



Scottish Intercollegiate Guidelines Network

54

Perioperative Blood Transfusion for Elective Surgery

A national clinical guideline

1	Introduction	1
2	Risks of allogeneic blood transfusion	3
3	Haemoglobin transfusion thresholds	7
4	Aids to effective blood ordering	10
5	Blood sparing strategies	13
6	Cardiac surgery	18
7	Orthopaedic surgery	21
8	Implementation and audit	24
9	Development of the guideline	26
	References	28
	Abbreviations	32

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KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1 ⁺⁺	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1 ⁺	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2 ⁺⁺	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

A	At least one meta-analysis, systematic review, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; <i>or</i> A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; <i>or</i> Extrapolated evidence from studies rated as 2 ⁺

GOOD PRACTICE POINTS

<input checked="" type="checkbox"/>	Recommended best practice based on the clinical experience of the guideline development group
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1 Introduction

1.1 THE NEED FOR A GUIDELINE

The importance of blood transfusion in the development of modern surgery and in the continued safe performance of major operations cannot be overstated. Without blood and blood donors, thousands of surgical procedures could not be performed safely. However, good clinical studies and outcome data establishing the benefits and risks of transfusion for a patient in a given surgical setting are not available. Nor are there good data on the optimal haemoglobin (Hb) concentration for recovery and rehabilitation following specific surgical interventions.

It is now seven years since variant Creutzfeldt-Jakob disease (vCJD) was first described in the UK,¹ with a total of 101 cases recorded to the end of June 2001.² How far this rare but lethal disease has spread in society is not known, making its impact on medical practice generally, and blood transfusion in particular, difficult to predict. Precautionary measures such as the exclusion of UK donor plasma from fractionation, and the universal leucodepletion of all blood for transfusion have been introduced to minimise the spread of vCJD by transfusion, but this risk cannot be discounted and remains a serious cause of concern for all who prescribe blood in the UK.

1.2 OBJECTIVE OF THE GUIDELINE

This guideline aims to provide a rational and practical framework on which to base transfusion decisions and practice. It aims to maximise patient safety by:

- helping clinicians to decide when allogeneic red cell transfusion is appropriate
- minimising the avoidable risks of transfusion
- helping clinicians to provide appropriate advice on options for treatment, in particular where patients are anxious about the risks of transfusion.

The guideline also provides more detailed information for cardiac and orthopaedic surgery teams, as the major users of red cells.

The provision of clear verbal and written information about the risks and benefits of allogeneic blood transfusion is emphasised as good clinical practice. Whenever possible, alternatives to transfusion should be discussed with the patient in advance of need, to allow arrangements for their delivery to be put in place.

This guideline and its recommendations do not address the emergency management of acute blood loss, but could affect the decision to transfuse once the patient has been stabilised. Neither does the guideline address perioperative blood transfusion in paediatric surgery.

1.3 USE OF DONOR BLOOD IN ELECTIVE SURGERY

In the UK, transfusion of donor (allogeneic) red blood cells (RBCs) remains the mainstay of the management of the patient who has, or is considered to be at risk of, major surgical bleeding. Over 313,000 units of concentrated red cells (CRCs) were issued in Scotland in 1999.³ The majority of patients transfused are aged over 65 years.

Although there are no national figures for the number used for all elective surgery, Table 1 shows the actual number of units of red cells transfused in the South Glasgow University Hospital NHS Trust during the year 2000. Over 50% of red cells transfused were prescribed in the surgical specialties, though the increasing use of standard and high dose chemotherapy has produced a steady rise in medical, oncological and haematological transfusion. The most widely used blood bank computer systems do not discriminate between blood used in an emergency and that used as part of an elective surgical programme. A 1996 Canadian survey indicated that cardiac operations were responsible for 15% of all red cell transfusions and that cardiac and orthopaedic patients together used 31% of total red cell transfusions.⁴

Table 1: Total concentrated red cells (CRC) transfused January-December 2000
South Glasgow University Hospital NHS Trust (reproduced with permission)

Specialty	Cross-matched units	Transfused units	C:T ratio*	Specialty usage (% total units transfused)
General and vascular surgery	4,035	2,468	1.6 :1	18%
Orthopaedics	4,110	1,983	2.1 :1	14%
Neurosurgery	3,340	1,123	2.9 :1	8%
Urology	616	343	1.8 :1	2.5%
Other surgical	-	1,454	-	10.5%
Obstetrics	515	159	3.2 :1	1%
Gynaecology	407	297	1.4 :1	2%
Haematology	3,287	3,040	1.1 :1	22%
General medicine and geriatrics	3,832	3,021	1.3 :1	22%

