell disease, was large enough to rule out clinically important differences in its primary outcome, perioperative sickle-cell crises (Vichinsky et al 1995). The remaining studies enrolled too few patients to draw conclusions about outcomes from the use of red blood cells and did not result in evidence to support an optimal transfusion threshold.

The Hill et al review identified seven randomised controlled trials (including four evaluated in the Hébert et al review) and five non-randomised studies that investigated the impact of transfusion thresholds. There was considerable variation from study to study with regard to the transfusion threshold used, although many of the studies measured similar outcomes, such as mortality, length of hospital stay and blood use. In general, the strategies compared were either maintaining haemoglobin concentration or haematocrit above a specified level (a 'liberal' transfusion strategy) or not initiating transfusion unless the haemoglobin level/haematocrit fell below a specified level (a 'restrictive' strategy). The thresholds for the restrictive strategies ranged from haemoglobin levels of 70g/L to 90g/L or haematocrits of <25 per cent to 30 per cent.

Table A2.1 (see page 53) summarises the results of those randomised controlled trials from the Hébert et al and Hill et al reviews that reported on mortality, length of hospital stay and blood use.

Transfusion thresholds in patients with special considerations

Anaemia is less well tolerated in the severely ill and in people with coronary, cerebrovascular or respiratory disease (NIH Consensus Conference 1988; Audet & Goodnough 1992; American Society of Anesthesiologists 1996). However, there is little clinical evidence to confirm that these factors are independently associated with an increased risk of adverse outcome (Hébert et al 1997a). Studies of perioperative and critically ill patients have suggested that complications from anaemia are greatest in those with cardiac disease (Carson et al 1996; Hébert et al 1997b). Associations between anaemia and adverse outcomes, as well as modification in the degree of risk in people with other potential risk factors such as increased age and disease severity, respiratory and cerebrovascular disease, have not been clearly established (Hébert et al 1997a).

Evidence on the use of platelets

Indications for the therapeutic use of platelets in most clinical settings are based on observation or consensus, with little evidence from clinical trials. For prophylactic use there are a limited number of randomised and non-randomised clinical trials examining different transfusion thresholds in haematological and oncological patients (Gmur et al 1991; Gil-Fernandez et al 1995; Heckman et al 1997; Wandt et al 1998; Lawrence et al 2001). Taken together, there is no evidence that the lower transfusion threshold of $10 \times 10^9/L$ is associated with a worse outcome than the tradition transfusion trigger of $20 \times 10^9/L$ in the absence of risk factors.

These results are in keeping with a recent prospective and randomised multicentre trial of 255 patients with acute myeloid leukaemia undergoing induction chemotherapy. The study showed no significant difference in bleeding episodes, red blood cell use, hospital inpatient days or mortality in patients randomised to a platelet trigger of $10 \times 10^9/L$ or to a trigger of $20 \times 10^9/L$ (Rebulla et al 1997). Further reduction in the threshold for prophylactic use of platelets may be possible (Gmur et al 1991). A reduction in platelet use could not only reduce transfusion-related risks, but also markedly diminish costs (Wandt et al 1998).

Table A2.2 (see page 54) outlines selected studies investigating different platelet transfusion triggers.

Some studies have suggested that spontaneous bleeding is uncommon with platelet counts $>20 \times 10^9/L$ (Gmur et al 1991). However, controlled trials have not been carried out to investigate the platelet count at which surgical patients are likely to experience increased bleeding (American Society of Anesthesiologists 1996). In general most guidelines recommend that the platelet count should be $>50 \times 10^9/L$ for surgical procedures. For operations in critical sites such as the brain or eyes, it may be appropriate to maintain the platelet count at $100 \times 10^9/L$ (British Committee for Standards in Haematology 1992a).

Massive transfusion often causes thrombocytopenia proportional to the amount of blood transfused. Coexisting clinical conditions influence the value of platelet counts in predicting the occurrence of bleeding, but the probability of clinically significant thrombocytopenia increases in proportion to the number of units of blood transfused (Counts et al 1979; Reed et al 1986; Ciaverella et al 1987; Leslie & Toy 1991). Clinically significant problems occur after transfusion of 1.5–2.0 blood volumes (Norfolk et al 1998). Consumption of platelets, as well as simple dilution, can also lead to microvascular bleeding (Ciaverella et al 1987).

There is no evidence to support the use of platelets in situations of immune-mediated platelet destruction, thrombotic thrombocytopenic purpura, which may be worsened by platelet transfusion (Harkness et al 1981) or haemolytic uraemic syndrome.

Platelet function defects and some degree of thrombocytopenia frequently occur after cardiac bypass surgery (Slichter 1980). However, controlled trials of prophylactic platelet transfusion have not demonstrated benefit for patients following uncomplicated cardiac bypass surgery (Simon et al 1984).

Evidence on the use of fresh frozen plasma

While there have been clinical trials evaluating the use of FFP for a range of patients (Leese et al 1987; Leese et al 1991; Consten et al 1996; Dupont et al 1996), most recommendations are based on clinical observations and the results of coagulation tests.

There are few well-documented and universally accepted indications for the use of FFP, limited to treatment of bleeding episodes or preparation for surgery in patients with factor deficiencies where specific factor concentrates are not available.

Few studies have been performed to determine whether perioperative administration of FFP improves clinical outcome (American Society of Anesthesiologists 1996). A retrospective review of patients having coronary artery bypass (Roy et al 1988) and given either albumin or an average of six units of FFP did not demonstrate any differences in blood loss or transfusion requirements. A prospective randomised trial of patients undergoing cardiopulmonary bypass found no significant differences between patients receiving FFP and those receiving plasma substitute (Consten et al 1996). A review of evolving issues in coronary artery bypass grafting found that transfusion of FFP is of no benefit and therefore carries an unnecessary risk to the patient (Goodnough et al 1990).

FFP has been widely used to provide prophylaxis against coagulation disorders and severe bleeding following uncomplicated cardiac bypass surgery, but there is little justification for this either because no substantive evidence of efficacy exists or because safer, equally effective alternative therapies exist (NIH Consensus Conference 1985; Roy et al 1988; Goodnough et al 1990; Consten et al 1996).

It is generally accepted that for the immediate reversal of warfarin overdose associated with life-threatening haemorrhage, FFP alone or in combination with concentrates of vitamin-K-dependent factors is indicated. A study into the relative efficacy of infusions of FFP and clotting factor concentrate on correction of the anticoagulation effect found that haemostatically effective levels of factor IX could not be achieved, in most instances, by the conventional use of FFP (Makris et al 1997).

While FFP is a reliable solution for intravascular volume replacement in acute blood loss, alternative therapies are equally satisfactory and considerably safer. Table A2.3 (see page 55) outlines selected studies evaluating the use of FFP.

EVIDENCE ON THE USE OF CRYOPRECIPITATE

Cryoprecipitate cannot as yet be virally inactivated and therefore should no longer be used for the treatment of bleeding unless other measures have clearly failed (Association of Hemophilia Clinic Directors of Canada 1995).

Use of cryoprecipitate may be justified in patients with fibrinogen deficiency where there is clinical bleeding, invasive procedures, trauma or DIC (British Committee for Standards in Haematology 1992b; College of American Pathologists 1994; American Society of Anesthesiologists 1996).

Indirect observational evidence suggests a beneficial effect from the use of cryoprecipitate in patients with factor VIII deficiency and certain types of von Willebrand's disease (Green & Potter 1976; Holmberg & Nilsson 1992). However, most patients with factor VIII deficiency are treated with factor VIII concentrates, and patients with some subtypes of von Willebrand's disease respond to

administration of desmopressin (Aledort 1991; Schulman 1991; Rodeghiero et al 1992; Hoyer 1994).

A randomised crossover study to assess the efficacy of virally inactivated factor VIII concentrates in the treatment of von Willebrand's disease indicated that variable success can be expected (Mannucci et al 1992).

It has not been conclusively shown that cryoprecipitate is of clinical use in patients with fibronectin deficiency.

Table A2.1 Summary of outcomes from randomised controlled trials into restrictive use of red blood cells

Study population	n	Intervention	30-day mortality	LOS hospital (days)	Blood use (units/pt)	Comments
<i>Hébert et al (1999)</i> Critically ill patients with Hb<90g/L within 72 hr admission	420	Liberal group: Hb 100–120g/L maintained and transfused if Hb<100g/L Restrictive group: Hb 70–90g/L maintained and transfused if Hb<70g/L	23.3% 18.7%	35.5±19.4 34.8±19.5	5.6±5.3 2.6±4.1	Restrictive transfusion is as effective as liberal transfusion in critically ill patients, with the possible exception of patients with acute myocardial infarction and unstable angina.
<i>Carson et al (1998)</i> Surgical repair of hip fracture	40 40	Symptomatic group: Hb<80g/L + symptoms Threshold group: maintained at Hb>100g/L	2.4% 2.4%	6.3±3.4 6.4±3.4	— —	Symptomatic transfusion may be associated with reduced blood usage and lower mean Hb levels than the threshold transfusion policy.
<i>Bush et al (1997)</i> Elective aortic/inguinal arterial reconstruction	49 50	Liberal group: maintained at Hb⊕100g/L Restrictive group: maintained at Hb<90g/L	8% 8%	11.0±9.0 10.0±6.0	3.7±3.5 2.8±3.1	A lower Hb level was tolerated without adverse clinical outcome.
<i>Hébert et al (1995)</i> Critically ill patients	69	Liberal group: maintained at 100–120g/L Restrictive group: maintained at 70–90g/L	25% 24%	— —	4.8 2.5	Neither mortality nor development of organ dysfunction was affected by the transfusion strategy.
<i>Vichinsky et al (1995)</i> Patients with sickle cell disease	278 301	Liberal group: Hb=100g/L and HbS≤30% Restrictive group: Hb=100g/L regardless of HbS%	n=2 n=0	8 (mean) 8 (mean)	5.0 2.5	Restrictive transfusion was as effective as liberal transfusion in preventing perioperative complications in patients with sickle cell disease and resulted in half as many transfusion-associated complications.
<i>Johnson et al (1992)</i> Elective myocardial revascularisation	18 20	Liberal group: Hct=32% Restrictive group: Hct <25%	— —	7.6±1.9 7.9±4.3	2.05±0.93 1.0±0.86	Postoperative blood transfusion in revascularised patients should be guided by clinical indications and not by specific haematocrit values.
<i>Blair et al (1986)</i> Acute gastrointestinal haemorrhage	24 26	Liberal group: given at least 2 units at admission Restrictive group: not transfused unless Hb<80g/L or shock	8.3% 0%	— —	4.6±0.3 2.6±0.6	Early blood transfusion appears to increase the chances of rebleeding.

LOS = length of stay; Hb = haemoglobin; HbS = sickle cell haemoglobin; Hct = haematocrit Source: Adapted from Hill et al (1999).

Table A2.2 Selection of recent studies investigating different platelet transfusion triggers

Study design	Study population	n	Intervention	Outcome measures	Outcomes
<i>Rebulla et al (1997)</i> Prospective randomised clinical multicentre trial	Acute myeloid leukaemia (1st course of induction chemotherapy)	255	Restrictive group: $10 \leftrightarrow 10^9/L$ Liberal group: $20 \leftrightarrow 10^9/L$	Primary—Frequency of major haemorrhage Secondary—Transfusion rates; rates of complete remission; mortality	No significant difference in total number of major haemorrhages. 21.5% fewer platelets in restrictive group. No significant differences in rates of remission and mortality.
<i>Heckman et al (1997)</i> Prospective randomised clinical, single-institution trial	Acute leukaemia (induction therapy)	78	Restrictive group: $\leq 10 \leftrightarrow 10^9/L$ Liberal group: $\leq 20 \leftrightarrow 10^9/L$	Primary—Bleeding episodes; number of platelet transfusions Secondary—Number of RBC transfusions; febrile days; LOS; days thrombocytopenic; need for HLA-matched platelets; remission rate; death during induction therapy	No significant differences in the total number of bleeding episodes. More platelets for bleeding in restrictive group; more prophylactic platelets in liberal group. Total number of platelets used higher (nearly significant) in liberal group. No significant differences in other outcomes.
<i>Wandt et al (1998)</i> Prospective clinical multicentre trial	Acute myeloid leukaemia (induction of consolidation therapy)	105	Restrictive group: $\leq 10 \leftrightarrow 10^9/L$ Liberal group: $\leq 20 \leftrightarrow 10^9/L$	Primary—Bleeding complications; number of platelet transfusions; number of RBC transfusions Secondary—costs for each transfusion strategy	No correlation between serious bleeding events and platelet count. Significantly lower number of platelets used in the restrictive group. No significant difference in the number of RBCs used. Costs of platelet therapy one-third lower in restrictive group.
<i>Gmur et al (1991)</i> Prospective clinical single-institution trial	Acute leukaemia	102	No risk factor group: $\leq 5 \leftrightarrow 10^9/L$ Restrictive group: $\leq 10 \leftrightarrow 10^9/L$ (with fever or minor bleeding) Liberal group: $\leq 20 \leftrightarrow 10^9/L$ (heparin therapy, coagulation disorders, invasive procedures)	Bleeding episodes	Bleeding episodes on 1.9% of study days in the without risk factors group and on 0.07% days in the restrictive group.
<i>Gil-Fernandez et al (1995)</i> Retrospective analysis	Bone marrow transplant patients	190	1990–1991 policy: $\leq 20 \leftrightarrow 10^9/L$ 1993–1994 policy: $\leq 10 \leftrightarrow 10^9/L$ (stable); $\leq 20 \leftrightarrow 10^9/L$ (higher platelet consumption)	Major haemorrhage; number of platelet transfusions.	Significantly lower use of platelet units in the $\leq 10 \leftrightarrow 10^9/L$ group.

RBC = red blood cell; LOS = length of stay; HLA = human leucocyte antigen Source: Adapted from EC (1998).

Table A2.3 Selection of clinical studies evaluating the use of fresh frozen plasma in different settings

Study design	Study population	n	Intervention	Outcome measures	Outcomes
<i>Consten et al (1996)</i> Randomised clinical single-institution trial	Surgery, elective cardiac bypass	50	Group I: 3 units of FFP after operation Group II: equal volume of plasma substitute	Perioperative blood loss; perioperative transfusion requirements; coagulation parameters; platelet count	No significant difference in blood loss, transfusion requirement, coagulation parameters or platelet count.
<i>Dupont et al (1996)</i> Observational study	Surgery, orthotopic liver transplantation	28	Group I: preoperative factor V 10–60% Group II: preoperative factor V >60%	Bleeding during operation and up to 48hrs after operation; coagulation factors	Total intraoperative bleeding 3460±2700mL in Group I; 3470±2110mL in Group II.
<i>Leese et al (1991)</i> Prospective randomised clinical multicentre trial	Patients with predicted severe pancreatitis	72	Group I: 8 units/day FFP over 3 days Group II: equal volume of colloid	Mortality within hospital stay	No significant difference in clinical outcome. Mortality 20% in Group I and 18% in Group II.
<i>Leese et al (1987)</i> Randomised clinical multicentre trial	Patients presenting acute pancreatitis	202	Group I: 2 units/day FFP over 3 days Group II: equal volume of colloid		No significant differences in clinical outcome.

FFP = fresh frozen plasma Source: Adapted from EC (1998)

APPENDIX 3

REVIEW OF MEASURES TO IMPROVE TRANSFUSION PRACTICE

Several approaches have been developed with the aim of reducing inappropriate use of blood components. Interventions that directly affect clinical decision-making, such as clinical practice guidelines, education programs, conferences and audits, may improve a clinician's transfusion practice. This appendix outlines guidelines on the appropriate use of blood components that have been endorsed by medical organisations overseas and reviews the evidence on interventions to change transfusion practice.