*crossmatched to transfused ratio (see section 4)

1.4 VARIATION IN TRANSFUSION PRACTICE

Many reports show variation in transfusion practice for comparable groups of surgical patients between hospitals.^{5,6,7} Blood use audits in Scotland show that large variations also exist among individual practitioners or operating teams within a hospital.⁶ Variations in rates of transfusion may be due to many factors, including differing opinions on the threshold level of haemoglobin below which a patient needs to be transfused, differences in surgical and anaesthetic techniques, and differences in casemix. The first may reflect uncertainty about the relative benefits and risks of transfusion and the second different perceptions of the value of minimising blood loss and subsequent transfusion.

A retrospective cohort study of hip fracture patients with significant comorbidities used a statistical model to take account of the clinical variables in this patient population.⁸ Existing variations in transfusion practice between university, teaching and community hospitals changed as more variables were introduced into the model. In the final analysis, despite making allowance for these variables, considerable practice variation remained. Therefore, extreme care is required in interpreting variation in transfusion practice.

In the absence of controlled trials on the risk and benefits of transfusion there is no "ideal transfusion rate" for a given operation such as hip replacement. Analysis cannot determine which hospitals have the best transfusion practices, only whether transfusion rates are high or low.

1.5 REVIEW AND UPDATING

This guideline was issued in October 2001 and will be considered for review in 2004, or sooner if new evidence becomes available. Any updates to the guideline will be available on the SIGN website: www.sign.ac.uk.

2 Risks of allogeneic blood transfusion

The risk of transfusion in terms of morbidity and mortality is not known, mainly as the direct impact of a transfusion can be impossible to separate out in complex clinical circumstances. If a potentially life saving operation can only be undertaken with transfusion support, the benefits of transfusion are likely to far outweigh the risks. In contrast, a postoperative transfusion given to raise haemoglobin level in a stable patient may provide little or no clinical benefit. Here, the transfusion risk, although small, may not be balanced against any predictable benefit.

Confidential reports of more serious complications and transfusion-related deaths are collated as part of the Serious Hazards of Transfusion (SHOT) scheme which covers a substantial proportion of all UK red cell transfusions, amounting to three million units per annum (see Table 2).⁹⁻¹³

Table 2: Transfusion transmitted infections reported to SHOT

	1995	1996	1997	1998	1999	Total
Hepatitis A	-	1	-	-	-	1
Hepatitis B	1	1	-	2	1	5
Hepatitis C	-	1	-	1	1	3
HIV	-	3	-	-	-	3
Bacteria	1	1	3	1	5	11
Malaria	-	-	1	-	-	-

2.1 TRANSFUSION TRANSMITTED INFECTIONS

2.1.1 VIRAL

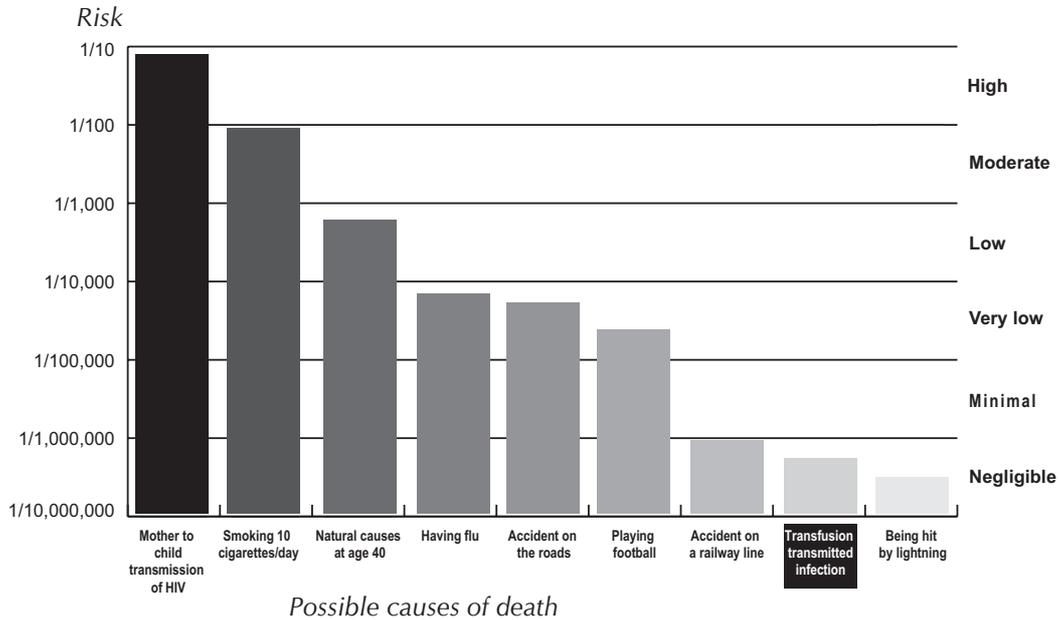
Since 1996, only 12 incidents of viral infection have been recorded.⁹⁻¹² Given this very low incidence, direct assessment of transfusion transmitted infection (TTI) by virus is difficult and this has led to the development of mathematical models. The total TTI risk has been estimated at between 1:100,000 and 1:1,000,000 in the American population.¹⁴ The European Protein Fractionation Association, analysing retrospective data from the US, Australia and Europe, found that in repeat donors seroconversions are detected as follows: 1:2,323,778 for anti-HIV screening, 1:620,754 for anti-hepatitis C (HCV), and 1:398,499 for hepatitis B (HBV).¹⁵