Guidelines

Red blood cells

Nine clinical practice guidelines addressing the use of red blood cells were reviewed (Petz & Tomasulo 1987; NIH Consensus Conference 1988; Goodnough et al 1990; Audet & Goodnough 1992; Royal College of Physicians of Edinburgh 1994; ACOG 1995; Spence 1995; American Society of Anesthesiologists 1996; Canadian Medical Association 1997). Of these, three addressed general patient populations (Petz & Tomasulo 1987; Audet & Goodnough 1992; Royal College of Physicians of Edinburgh 1994; Canadian Medical Association 1997), two focused on specific patient populations—patients undergoing coronary artery bypass grafting (Goodnough et al 1990) and obstetric patients (ACOG 1995)—and three addressed the administration of red blood cells solely in the perioperative period (NIH Consensus Conference 1988; Spence 1995; American Society of Anesthesiologists 1996). With the exception of the surgical red blood cell transfusion practice policies (Spence 1995), all the guidelines were endorsed by a medical society or organisation. Table A3.1 gives examples of the recommendations of the guidelines.

Table A3.1 Examples of guidelines on the use of red blood cells

Recommendations	Comments
<i>Guidelines for red blood cell and plasma transfusion in adults and children (Canadian Medical Association 1997)</i>	
There is no single haemoglobin level that justifies or requires transfusion; an evaluation of the patient's clinical situation should also be a factor in the decision.	A physician prescribing red blood cells should be familiar with the indications for and the benefits and risk from their use.
<i>Practice guidelines for blood component therapy (American Society of Anesthesiologists 1996)</i>	
Use of red blood cells: Hb > 100g/L—rarely; Hb < 60g/L—almost always; Hb 60–100g/L—consideration of patient's risk factors for complications of inadequate oxygenation.	Haemoglobin level alone is an inadequate measure of oxygen delivery, but suggestion of a range of 60–100g/L.
<i>Guidelines for therapy with blood components and plasma derivatives (German Medical Association 1995)</i>	
Patients without reduction of vital functions—loss of blood volume up to 20% should be restored with crystalloids; Hb 60–70g/L sometimes tolerated without signs of hypoxic organ damage; Hb < 40–50g/L critical.	No universally applicable lower limits for haemoglobin level or haematocrit can be given as an indication for use of red blood cells.
Older patients and patients with cardiac and/or pulmonary disease should be transfused earlier.	Duration, severity and cause of anaemia, the clinical condition, age and gender of patient should always be taken into consideration.
<i>Surgical red blood cell transfusion policies (Spence 1995)</i>	
Transfusion at Hb of 100g/L in cardiopulmonary affected patients; 70g/L in healthy, low-risk patients with no evidence of cardiopulmonary disease.	Case-by-case and one unit at a time approach.
<i>Consensus statement on red cell transfusion (Royal College of Physicians Edinburgh 1994)</i>	
Transfusion decision should be made by an experienced medical practitioner. Consideration should be given to the patient's individual risk factors for complications of inadequate oxygenation.	There is no single critical haemoglobin level or haematocrit value applicable to all patients.
<i>Practice strategies for elective red blood cell transfusion (Audet & Goodnough 1992)</i>	
Use of red blood cells to be avoided where possible. In case of transfusion, patient's individual risk factors for complications of inadequate oxygenation should be considered.	Elective homologous transfusion should be regarded as an outcome to be avoided. No transfusion threshold. Anaemia with normal blood volume can be well tolerated in symptomatic patients.
<i>Perioperative red blood cell transfusion (NIH Consensus Conference 1988)</i>	
Red blood cell transfusion: rarely required in healthy patients with Hb > 100g/L; frequently required in patients with Hb < 70g/L.	Available evidence does not support the use of a single criterion for transfusion. No single measure can replace good clinical judgment as the basis for decision-making regarding perioperative transfusion.

Source: Adapted from EC (1999).

Platelets

Four clinical practice guidelines addressing the use of platelets have been published in English and endorsed by a medical society or organisation (British Committee for Standards in Haematology 1992a; College of American Pathologists 1994; American Society of Anesthesiologists 1996; Royal College of Physicians of Edinburgh 1998). Of these, one was dedicated to perioperative and obstetric use (American Society of Anesthesiologists 1996) and the others provided general indications for use.

Table A3.2 summarises the recommendations of the guidelines.

Table A3.2 Examples of guidelines on the use of platelets

Recommendations	Comments
<i>Consensus conference on platelet transfusion (Royal College of Physicians of Edinburgh 1998)</i>	
<p>Prophylactic platelet transfusion —</p> <ul style="list-style-type: none"> • is appropriate in patients with haematological malignancies and bone marrow failure—threshold of $10 \times 10^9/L$ in patients without risk factors; higher thresholds in those with risk factors or planned invasive procedures. 	<p>Recommendations are supported by broad review of the literature with consideration of clinical studies. Precise indications and optimal specifications still need to be defined. There is a need for prospective randomised trials and clearly defined protocols.</p>
<p>Therapeutic platelet transfusion —</p> <ul style="list-style-type: none"> • is appropriate for massive haemorrhage with a platelet count of $50 \times 10^9/L$ and consideration of clinical criteria. 	<p>Inappropriate uses —</p> <ul style="list-style-type: none"> • platelet transfusion is rarely appropriate in surgical patients (including cardiac and vascular); and • platelet transfusion is not appropriate in patients with heparin-induced thrombocytopenia, thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome.
<i>Practice guidelines for blood component therapy (American Society of Anesthesiologists 1996)</i>	
<p>Prophylactic platelet transfusion —</p> <ul style="list-style-type: none"> • is ineffective and rarely appropriate when thrombocytopenia is due to increased platelet destruction; • is rarely appropriate in surgical patients with thrombocytopenia due to decreased platelet production when the platelet count is $>100 \times 10^9/L$ and usually appropriate when the count is $<50 \times 10^9/L$; • determination of whether patients with intermediate counts ($50\text{--}100 \times 10^9/L$) require therapy should be based on the risk of bleeding. 	<p>Recommendations are based on controlled and uncontrolled observational clinical studies and apply to patients in the perioperative or obstetric setting. The need for platelet transfusion is dependent on multiple risk factors and not a single laboratory value (eg platelet count, bleeding time). The risk in surgical and obstetric patients is defined by the type and extent of surgery, the ability to control bleeding, the actual and anticipated rate of bleeding and the presence of factors that adversely affect platelet function (eg extra-corporeal circulation, renal failure, medications).</p>
<p>Therapeutic platelet transfusion —</p> <ul style="list-style-type: none"> • is usually appropriate in surgical and obstetric patients with microvascular bleeding if the platelet count is $<50 \times 10^9/L$ and rarely required if it is $>100 \times 10^9/L$; • may be appropriate despite an apparently adequate platelet count if there is known platelet dysfunction and microvascular bleeding. 	<p>In the absence of evidence, the opinion of the task force is that platelet transfusion is justified in bleeding patients at higher platelet counts than recommended for non-bleeding patients because of the increased risk of complications due to bleeding in the surgical patient.</p>

continued

Table A3.2 Examples of guidelines on the use of platelets (continued)

Recommendations	Comments
<i>Practice parameter for the use of fresh-frozen plasma, cryoprecipitate and platelets (College of American Pathologists 1994)</i>	
<p>Platelet transfusion may be appropriate—</p> <ul style="list-style-type: none"> • when the platelet count is $<5 \times 10^9/L$ regardless of apparent bleeding; • when the platelet count is between $5 \times 10^9/L$ and $30 \times 10^9/L$ prophylactically or on the basis of significant bleeding risks; • for patients undergoing major surgery when the platelet count is $<50 \times 10^9/L$ and there is evidence of microvascular bleeding; • when the platelet count is between $<20 \times 10^9/L$ and $50 \times 10^9/L$ and there is unexpected excessive bleeding; • to treat platelet dysfunction. 	<p>Parameters are provided as an educational tool to assist physicians in providing quality care. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of the individual circumstances presented by a specific patient.</p>
<i>Guidelines for platelet transfusions (British Committee for Standards in Haematology 1992a)</i>	
<p>Prophylactic platelet transfusion —</p> <ul style="list-style-type: none"> • for bone marrow failure, risk of haemorrhage is reduced by platelets to keep the count $>10 \times 10^9/L$ without risk factors, or $>20 \times 10^9/L$ with factors associated with bleeding; • for lumbar puncture, epidural anaesthesia, insertion of indwelling lines, transbronchial biopsy, liver biopsy, laparotomy or similar procedures, the platelet count should be raised to at least $50 \times 10^9/L$. For operations in critical sites such as the brain or eyes, the platelet count should be raised to $100 \times 10^9/L$. 	<p>In general, the cause of the thrombocytopenia should be established before a decision about the use of platelets is made because the role of platelets depends on the underlying disorder.</p>
<p>Therapeutic platelet transfusion —</p> <ul style="list-style-type: none"> • may be appropriate to maintain a count of $>50 \times 10^9/L$ in patients receiving massive blood transfusions. 	<p>Inappropriate use —</p> <p>Platelets are not appropriate:</p> <ul style="list-style-type: none"> • as long-term prophylaxis for patients with chronic failure of platelet production due to aplastic anaemia or myelodysplasia; • for patients with platelet disorders unless they are undergoing surgical procedures; • for TTP; • for DIC unless there is bleeding; • for cardiopulmonary bypass surgery; • for autoimmune thrombocytopenia except in patients with major haemorrhage.