A study prospectively following up 20,000 units transfused in the UK in 5,579 patients over a nine month period detected no transfusion-associated episodes of human T-lymphocytic virus (HTLV), HIV, HCV or HBV. The risks of viral TTI should be regarded as being very low or minimal compared to other life risks¹⁶ (see Figure 1).

2.1.2 BACTERIAL

SHOT has recorded 10 significant episodes of bacterial TTI over the last four years, the majority associated with platelet therapy. In 1998/9 two fatalities occurred, one due to *Yersinia Enterocolitica*, the other to *Escherichia Coli*, indicating a high mortality from a rare complication. In New Zealand between 1992 and 1997 *Y. Enterocolitica* infection led to eight transfusion transmitted infections resulting in four deaths.¹⁷ This incidence of 1:65,000 transfusions is higher than the 1:500,000 infection rate reported in the US.¹⁸ In both countries there was a similar rapidity of onset of symptoms and a high mortality, at 12 out of 20 reported cases. The UK incidence of bacterial transmitted infection remains similar to the American experience at approximately 1:400,000 transfusions.¹²

Figure 1: Transfusion risks in context ¹⁹



2.2 DIRECT IMMUNE INJURY

There were five major transfusion reactions (acute and delayed) in 1999, three of which were fatal.¹² Other syndromes, such as post-transfusion purpura, transfusion-related acute lung injury and transfusion-associated graft versus host disease, were collectively responsible for eight deaths amongst 20 serious transfusion incidents. These complications could not have been predicted, although early recognition and appropriate therapy might help to reduce the associated morbidity. 3

2.3 IMMUNOMODULATION

In the laboratory setting, allogeneic blood has been shown to have the capacity to depress immune function,²⁰⁻²³ an effect mediated mainly by transfused white blood cells.^{20,21,24,25} 3

This, together with concern over the potential for increased risk of cancer recurrence²⁶⁻²⁸ when transfusing allogeneic blood in the perioperative period, has historically led to some surgeons adopting a conservative transfusion policy. 2+

Randomised controlled trials using both leucodepleted and autologous blood have not demonstrated an increase in either the risk of cancer recurrence or of infection.²⁹⁻³¹ Attempts to demonstrate this effect in a clinical context have been confounded by the difficulty of establishing an appropriate control group. In addition, any risk of postoperative infection is likely to be minimised by the leucodepletion process.

A meta-analysis³² of three randomised³³⁻³⁵ and two cohort studies^{36,37} where control groups received either leucodepleted or autologous blood transfusion found no significant difference in cancer recurrence. Due to the small number of patients taking part in trials, the meta-analysis was insufficiently powerful to detect a difference of less than 20% in risk. The inability of these studies to exclude a small effect is of less significance now that leucodepletion of blood for transfusion is universal in the UK. 1+

B Transfusion of leucodepleted allogeneic blood should not be limited by concerns over increased cancer recurrence or perioperative infection.

2.4 PROCEDURAL ERROR

The blood transfusion process can be complex and crosses many disciplines and professions. One study identified over 40 steps between the patient and their transfusion, all of which involve potential human error.³⁸ When an error leads to the incorrect administration of crossmatched blood, the consequences can be disastrous. It has been suggested that in the US, human error occurs in approximately 1:24,000 transfusions.³⁹ SHOT estimates that in the UK, human error affects around 1:25,000 transfusions. This reduces to 1:67,000 if only serious complications are considered.¹²

3

Given the paucity of data and the lack of evidence about safe systems of blood handling, administration should follow best practice as set out in the British Committee for Standards in Haematology (BCSH) guideline, with educational initiatives undertaken to establish the use of safe protocols by staff.^{40,41}

4

D The BCSH collaborative guideline for the administration of blood and blood components and management of transfused patients should be implemented in all Scottish hospitals where transfusion takes place.

A final check of the patient's wrist identity band against the identity given on the blood component to be transfused is essential for safe practice.

2.5 ALL RISKS

Overall, the total risk from blood transfusion in Scotland is low, at approximately one incident per 12,000 transfusions (derived from SHOT reports).⁹ Serious complications, such as intravascular haemolysis, transfusion-induced coagulopathy, renal impairment and failure, admission to intensive care, persistent viral infection, and death, occur at a rate of 1 in 67,000 transfusions. Since the SHOT scheme started in 1996, 47 deaths have been reported that were associated with transfusions. Over the same period more than 12 million blood components were issued in the UK.⁹⁻¹²

3

The actual contribution of transfusion morbidity and mortality for an individual patient is difficult to evaluate, mainly as the direct impact of a transfusion can be impossible to assess. Confounding factors include:

- **Patient factors:** age, preoperative haemoglobin, general health (e.g. based on the American Society of Anesthesiologists preoperative risk score, which assess comorbidity at the time of surgery).⁴²
- **Surgical factors:** type and complexity of surgery, duration of anaesthesia, presence of drains, expertise of surgeon.
- **Type of illness:** local or systemic, benign or malignant.

In the past, infections caused by HBV, HCV, and HIV were the main causes of concern in the UK. In each case, once the causal agent was identified, procedures were introduced to protect patients from infection. Unfortunately, by the time preventive testing had been introduced many individuals had been infected.

Nowadays the risk of contracting HBV, HCV or HIV from blood transfusion is minimal (see section 2.1.1) and probably falling. Other viruses such GB virus C, human herpes virus⁸, and TT virus still need to have their transmissibility assessed and their prevalence in the donor population established, although none has yet been relevant to transfusion practice.⁴³

3

No transmission of variant Creutzfeldt-Jakob disease (vCJD) by transfusion has as yet been documented. The four UK Departments of Health have instituted major precautionary measures, including the exclusion of UK donor plasma from fractionation, and the introduction of universal leucodepletion of all blood prepared for transfusion. Such well-publicised actions, designed to protect the public, may well have increased awareness and concern about transfusion risks. Allogeneic blood transfusion can never be risk-free, reflecting as it does the current state of health of society. Just as new illnesses and infections will influence the overall health picture, their impact on blood safety cannot be predicted.

D Given the potential risks, however small, each allogeneic transfusion must have a valid, defined and justifiable indication.

- The indication for each transfusion should be documented in the patient's records.
- In a haemodynamically stable patient, one unit of concentrated red cells should be transfused at a time, allowing the benefit of each to be assessed at 24 hourly intervals.

2.6 RISKS OF NOT BEING TRANSFUSED

The safer blood transfusion becomes, the more the risk of not transfusing blood must be considered, i.e. the risk of perioperative anaemia. The rate of fatal complications due to anaemia in 16 reports of the surgical management in Jehovah's Witnesses ranges between 0.5% and 1.5%.⁴⁴

A more recent retrospective survey of a similar patient population indicates that, if confounding factors are taken into consideration, mortality does not increase as the haemoglobin (Hb) falls to 80 g/l.^{45,50} It is not possible to comment on mortality changes at Hb levels below 80 g/l, as 90% of such patients receive transfusions. Evidence from observational studies suggests that the elderly and those patients suffering from cardiovascular and peripheral vascular disease are less tolerant of perioperative anaemia and should therefore be transfused at a higher haemoglobin level (i.e. a lower threshold for transfusion).⁴⁵

2+

The decision to transfuse any patient for a given indication must balance the risks of not transfusing, influenced for example by disease prognosis, against the risks of transfusion, influenced for example by the probable duration of patient survival and the incubation time of known infective agents.

2.7 PREOPERATIVE ANTICOAGULANT THERAPY

The treatment of patients with atrial fibrillation with oral anticoagulant therapy is becoming increasingly common. In addition, outpatient management of patients with thromboembolic disease using low molecular weight heparin is also widely practised. Both of these medications reduce the risk of thrombosis by prolonging clotting times. Their principal complication is to increase the risk of haemorrhage. Patients on either of these treatments who present for surgery for which anticoagulant dose attenuation is required should have their doses modified in good time, i.e. days prior to surgery, to reduce the risk of increased blood loss.^{46,47}

4

- D** All surgical and anaesthetic units should have protocols:
- to prepare anticoagulated patients for all types of surgery
 - for deep vein thrombosis prophylaxis in the preoperative period.