DIC = disseminated intravascular coagulation; TTP = thrombotic thrombocytopenic purpura

Source: Adapted from EC (1999).

Fresh frozen plasma

Nine clinical practice guidelines addressing the use of plasma were reviewed (NIH Consensus Conference 1985; Petz & Tomasulo 1987; Goodnough et al 1990; British Committee for Standards in Haematology 1992b; Ali et al 1994; College of American Pathologists 1994; ACOG 1995; American Society of Anesthesiologists 1996; Canadian Medical Association 1997). Of these, four were dedicated to the use of plasma in specific clinical settings: massive transfusion (Ali et al 1994), coronary artery bypass grafting (Goodnough et al 1990), obstetrics (ACOG 1995) and perioperative and obstetric use (American Society of Anesthesiologists 1996).

The remaining guidelines provided general indications for use, particularly the appropriate clinical settings (NIH Consensus Conference 1985; British Committee for Standards in Haematology 1992b; College of American Pathologists 1994; Canadian Medical Association 1997). All guidelines were developed and endorsed by major medical societies or organisations.

Table A3.3 gives examples of the recommendations of the guidelines.

Table A3.3 Examples of guidelines on the use of fresh frozen plasma

Recommendations	Comments
<i>Guidelines for red blood cell and plasma transfusion in adults and children (Canadian Medical Association 1997)</i>	
Use of FFP is appropriate for patients with multiple coagulation factor deficiencies with— <ul style="list-style-type: none"> • serious bleeding or prophylactically before surgery or invasive procedures in patients with vitamin K deficiency or on warfarin therapy; • bleeding in patients with liver disease; • DIC with active bleeding; • massive transfusion and microvascular bleeding. 	Recommendations are based on systematic review of the literature by an expert panel.
Plasma should be used in the treatment of TTP.	
Use is appropriate in patients with acquired deficiencies of a single coagulation factor when desmopressin or appropriate factor concentrates are unavailable and bleeding has occurred or is expected to occur.	
<i>Practice guidelines for blood component therapy (American Society of Anesthesiologists 1996)</i>	
Use of FFP is appropriate for— <ul style="list-style-type: none"> • urgent reversal of warfarin therapy; • correction of known coagulation factor deficiencies for which specific concentrates are unavailable; • correction of microvascular bleeding when PT and PTT are >1.5 times normal. It is contraindicated for augmentation of plasma volume or albumin concentration. 	Recommendations are based on controlled and uncontrolled observational clinical studies and apply to patients in the perioperative or obstetric setting.
<i>Practice parameter for the use of fresh-frozen plasma, cryoprecipitate and platelets (College of American Pathologists 1994)</i>	
Use of FFP may be appropriate for— <ul style="list-style-type: none"> • history or clinical course suggestive of a deficiency of coagulation factors, with active bleeding or before surgery or an invasive procedure; • massive blood transfusion; • reversal of warfarin effect (to stop active bleeding or prior to emergency surgery or an invasive procedure); • documented coagulation factor deficiency when used for bleeding or before surgery or an invasive procedure; • plasma exchange for thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome. 	Parameters are provided as an educational tool to assist physicians in providing quality care. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of the individual circumstances presented by a specific patient.

continued

Table A3.3 Examples of guidelines on the use of fresh frozen plasma (continued)

Recommendations	Comments
<i>Guidelines for the use of fresh frozen plasma (British Committee for Standards in Haematology 1992b)</i>	
<p>Use of FFP is appropriate for:</p> <ul style="list-style-type: none"> • replacement of single coagulation factor deficiencies, where a specific or combined factor concentrate is unavailable; • immediate reversal of warfarin effect; • acute disseminated intravascular coagulation; and • thrombotic thrombocytopenic purpura. 	<p>Fresh frozen plasma should only be used to treat bleeding episodes or prepare patients for surgery in certain defined situations.</p> <p>There is no justification for the use of fresh frozen plasma in hypovolaemia, plasma exchange procedures, 'formula' replacement, nutritional support, or treatment of immunodeficiency states.</p>
<p>In the presence of bleeding and abnormal coagulation, fresh frozen plasma may also be indicated for massive transfusion; liver disease; and cardiac bypass surgery.</p>	
<i>Fresh-frozen plasma: indications and risks (NIH Consensus Conference 1985)</i>	
<p>Use of FFP is appropriate for:</p> <ul style="list-style-type: none"> • replacement of isolated factor deficiencies; • reversal of warfarin effect; • massive blood transfusion; • immunodeficiencies; and • thrombotic thrombocytopenic purpura. 	<p>Evidence indicates that other plasma concentrates that do not meet the criteria of FFP may have adequate levels of coagulation factors and are suitable for patients in whom FFP is indicated.</p>

PT = prothrombin time; PTT = partial thromboplastin time

Cryoprecipitate

Three guidelines have made recommendations on the use of cryoprecipitate (British Committee for Standards in Haematology 1992b; College of American Pathologists 1994; American Society of Anesthesiologists 1996). Of these, one is specific to the perioperative setting (American Society of Anesthesiologists 1996), and the others provide general indications for use.

Table A3.4 summarises the recommendations of the guidelines.

Table A3.4 Examples of guidelines on the use of cryoprecipitate

Recommendations	Comments
<p><i>Guidelines for the use of fresh frozen plasma (British Committee for Standards in Haematology 1992b)</i></p> <p>Use of cryoprecipitate may be appropriate for—</p> <ul style="list-style-type: none"> • massively transfused patients with micro-vascular bleeding when the fibrinogen level is less than 80mg/dL. 	<p><i>Practice guidelines for blood component therapy (American Society of Anesthesiologists 1996)</i></p> <p>Use of cryoprecipitate may be appropriate for—</p> <ul style="list-style-type: none"> • prophylaxis in non-bleeding patients with congenital fibrinogen deficiencies or von Willebrand's disease unresponsive to DDAVP; • bleeding patients with von Willebrand's disease; • correction of microvascular bleeding in massively transfused patients with fibrinogen levels below 80–100mg/dL. <p><i>Practice parameter for the use of fresh-frozen plasma, cryoprecipitate and platelets (College of American Pathologists 1994)</i></p> <p>Use of cryoprecipitate may be appropriate for—</p> <ul style="list-style-type: none"> • hypofibrinogenaemia in patients with clinical bleeding or those at greater risk due to imminent invasive procedures or trauma; • von Willebrand's disease unresponsive to desmopressin; • haemophilia A (when factor VIII concentrate is not available).
	<p>Recommendations are based on uncontrolled observational clinical studies and apply to patients in the perioperative or obstetric setting.</p> <p>Parameters are provided as an educational tool to assist physicians in providing quality care. The ultimate judgement regarding the propriety of any specific procedure must be made by the physician in light of the individual circumstances presented by a specific patient.</p>

Other strategies to improve practice

Relatively few studies have investigated the effectiveness of measures to change red blood cell transfusion practice (Hébert et al 1997a). Only two randomised controlled trials have demonstrated that specific interventions, education and transfusion algorithms, may improve red blood cell transfusion practice. Focused teaching sessions have been found to increase compliance with transfusion guidelines (Soumerai et al 1993) and the use of an intra-operative transfusion algorithm has been found to have a significant impact on transfusion practice, assist in decision-making and serve as an effective teaching tool (Despotis et al 1994). The Hill et al review examined the same two randomised controlled trials as well as 12 non-randomised studies.