*Advice is also given in the SIGN guideline on prophylaxis of venous thromboembolism, which contains a section on the management of anticoagulation in the perioperative period.*⁴⁸

3 Haemoglobin transfusion thresholds

The transfusion threshold is the haemoglobin value at which transfusion will normally be indicated, under stable conditions and in the absence of other clinical signs or symptoms of anaemia. Transfusion should be limited to the smallest amount of blood required to lift the patient above the transfusion threshold. Each hospital laboratory has its own definition of anaemia, based on the normal range for the local population.

- A transfusion threshold should be defined as part of an overall strategy to provide optimal patient management.
- The transfusion threshold should be viewed as the haemoglobin value below which the patient should not fall during the perioperative period, particularly in the context of ongoing or anticipated blood loss.

3.1 PREOPERATIVE

Preoperative anaemia increases the likelihood of allogeneic transfusion⁴⁹ and should be investigated and, where possible, corrected prior to major elective surgery (in this context major surgery refers to procedures for which blood is routinely grouped preoperatively). However, there is limited evidence available on appropriate preoperative haemoglobin concentrations. When a patient refuses a blood transfusion, preoperative haemoglobin is an important determinant of operative outcome, particularly in patients with ischaemic heart disease.⁴⁹⁻⁵¹

2+

- All patients undergoing major elective surgery should have a full blood count performed prior to surgery to avoid short term cancellation and to allow those patients presenting with anaemia to be investigated and treated appropriately (e.g. iron therapy).

C Where possible, anaemia should be corrected prior to major surgery to reduce exposure to allogeneic transfusion.

3.2 INTRAOPERATIVE

When there is ongoing surgical blood loss, haemoglobin measurements should be interpreted in the context of a multifaceted clinical assessment, which should include clinical evaluation of blood volume status. There is no indication that thresholds should differ during this period, but the use of intraoperative transfusion must reflect the ongoing rate of surgical blood loss, continued haemodynamic instability, and anticipated postoperative bleeding.⁵²

3

Accurate measurement of intraoperative blood loss is difficult, although during cardiopulmonary bypass (CPB) frequent haematocrit evaluations are available. Two large prospective observational studies of patients undergoing CPB for primary coronary artery bypass graft (CABG) showed that postoperative mortality and severe ventricular dysfunction were related to low haematocrit during bypass. Though both studies showed increased risk when the haematocrit fell below 0.17, there was no agreement about the safe critical haematocrit value that indicated the need for transfusion.^{53,54}

2+

Rapid intraoperative measurement of haemoglobin levels using near patient testing may improve safety margins and avoid unnecessary transfusion.^{55,56} Prospective assessment of the impact of these new techniques during the intraoperative and immediate postoperative periods is urgently required.

3.3 POSTOPERATIVE

Three systematic reviews,^{52,57,58} five randomised controlled trials,⁵⁹⁻⁶³ seven cohort studies^{45,49-51,64-66} and seven consensus statements⁶⁷⁻⁷³ were judged to be of an appropriate standard for inclusion in the evidence base for the guideline. All trials and studies were performed using non leucodepleted red cells and differences in haemoglobin and/or transfusion thresholds were described in relation to the intraoperative and postoperative periods only. However, no trial or study has examined transfusion thresholds in patients with chronic disease undergoing elective surgery so it has not been possible to make evidence-based recommendations for this group of patients.

Over the last 12 years, guidelines and consensus statements have consistently expressed the transfusion threshold as a range, usually between 70 and 100 g/l haemoglobin, with clinical indicators further defining the need for allogeneic transfusion in between.^{67,69,73} 4

Spieß et al⁶⁴ found a statistically significant increase in postoperative myocardial infarction (MI) in CABG patients whose haematocrit was greater than 0.33 on the first postoperative day. However, this was not confirmed by a retrospective assessment of a similar postoperative CABG population in Canada, despite the fact that both studies had a similar overall mortality and postoperative MI rate.⁷⁴ No evidence was found to suggest that cardiovascular function is improved at haemoglobin values > 100 g/l. 2+

D Transfusion is unjustified at haemoglobin levels > 100 g/l.