Studies have suggested that use of fresh frozen plasma can be reduced by programs that include chart audits and the review of results with ordering physicians, dissemination of practice guidelines, case presentations, house staff education and review of transfusion orders (Shanberge 1987; Solomon et al 1988; Ayoub & Clark 1989; Barnette et al 1990; Tuckfield et al 1997). Similar results have been achieved for platelet use (Simpson 1987; McCullough et al 1988).

Table A3.5 summarises the effectiveness of trialed interventions.

Table A3.5 Summary of studies of interventions to alter transfusion practice

Strategy	Effective	Comments
<i>Rosen et al (1993)</i> Transfusion guidelines, education + monitoring	✓	Over a 3-year period numbers of transfusions decreased.
<i>Marconi et al (1996)</i> Quality improvement program + computer audit	✓	Prospective audit is a useful tool for assuring the quality of blood requesting.
<i>Rehm et al (1998)</i> New transfusion information form + audit	✓	Use of a transfusion request sheet as an educational tool improved transfusion practices.
<i>Tuckfield et al (1997)</i> Prospective transfusion monitoring	✓	Prospective monitoring of transfusion request forms can reduce rates of inappropriate transfusions.
<i>Williams et al (1997)</i> Revised transfusion guidelines + audit	✓	Audit showed reductions in cross-match requests and decrease in cross-match / transfusion ratios without any patient morbidity.
<i>Joshi et al (1997)</i> Quality assessment + transfusion guidelines	✓	Improvement in transfusion practice may be due to ongoing quality improvement program and use of transfusion guidelines.
<i>Lam et al (1997)</i> Clinician self-audit	✗	Reduction in blood usage was hypothesised to be due to awareness of the research study.
<i>Brandis et al (1994)</i> Transfusion policies + audit	✓	Transfusion policies reduce rates of inappropriate transfusion.
<i>Morrison et al (1993)</i> Provider education + audit	✓	Education on appropriate blood usage and concurrent quality improvement audit can safely reduce red blood cell usage.
<i>Giovanetti et al (1988)</i> Quality improvement program + audit	✓	Comparison of audit data showed a reduction in overtransfusion but no change in rates of over-request or predeposit.
<i>Soumerai et al (1993)</i> Educational outreach program + audit	✓	Educational outreach visits by transfusion specialists can improve appropriateness and cost-effectiveness of blood use in surgery.
<i>Lam et al (1996)</i> Retrospective peer-review	✓	Retrospective peer-review systems were found to have no effect on reducing red blood cell usage.
<i>Despotis et al (1994)</i> Treatment algorithm	✓	The use of algorithms by transfusion decision-makers can serve as an effective clinician education intervention.

Source: Adapted from Hill et al (1999).

The use of transfusion thresholds in transfusion guidelines or policies can be effective in changing practice. However, it appears from the small number of high-quality studies that a complex intervention is likely to be more effective, combining a number of approaches such as educational programs and guidelines combined with repeated measurement of adherence to the guidelines using audits (Hill et al 1999). This is consistent with studies of changing physician practice in other areas (Grimshaw & Russell 1993; Bero et al 1998). Quality improvement measures also need to be integrated into systems, emphasising informed consent, documentation of rationale for each transfusion, and clinical reassessment between transfusion events (Audet et al 1996).

It is not clear from the evidence how long change in practice can be sustained. It is clear that change can be sustained for at least six months (Soumerai et al 1993) and some of the non-randomised studies suggest that change can be sustained for at least 12 months. To ensure that initial performance improvements are sustained, programs to modify clinician transfusion practice should incorporate renewal of the initial intervention as well as performance monitoring and clinical guidance efforts (Tobin et al 2001). It is likely that educational programs need to be repeated at regular intervals, if only to ensure that new hospital staff are aware of transfusion policies (Hill et al 1999).

APPENDIX 4

DOSAGE AND VOLUME

Red blood cells

A unit of red blood cells is usually 300mL in volume and has a haemoglobin concentration of 180–230g/L. One unit of red blood cells will raise the haemoglobin level of an average sized adult by approximately 10g/L.

The dose of the red blood cells is therefore based on the patient's haemoglobin level and their volume requirements. It is desirable to repeatedly measure the patient's haemoglobin level to assess the effect of the use of red blood cells.

Platelets

The dose of platelets is determined by the pretransfusion platelet count, blood volume and the presence of additional risk factors. A dose of one random donor unit (~5 × 10¹⁰ platelets) per 10 kg body weight may be used as a guide. Therapeutic efficacy should be judged by the clinical result and the 1 hour post-transfusion platelet count. Stable patients who are not refractory to platelet transfusions can be expected to have a platelet count increase between 5–7 × 10⁹/L with each unit infused.

Fresh frozen plasma

The amount of FFP needed depends on the patient's clotting factor levels, the levels needed to attain a therapeutic result, whether or not the patient is bleeding, and the patient's blood volume. The recommended dose is 10–20mL/kg (College of American Pathologists 1994). As 1mL of FFP/kg of patient weight will raise most factors by approx 1 per cent, a dose of 10–20mL/kg would be expected to increase the level of coagulation factors by 15–20 per cent immediately after transfusion of a bolus dose. The infusions need to be in bolus form and given as rapidly as the patient's vascular system can tolerate.

Cryoprecipitate

Where there is a fibrinogen deficiency, values are below 1.0G/L and there is associated haemorrhage, the use of cryoprecipitate may be justified. The exact dose will depend on the patient's blood volume, the level of fibrinogen, the severity of the haemorrhage, and the quality of the available cryoprecipitate. A single cryoprecipitate made from a single unit of plasma will normally contain 200–400mg of fibrinogen but levels may vary widely depending on the method of production, and the initial level of fibrinogen in the plasma.

The recommended dose in a 70kg patient would be 1–2g of fibrinogen and this would require 5–10 individual cryoprecipitates. Further infusions should only be administered based on fibrinogen levels. The infusion should be given rapidly as the volume is relatively small.

As this product is not virally inactivated, only sufficient should be given to control clinical symptoms as this will reduce the number of donor exposures to the patient.

APPENDIX 5

COMMONLY USED TESTS FOR INVESTIGATING FOR SYSTEMIC HAEMOSTATIC FAILURE

Platelet count (PC) (normal 150–400 ↔ 10⁹/L)

The counting of platelets is performed as part of the full blood count by automated cell counters. It is not possible to perform accurate platelet counts on 'fingerprick' blood.

Bleeding time (BT) (normal 3–9 minutes)

The BT is progressively prolonged when the platelet count falls below 75–100 10⁹/L assuming platelet function is normal. The BT is also prolonged when platelet function is defective, in capillary/vascular disease and in some coagulation defects. The testing of bleeding time is invasive and operator-dependent test and is not good for screening unselected patients. Its role is generally in elective settings for investigation of selected patients who have good clinical evidence for a systemic haemostatic disorder. It should be noted that thrombocytopenia is a contraindication for the BT test.

Prothrombin time (PT) (normal range <3 seconds above the control)

The PT is a test of the extrinsic coagulation system. Prolongation may be caused by factor VII deficiency, liver disease, vitamin K deficiency or oral anticoagulant therapy. The PT is also expressed as the International Normalised Ratio (INR) especially when used for anticoagulant control.

Activated partial thromboplastin time (APTT) (<6 seconds above control)

The APTT is a test of the intrinsic coagulation system. The result must be interpreted with caution. There may be significant variation between laboratories about the sensitivity and specificity of the test, as in unselected patients there may be poor correlation between the APTT prolongation and the presence of haemostatic failure and the likelihood of a patient bleeding. In the context of a suspected systemic haemostatic defect, an isolated prolongation of the APTT may represent deficiency or inhibition of factor VIII or IX. If there is a marked isolated prolongation, there may be a deficiency in the contact phase of the coagulation cascade and there is poor correlation with failure of haemostasis. Prolongation of APTT and PT may be due to deficiencies of factors X, V or II. If prolongation is due to deficiency of factors in the contact phase of the haemostatic system there is no correlation with the likelihood of haemorrhage

and the lupus anticoagulant may prolong the APTT and represent a prothrombotic state. Prolonged APTT can also be investigated using correction studies.