Only limited experimental data and expert opinion were identified on which to base a recommendation on the lower limit of haemoglobin below which transfusion should take place. Experimental data from healthy animals indicates that electrocardiogram (ECG) changes of myocardial ischaemia appear at haemoglobin levels below 50 g/l.⁷⁵ Dogs with experimental stenoses of their coronary artery circulation developed ECG and functional changes at Hb 70 g/l.⁷⁶ During normovolaemic haemodilution in healthy fit resting adults it has been shown that adequate delivery of oxygen was sustained down to a haemoglobin of 50 g/l.⁷⁷

A review of consensus statements⁵⁸ supported a lower limit of 70 g/l and also suggested that patients with cardiovascular problems should have this limit raised to 80 g/l. A large retrospective study of surgical patients confirmed that, allowing for confounding factors, there was no difference in mortality using a lower threshold of either 80 or 100 g/l.⁴⁵ No conclusions could be drawn regarding a lower threshold, as 90% of patients were transfused at Hb < 80 g/l. 4

D Transfusion is required at haemoglobin levels < 70g/l.

More evidence exists on which to base an upper limit for the transfusion range. The largest randomised controlled trial (RCT) of transfusion thresholds was performed in over 800 patients admitted to intensive care.⁶³ Patients were randomised to a conservative (70-90 g/l) or liberal (100-120 g/l) threshold and no difference in 30 or 60-day mortality was found. In addition, there was no significance difference in severe ventricular dysfunction, with the overall mortality in this population exceeding 20%. 1+

Subgroup analysis indicated that patients under 55 years of age, or with less severe disease, had statistically better survival using the conservative policy, but clearly this requires care in interpretation. A large number of patients (598) were not entered in the study because of physician refusal. In addition, caution should be applied before extrapolating observations in patients in a critical care context to patients having routine surgery, as the patients' characteristics, patterns of morbidity and mortality and levels of physiological monitoring are all different.

In another study,⁶² 428 low risk CABG patients were randomised to a restrictive (< 80 g/l) or liberal (> 90 g/l) transfusion policy. No difference in mortality, postoperative MI, or significant ventricular complications was seen, nor was there any significant effect on patient rehabilitation. Although a statistically significant lower volume of red blood cells were transfused in the restrictive group, the percentage of patients receiving allogeneic blood was the same in both groups. 1+

A small RCT in elderly patients with fractured neck of femur found no difference in either mortality or the achievement of mobilisation targets in patients transfused when symptomatic or with Hb < 80 g/l compared with patients whose haemoglobin was maintained above 100 g/l.⁶¹ Another small randomised trial in patients undergoing elective vascular reconstruction found no difference in mortality or morbidity when comparing a transfusion threshold of 90 g/l to 100 g/l.⁵⁹ This is a group of patients in whom the incidence of cardiovascular disease would be expected to be very high. However, both trials had inadequate analytical power to show significant differences in mortality/myocardial events.

1⁻

A small observational study of similar patients found an increase in myocardial ischaemia and myocardial events in patients with a postoperative haemoglobin < 90 g/l. An increased incidence of myocardial ischaemia was also detected in an observational cohort study of elderly patients undergoing radical prostatectomy when their haemoglobin fell below 90 g/l.

2⁺

A further retrospective subgroup analysis of the original Transfusion Requirements in Critical Care (TRICC) study population⁶³ identified 357 patients who had a primary or secondary diagnosis of cardiovascular disease, or where cardiovascular disease represented a significant comorbid condition.⁷⁸ Despite having a significantly different mean haemoglobin compared to control patients (85 v 103 g/l), there was no difference in 30 or 60 day mortality, nor in ventricular dysfunction. As with the original study,⁶³ the authors felt that particular care should be exercised when patients had significant peripheral vascular disease, recent MI, or unstable angina.

1⁺

C Patients with cardiovascular disease, or those expected to have covert cardiovascular disease (e.g. elderly patients or those with peripheral vascular disease) are likely to benefit from transfusion when their haemoglobin level falls below 90 g/l.

4 Aids to effective blood ordering

4.1 PREDICTORS OF ALLOGENEIC TRANSFUSION

A series of nine risk factors which predict the need for allogeneic transfusion has been defined in a series of studies covering a heterogeneous population (with regard to case-mix and comorbidity) of over 10,000 patients, including a wide variety of surgical procedures.^{5,79-82} All the studies made attempts to reduce confounding factors and were remarkably consistent in the risk factors found to show high levels of statistical significance.

The factors determining risk of allogeneic transfusion are:^{5,79-82}

- low preoperative haemoglobin/haematocrit, either before intervention or on day of surgery
- low weight
- small height
- female sex
- age over 65 years
- availability of preoperative autologous blood donation (PABD)
- estimated surgical blood loss
- type of surgery
- primary or revision surgery.

2+

C When ordering blood, all nine factors determining the risk and degree of transfusion should be taken into account, for example by using Mercuriali's formula (see below).

4.2 BLOOD ORDERING EQUATIONS

4.2.1 MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE

The intention behind blood ordering schedules is to relate the ordering of blood to the likelihood that a transfusion will be required. At a simple level this is done through a maximum ordering schedule related to the type of operation, but this has been extended to try and take account of an individual patient's risk factors (see section 4.2.2).

Maximum surgical blood ordering schedules (MSBOS) have been introduced in Scotland by most hospital transfusion departments. Each surgical operation is allocated a tariff of transfusion, which is influenced by national and hospital practice but locally agreed by clinicians and blood providers. The ratio of the number of units of crossmatched red cells for a given operation to the number of units actually transfused – the C:T ratio – should not exceed 2:1.^{83,84}

Using MSBOS, patients for whom the likelihood of blood transfusion is less than 30% do not have blood crossmatched but instead have their blood group established and their serum checked for antibodies. This "group and save" provision allows rapid blood delivery in an emergency. The extent to which surgery can be covered by this provision largely depends on practical, local issues, such as the distance between operating theatre and transfusion department.

3

Although MSBOS has improved the efficiency of blood ordering,⁸³ it does not account for individual differences in transfusion requirements between different patients undergoing the same surgical procedure. MSBOS cannot identify over-transfusion, nor does it impact on institutional variation in transfusion practice.

C All hospitals should use a maximum surgical blood ordering schedule to provide concentrated red cells.

4.2.2 OTHER BLOOD ORDERING EQUATIONS

Using basic physiological principles, simple equations can be derived which involve some of the risk factors for transfusion directly and can be altered by others:^{85,86}

$$\text{Blood loss} = \text{Circulating red cell volume reduction (preop to postop)} + \text{Red cells transfused}$$

Larocque⁸⁷ used the risk factors listed in section 4.1 to allocate points for preoperative haemoglobin, weight in kg, type of surgery (knee versus hip) and primary or revision. A score exceeding five meant a high risk of allogeneic transfusion. When prospectively applied, this scoring system appeared to work in practice, with a high point score being associated with greater than 22% allogeneic transfusion rates.⁸⁸ When a similar formula was used in 250 consecutive radical prostatectomies, a very close relationship was found between the equation-derived blood estimate and the calculated blood loss in theatre. No relationship was found between operating room staff blood loss estimates and actual blood loss.⁸⁵ 3

Mercuriali⁸⁹ produced an algorithm based on an accurate calculation of patients' preoperative red cell volume, taking height and weight into account:

$$\text{Preoperative red cell volume} - \text{Postoperative red cell volume} = \text{Operative blood loss} - \text{Extra transfusion support/demand}$$

Using the same data and a threshold haematocrit, the **lowest** red cell volume acceptable to the surgical team for that operation can be established. The level of postoperative haemoglobin/haematocrit should be set following clinical assessment, local transfusion protocols and national guidelines. Using this algorithm over a 10 year period, Mercuriali demonstrated that allogeneic blood exposure in primary total hip surgery was restricted to less than 20% of patients, with a wastage rate of only 10% of autologous units. 2+

Table 3 indicates how patient-specific, independent risk factors for transfusion can fit into and influence Mercuriali's equation. The patient's age, height, weight, sex, pre- and postoperative haemoglobin assessments form the basic data set, along with the type of surgery. The level of postoperative haemoglobin/haematocrit should be set following clinical assessment of the patient.

Table 3: Patient factors influencing Mercuriali's blood ordering equation

Preoperative red cell volume	Postoperative red cell volume	Operative blood loss	Extra transfusion support/demand
<ul style="list-style-type: none"> ■ Preoperative Hb ■ Weight/height ■ Sex 	<ul style="list-style-type: none"> ■ Postop/target Hb ■ Weight/height ■ Sex ■ Age/medical history 	<ul style="list-style-type: none"> ■ Primary/revision ■ Knee/hip ■ Local factors 	<ul style="list-style-type: none"> ■ Allogeneic salvage ■ PABD ■ ANH

Nuttall⁹⁰ also developed a surgical blood ordering equation which accounted for Hb levels, allowing blood provision to be tailored more closely to the individual patient. This schedule resulted in a lower cross match to transfusion ratio than MSBOS, indicating a higher efficiency in blood ordering. 4

This approach, as well as individualising each patient's transfusion requirements, would allow:

- each surgical team to develop its own local transfusion system
- each surgical team to set its own minimum transfusion levels for fit and unfit patients
- each surgical/anaesthetic team to audit operative blood loss for different operations
- prospective audit of outcomes and more realistic comparison between institutions or teams
- flexible and rapid local responses to changes in information, safety, or national supply of blood.