Thrombin clotting time (TCT) (normal <2 seconds longer than control)

This is a test of the final conversion of fibrinogen to fibrin. Prolongation of TCT is due to hypofibrinogenaemia, dysfibrinogenaemia, heparin, and fibrin degradation products.

D-Dimer (normal <0.25 µg/mL)

The D-Dimer assay measures cleavage fragments resulting from the proteolytic action of plasmin of fibrin. Elevation of D-Dimer may be seen in the postoperative state, trauma, renal impairment, sepsis and venous thrombosis. High levels of D-Dimer suggest excessive fibrinolysis, as seen in DIC. The test is specific for fibrinolysis and not primary fibrinogenolysis.

Specific coagulation factor assays (normal 2–4g/L)

Fibrinogen is the most common routinely measured coagulation factor in patients suspected of systemic haemostatic failure. Other assays are usually performed in the investigation for specific defects, usually after consultation with a haematologist.

APPENDIX 6

PROCESS REPORT

The *Clinical Practice Guidelines for the Use of Blood Components* were developed in two stages. The first stage involved the development of material and recommendations on the use of red blood cells. These recommendations were endorsed by NHMRC in March 2001. In the second stage, material on platelets, fresh frozen plasma and cryoprecipitate was developed and incorporated into the red blood cell guidelines.

The development of the guidelines involved extensive consultation as follows.

- At the outset of the developmental process, specific professional colleges and known interested parties were asked to forward submissions about the appropriate use of red blood cells. No submissions were received.
- Submissions were invited on the draft guidelines on the use of red blood cells and the Working Party met to discuss their inclusion in the guidelines.
- Face-to-face workshops involving professional colleges and societies, hospital staff and private pathologists were conducted around Australia.
- Submissions were invited on the draft guidelines on the use of platelets, fresh frozen plasma and cryoprecipitate and the Working Party met to discuss their inclusion in the guidelines.

Consultation on the use of red blood cells

The second round of consultations on the draft guidelines on the use of red blood cells took place during December 2000 and January 2001 and involved the following:

A call for submissions on draft guidelines on the use of red blood cells, publicised in the *Government Notices Gazette* and *The Weekend Australian*, and invitations forwarded to all professional colleges and known interested parties.

Submissions were received from the following individuals/organisations:

Jeff Adams

Janssen-Cilag Pty Ltd

Sally Argent

ARCBS National End User Liaison Program

Dr Simon Towler

Australasian Association for Blood Conservation

Dr Vladimir Martyn

Mr Shannon Farmer

Mrs Lee Best	
Ms Chris Hanna	
Dean Beaumont	The Australasian Society of Oto-Laryngology Head and Neck Surgery
Dr Jim P Bradley	Australian Society of Anaesthetists
Jenny Brown	Mater Misericordiae Hospitals
Professor Bryan Campbell	Queensland Health
Julie Cairns	Royal College of Nursing Australia
Dr Ralph Cobcroft	Princess Alexandra Hospital & Queensland Health Blood and Blood Products Advisory Committee
Dr N I Demediuk	Dandenong Division of General Practice
Dr NI Demediuk	The Royal Australian College of General Practitioners
Dr Wendy Erber	Sir Charles Gairdner Hospital Transfusion Committee
Andrew Fitzhardinge	Concord Repatriation General Hospital
Dr Steve Flecknoe-Brown	Barwell Avenue Medical Centre
Ian Fletcher	Territory Health Services
Dr Debra Graves	The Royal College of Pathologists of Australasia
Dr Kerry Gunn	New Zealand Committee of the Australian and New Zealand College of Anaesthetists
Professor Brendon Kearney	Department of Human Services, South Australia
Dr David Kennett	Western Australian Blood Products User Group
Dr Katherine Marsden	Royal Hobart Hospital
Dr Clare Morgan	On behalf of Sullivan Nicolaides Pathology and Queensland Medical Laboratories
Professor Kerin O'Dea	Menzies School of Health Research
Professor Garry Phillips	Australia and New Zealand College of Anaesthetists
Dr Bill Ping	Australian Medical Association Public Health and Aged Committee
Hatem H Salem	Faculty of Medicine Monash University
Dr Russell Schedlich	Far West Area Health Service
Joan Sheales	Australian and New Zealand College of Anaesthetists
Greg Taylor	Australian Pacific Health Group
Dr Amanda Thomson	Concord Hospital
Shannon Farmer & David Webb	David Webb and Associates
Erica Wood	ARCBS Melbourne

A Working Party meeting was held on 6 February 2001 to discuss the submissions and their inclusion in the draft guidelines.

Workshops

Face-to-face workshops were conducted in the States and Territories in February 2001. Consultations were not conducted in the Northern Territory however interested parties were invited to attend consultations in either Adelaide or Cairns. The workshops were used to refine the sections of the report dealing with evaluation, education, dissemination, implementation, monitoring and consumer issues. The following individuals/organisations attended the workshops:

Dr Rick Abbott	Australian Medical Association, SA
Ms Gina Aitken	Royal Hobart Hospital
Mrs Jean Allwright	Monash MC
Dr Stephanie Armstrong	Royal Adelaide Hospital
Dr Chris Ashton	Calvary Hospital
Ms Catherine Austen	Launceston General Hospital
Ms Margaret Baker	Beleura Private Hospital
Ms Suzanne Baker	Liverpool Hospital
Mr Geoff Barlow	Dorevitch Pathology
Mr Grant Barrett	Northern Hospital
Dr John Barry	Cairns Base Hospital
Dr Jenny Bartlett	Royal Melbourne Hospital
Professor R Beal	
Ms Stephanie Beeton	Hunter Health Bone Bank
Mrs Lee Best	Fremantle Kaleeya Hospital
Ms Christine Beswick	Launceston General Hospital
Ms Toni Bickley	Wakefield Hospital
Ms Joan Biddle	
Dr Helen Bidstrup	John James Memorial Hospital
Dr Robert Bird	Cairns Base Hospital
Dr Jonathon Blackwell	Douglass Hanly Moir
Ms Gail Blakeney	Sugermans Hampson's Pathology
Miss Tatiana Borisow	Health Consumers Council WA
Dr Cynthia Bowman	Calvary Hospital
Associate Professor Neil Boyce	ARCBS
Ms Jackie Braemar	Mountain District Private Hospital
Simon Brown	Royal Hobart Hospital
Ms Helen Bryan	Launceston General Hospital
Ms Sue Burtt	ARCBS
Ms Michelle Callard	Murwillumbah District Hospital

Dr Philip Campbell	St John of God Health Care Ballarat
Professor Alex Candon	
Ms Jeanette Cann	The Valley Private Hospital
Ms Cleo Cheng	Department of Human Services, Statewide Division
Ms Penny Clayton	Beleura Private Hospital
Dr Andrew Clime	Royal Hobart Hospital
Mr Trevor Cobain	ARCBS
Dr Ralph Cobcroft	Queensland Health
Mr John Cochran	Dorevitch Pathology
Dr Patrick Coghlan	ARCBS
Dr Cathy Cole	Princess Margaret Hospital
Ms Jennifer Condon	ARCBS
Ms Lisa Connell	St Helen's Private Hospital
Ms Kerrie Connley	Colac Community Health Services
Mr E Cooper	Cabrini Hospital
Dr John Copeland	Peninsula Health
Mrs Deirdre Cowan	Holy Spirit Hospital
Ms Fiona Craig	Royal North Shore Hospital
Ms Deb Crane	Peel Health Campus
Mrs Annette Creighton	Ipswich Hospital
Ms Jill Croft	Sydney Adventist Hospital
Ms Josephine Cummins	ACT Pathology—Core Laboratory
Ms Annette Dahler	Royal College of Nursing
Dr PW Danby	Consulting Physician Maroondah Hospital
Ms Nicki Dantalis	Department of Human Services, Statewide Division
Dr Geoff Dart	QEH
Dr Geoff Davey	Pathcare Geelong
Associate Professor Michael Davies	Australian and New Zealand College of Anaesthetists
Dr Ken Davis	Royal Adelaide Hospital
Mrs Fiona De Sousa	St Vincent's Hospital
Dr Peta Dennington	ARCBS
Ms Kathy Doolan	Beleura Private Hospital
Pip Duke	
Mrs Sue Dunbar	Gippsland Pathology Service
Dr John Earle	Gribbles Pathology
Dr Wendy Erber	WA Centre for Pathology and Medical Research
Ms Lin Evans	St Andrew's Hospital Inc
Mrs Kethly Fallon	Western Hospital

Mr Shannon Farmer	Fremantle Kaleeya Hospital
Ms Ann Farrell	St Helen's Private Hospital
Robin Filshie	St Vincent's Hospital
Mr Gavin Finkelstein	Haemophilia Foundation Australia (WA)
Mr George Fisher	Prince of Wales Hospital
Dr Robert Flower	Royal North Shore Hospital
Dr Craig French	Faculty Intensive Care
Dr Elizabeth Fugaccia	Concord Hospital
Ms Marilyn Garnham	Box Hill Hospital
Ms Vivienne Garrick	St John of God Health Care Subiaco
Mr David Gaunt	Cairns Base Hospital
Mrs Denise Gee	St John of God Calvary Hospital
Mr Tony Ghent	
Ms Julie Grassi	St Helen's Private Hospital
Ms Terri-Anne Grebert	Calvary Hospital
Dr Malcolm Green	Royal College of Pathologists of Australasia
Ms Dianne Grey	WA Centre for Pathology and Medical Research
Mrs Margaret Gunn	St Johns of God Pathology
Ms Dana Hall	Calvary Hospital
Dr Paul Handley	Gribbles Pathology
Dr Francis Hanley	Douglass Hanly Moir
Ms Prue Harding	Cairns Base Hospital
Ms Rebecca Hardy	St Andrew's Hospital Inc
Dr Rob Harris	Melbourne Pathology
Ms Bernie Harrison	NSW Department of Health
Ms Sue Hawkley	Free Masons
Ms Ruth Heady	Haemophilia Foundation Australia (WA)
Dr Philippa Hetzel	ARCBS
Kirren Higginbottom	Cairns Base Hospital
Dr Chris Hogan	Royal Melbourne Hospital
Ms Angela Holzberger	Launceston General Hospital
Mr Christopher Horwig	Calvary Hospital
Ms Barbara Howard	Royal Newcastle Hospital
Ms Pam Hudson	Westmead Blood Transfusion Service
Professor John Hunn	
Mr Doug Hutchinson	St Johns of God Pathology, Stawell
Ms Naida C Hutton	Vimy House Private Hospital
Dr Mariko Hylands	Wollongong Hospital
Ms Sue Ireland	Department of Human Services, Statewide Division

Mr Mark Jacobs	Public and Environmental Health
Ms Jackie Janssens	Wakefield Hospital
Mrs Suzi Jarkicic	Western Hospital
Mrs Sally Johnson	Douglass Hanly Moir
Mr Arthur Joyce	Mater Public Hospitals
A/Professor Surrender Juneja	Royal Melbourne Hospital
Dr David Jupe	Royal Hobart Hospital
Dr David Kennett	ARCBS
Dr Michelle Knuckey	ARCBS
Ms Diana Kropp	ACT Pathology – Core Laboratory
Dr Peter Kruger	
Dr Peter Kyle	St George Hospital
Sue Leimann	Modury Hospital
Dr Jill Leyton	Hamilton Base Hospital
Dr Andrew Lu	St Andrew’s Toowoomba Hospital
Dr Martin Mackertich	Prince of Wales Hospital
Ms Joanne Malpas	ACT Department of Health
Ms Wendy Manning	NSW Department of Health
Dr Vlad Martyn	Australasian Association of Blood Conservation, Fremantle Kaleeya Hospital
Dr Paul McCann	Hospitals & Ambulance Service—Department of Health
Dr Anne McDonald	ACT Pathology—Core Laboratory
Mr Russell McGowan	Consumers Health Forum
Ms Stephanie McIntosh	Royal Newcastle Hospital
Dr Steven McKay	Hobart Pathology
Dr Julie McMorro	Royal Perth Hospital
Dr Christopher McNamara	Royal Melbourne Hospital
Mrs Sandra Miedecke	University of Tasmania
Mr Peter Moffat	Sydney Adventist Hospital
Dr Paul Monagle	WCH
Ms Claire Moritz	Repatriation General Hospital
Dr Jon Mortimer	Southern Area Health Services
Ms Lynn Murray	Epsworth Hospital
Dr Kees Nidam	Bundaberg Base Hospital
Ms Roma North	Gribbles Pathology
Mrs Karen Olsen	Adelaide Hospital
Dr Chris Orlikowski	King Edward Hospital
Mrs Vivian Pang	Swan Health Service

Dr Rosalie Parton	Royal Hobart Hospital
Dr Ranish Patel	Calvary Hospital
Ms Lynne Penglase	Murwillumbah District Hospital
Dr Hamley Perry	Hopkins Street Clinic
Mr John Phillips	
Mr Greg Plummer	Mildura Base Hospital
Ms Hazel Popp	Blood Bank—Royal Prince Alfred Hospital
Ms Jennifer Posen	Sydney Adventist Hospital
Ms Catherine Powell	Strathfield Private Hospital
Ms Susan Quayle	Royal College of Nursing
Mrs Phyllis Quigley	Royal Darwin Hospital
Mrs Jovanka Ralevski	Douglass Hanly Moir
Mr Chris Rebeiro	Calvary Hospital
Mrs Janine Rogers	CHIP
Mr Rogers	Cabrini Hospital
Mr Trevor Roper	St John of God Health Care
Ms Maryanne Rose	Launceston General Hospital
Mr Phillip Rose	Westmead Blood Transfusion Service
Ms Jennifer Ross	Haemophilia Foundation Australia
Dr Beverley Rowbotham	Royal College of Pathologists of Australasia
Dr John Rowell	Royal Brisbane Hospital
Mr David Roxby	Flinders Medical Centre
Dr Roy	Royal Melbourne Hospital
Dr Helen Savoia	Women's and Children's Health Melbourne
Dr Ben Saxon	Women's and Children's Hospital
Dr Carl Scott	Nambour General Hospital
Dr Tim Semple	Royal Adelaide Hospital
Ms Gillian Sheldon-Collins	Royal Hobart Hospital
Dr Andrew Silvers	Anaesthetist, Alfred Hospital
Dr Carol Smith	Royal College of Pathologists of Australasia
Mr Gary Smith	Pathology Department RAAF Hospital
Dr John M Sparrow	Department of Health and Human Services
Ms Carmel Sporton	Knox Private Hospital
Mrs Diane Staniforth	St Vincents Hospital
Dr Stedman	Fremantle Hospital & Health Service
Dr Kate Stockhausen	Australian Medical Association
Dr Vera Stoermer	Douglass Hanly Moir
Dr Alison Street	The Alfred Hospital
Dr Noel Tait	Director, CHIP

Dr Kerry Taylor	Mater Public Hospitals
Dr Amanda Thomson	Concord Repatriation General Hospital
Ms Karen Thrift	Royal North Shore Hospital
Dr Michael Tong	Box Hill Hospital
Dr Graham Vaughan	
Dr Pauline Warburton	Royal College of Pathologists of Australasia
Mrs Jenny Watts	St Johns of God Pathology—St Arnaud Lab.
Dr Boyd Webster	Children's Hospital at Westmead
Dr Stephen Weinstein	
Mr Fred Wensing	Haemophilia Foundation
Dr David Westerman	Peter MacCallum Cancer Institute
Mr Ian Whan	Goulburn Valley Health
Mr Wayne Wheeler	Fremantle Hospital
Dr Nicholas Wickham	Townsville General Hospital North Queensland Oncology Service
Ms Denise Wilds	Cairns Base Hospital
Ms Margaret Wilshire	Nurse education—Calvary Hospital
Dr Janet Wong	ARCBS
Ms Colleen Woods	Calvary Hospital
Mrs Judy Worth	Westmead Blood Transfusion Service
Ms Janet Wren	ARCBS
Dr Brenton Wylie	ARCBS
Dr JL Young	University of Tasmania

Following are some of the main issues raised in the workshops.

- Training and education of both junior and senior staff is imperative to successful implementation.
- Computerised systems are needed in the longer term and will assist with monitoring and evaluation.
- To ensure compliance with the Guidelines, particularly those surrounding the collection of data and the establishment of a process of clinical review, indicators should be developed and included in the Australian Council on Healthcare Standards accreditation criteria.
- A national consumer information pamphlet should be developed. The pamphlet should include the risks and benefits of transfusion and frequently asked questions and answers.
- Comprehensive education resources must be developed appropriately to the needs of different stakeholders. The education resources should include:
 - pocket cards with transfusion guidelines;
 - posters for display in hospital and clinician waiting rooms;

- summary of guidelines;
- consumer information; and
- development of education materials for universities.
- Participants raised concerns about the resource implications of implementing the guidelines. Without the appropriate funding, the guidelines could not be successfully implemented.
- Participants agreed that the responsibility of implementing the Guidelines is a shared one and requires the support of health departments, professional colleges, clinicians and laboratory staff.
- Participants had no major concerns surrounding the recommended indications for the use of red blood cells. However, all workshops noted that the 70–100 g/L range is a 'grey' area and the decision of whether or not to transfuse is reliant on clinical judgement. It may be difficult to collect information in this area due to the absence of computerised systems.

Consultation on the use of platelets, fresh frozen plasma and cryoprecipitate

The draft *Clinical Practice Guidelines for the Appropriate Use of Blood and Blood Products* were advertised for consultation in *The Weekend Australian* on 12 May 2001. The consultation draft aimed to stimulate discussion among the wide range of health professionals and consumers with an interest in this area, and to encourage their input into the further development of the guidelines and their implementation. Submissions were received from the following individuals/organisations:

Baxter Healthcare Pty Ltd

Dr Margaret Buring	ARCBS—Queensland
Dr Ken Davis	Institute of Medical and veterinary Science, Adelaide
Dr Peter Flanagan	National Medical Director, New Zealand Blood Service
Dr Debra Graves	The Royal College of Pathologists of Australia
Sue Ireland	Principal Consultant, Statewide Division, Department of Human Services, SA
Dr Peter Kyle	Prince of Wales, St George, Sutherland and Sydney hospitals
Mater Misericordiae Mothers' Hospital,	Brisbane
John Simpson	Executive Director of Surgical Affairs (New Zealand), New Zealand Committee, Royal Australasian College of Surgeons.
Ann Webb	Australian Association of Pathology Practices Inc.

The Working Party met on 2 July 2001 to discuss these submissions and their inclusion in the guidelines.

ABBREVIATIONS AND ACRONYMS

ACHS	Australian Council on Healthcare Standards
ACOG	American College of Obstetricians and Gynecologists
AHMAC	Australian Health Ministers' Advisory Council
APTT	activated partial thromboplastin time
ARCBS	Australian Red Cross Blood Service
ASBT	Australasian Society of Blood Transfusion
BT	bleeding time
DIC	disseminated intravascular coagulation
EC	European Community
EHCB	Effective Health Care Bulletin
EPFA	European Plasma Fractionation Association
FBC	full blood count
FFP	fresh frozen plasma
Hb	haemoglobin
HbS	sickle cell haemoglobin
Hct	haematocrit
HIV	human immunodeficiency virus
HLA	human leucocyte antigen
INR	International Normalised Ratio
LOS	length of stay
MeSH	medical subject heading
NAT	nucleic acid amplification technology
NHMRC	National Health and Medical Research Council
NZBS	New Zealand Blood Service
PRP	platelet-rich plasma
PT	prothrombin time
PTT	partial thromboplastin time
RBC	red blood cell
SHOT	Serious Hazards of Transfusion

ABBREVIATIONS AND ACRONYMS

TCT	thrombin clotting time
TRAP	Trial to Reduce Alloimmunization to Platelets
TTP	thrombotic thrombocytopenic purpura
WHO	World Health Organization

GLOSSARY

Abnormal coagulation

For the purpose of this document, abnormal coagulation is defined as prolongation of the prothrombin time and/or the activated partial thromboplastin time to at least 1.5 times the mean of the reference range.

Activated partial thromboplastin time

The period required for clot formation in recalcified blood plasma after contact activation and the addition of platelet substitutes; used to assess the pathways of coagulation. A prolonged time can indicate a deficiency of a number of factors including Factors XII, XI, IX, VIII, V and II, and fibrinogen.

Apheresis

Any procedure in which blood is withdrawn from a donor, a portion (plasma, leucocytes etc) is separated and retained and the remainder is retransfused into the donor.

Autologous blood

The patient's own blood.

Disseminated intravascular coagulation

Widespread formation of thromboses in the microcirculation, mainly within the capillaries. The intravascular clotting may produce haemorrhage because of consumption of fibrinogen, platelets, prothrombin and clotting factors V, VIII and X.

Graft-versus-host disease

A condition that occurs when immunologically competent cells or their precursors are transfused into an immunologically incompetent recipient who is not histocompatible with the donor.

Haematocrit

Volume percentage of red blood cells in whole blood.

Haemodilution

The process by which the circulating blood dilutes as blood is shed. Red blood cells are not replaced in the short term. The patient's circulating blood volume is maintained by either transcapillary refill from the patient's own tissue fluid reserves or by the therapeutic intravenous infusion of clear fluids.

Haemodynamics

The study of the movements of the blood and the forces concerned therein.

Haemoglobin

A protein in red blood cells that transports molecular oxygen.

Haemolysis

Rupture of red blood cells with release of haemoglobin into the plasma.

Haemolytic uraemic syndrome

A syndrome of renal microangiopathy, microangiopathic haemolytic anaemia and platelet destruction leading to thrombocytopenia.

Haemostasis

The stoppage of bleeding through clot formation or vessel spasm.

Homologous blood transfusion

The transfusion of blood between members of the same species. The term allogeneic blood transfusion has exactly the same meaning and is increasingly the preferred term.

Hypovolaemia

Abnormally decreased blood volume.

Hypoxia

Diminished availability of oxygen to the tissues.

Infusion

The term 'infusion' is increasingly being used in place of 'transfusion'. The original term was accurate in the early days of transfusion medicine when blood was transfused from vein (donor) to vein (patient). With the increasing complexity of the process, there is now a greater gap between the collection of blood from a donor, its fractionation and its ultimate infusion into a patient.

Normovolaemia

Normal blood volume.

Pharmacological agents

Pharmacological agents to minimise blood loss include aprotinin, tranexamic acid and desmopressin. Erythropoietin, which stimulates the production of red blood cells, may also minimise the need for transfusion.

Prothrombin time

A test to measure the activity of factors I, II, V, VII and X, which participate in the extrinsic pathway of coagulation. Deficiency of any of these factors leads to a prolongation of the one-stage prothrombin time.

Randomised controlled trial

Experiment in which patients are randomly allocated to receive or not receive an experimental preventive, therapeutic or diagnostic procedure, then followed to determine the effect of the intervention.

Sickle cell disease

Any of the diseases associated with the presence of haemoglobin S.

Storage lesion

Lesions, such as those resulting from biochemical / physiological effects, that can develop in blood during storage.

Thrombocytopenia

A decrease in the number of platelets circulating in the blood.

Thrombotic thrombocytopenic purpura

A disease marked by thrombocytopenia, haemolytic anaemia, neurological manifestations, presence of nitrogen-containing compounds in the blood, fever and thromboses in terminal arterioles and capillaries.

Transfusion protocol

A set of guidelines to define the conditions under which a patient will be transfused and with what product.

Transfusion threshold

The laboratory result (eg haemoglobin level or platelet count) at which transfusion is instigated.

von Willebrand's disease

A congenital haemorrhagic disorder characterised by a prolonged bleeding time, deficiency of coagulation factor VIII and often impairment of platelet adhesion. The condition is associated with increased bleeding after trauma or surgery, nosebleeds, menorrhagia and postpartum bleeding.

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