These physiological relationships can be expressed in a simpler formula which assumes that one unit of blood lost or donated will decrease or increase patients' haemoglobin by 1 g/dl:

$$\text{No. red cell units required for a specific operation} = \text{Predicted Hb fall (g/dl)} - [\text{preoperative Hb (g/dl)} - \text{postoperative threshold Hb (g/dl)}]$$

Table 4: Examples of the starting haemoglobin level required to avoid transfusion in different sized people undergoing total hip arthroplasty

weight/height	Transfusion threshold (Hb g/l)		
	80	90	100
60kg/160cm	153	163	173
70kg/180cm	136	146	156
107.5kg/190cm	123	130	140

Table 5: Examples of blood loss in specific operations

Operation	Predictable Hb loss		
	No. RBCs (g/dl)		RC volumes (ml)
	Nuttall 2000 ⁹⁰	Mercuriali 1996 ⁸⁶	Mercuriali 1996 ⁸⁶
Primary hip	4.7 ± 1.7	4.8	907
Primary knee	3.8 ± 1.2	4.0	764
Revision hip	4.8 ± 2.4	8.0	1,531
Bilateral hip	-	-	2,020
Vertebral arthrodesis	-	11.0	890
Bilateral knee	5.4 ± 2.4	4.0	-
CABG	4.7	4.0	890

4.3 TRANSFUSION PROTOCOLS

Systematic reviews of allogeneic red cell transfusion^{40,91} have found only two RCTs that address methods of reducing variation in transfusion practice, using a transfusion treatment algorithm or an education outreach programme.^{92,93} Though both found statistically significant and sustained reductions in red blood cell prescribing, the total number of interventions was small (63 and 103).

A systematic review of observational studies⁴⁰ assessing the ability of education and protocol initiatives to improve practice has shown reductions in “transfusion triggers”. However, the approaches used and the quality of the individual studies were heterogeneous.

The generally poor quality of the literature in this area emphasises the need for careful evaluation of all types of transfusion intervention, ideally in a randomised controlled trial. It is worth emphasising that in two meta-analyses addressing autologous transfusion⁹⁵ and acute normovolaemic dilution,¹¹⁸ the presence of a transfusion protocol had an impact on allogeneic transfusion rates which was similar to the intervention being studied.

D Transfusion guidelines should be combined with audit and/or educational initiatives to reduce the number of allogeneic transfusions.

5 Blood sparing strategies

5.1 WHO WILL BENEFIT?

Blood sparing strategies should be considered for all patients who may require a transfusion, (Mercuriali's formula may be used to identify these patients) and who have consented to transfusion. There are also specific circumstances where blood sparing strategies should be given a high priority, for example for patients who:

- are Jehovah's Witnesses
- have multiple antibodies
- have serious anxieties about the transfusion of allogeneic blood.

However, a minimum provision should be made for every patient undergoing major blood losing surgery.

- All patients undergoing major blood losing surgery, and who have consented to transfusion, must have as a minimum provision a blood specimen grouped and screened by their hospital bank.

Blood sparing strategies currently available include:

- preoperative autologous blood donation (PABD) (see section 5.2)
- erythropoietin (see section 5.3)
- acute normovolaemic haemodilution (ANH) (see section 5.5)
- anti-fibrinolytic drugs (see sections 6.2, 7.2 and 7.3)
- cell salvage (see sections 6.4 and 7.5).

5.2 PREOPERATIVE AUTOLOGOUS BLOOD DONATION

In the elective surgical setting, preoperative autologous blood donation (PABD) is a convenient, predictable, safe and widely practised form of transfusion support. Though its introduction and use in Scotland has been very limited, it is regarded in many countries as the standard of care for major blood-losing operations, with the aim of minimising allogeneic blood exposure. Most studies cover cardiac, orthopaedic and cancer surgery in American and European populations. The type and extent of surgery in these studies is broadly similar to that practised in Scotland. PABD is not widely practised in Scotland, although the Scottish National Blood Transfusion Service (SNBTS) has established collection systems in the major population centres.

5.2.1 PRACTICAL ASPECTS OF PABD COLLECTION

PABD cannot be made available to all patients, since it requires time to pre-donate and a starting haemoglobin greater than 110 g/l,⁹⁴ which effectively excludes most emergency surgery. As part of a transfusion strategy, its use carries the same risk of collection, storage, identification and administration errors as allogeneic blood, but it does avoid the immunological and viral hazards of allogeneic transfusion. For a preoperative autologous blood donation programme to work, hospital admission and operative dates must be guaranteed, as donated blood has a limited storage life of 35 days.

From the patient's perspective, collection can often present logistical difficulties and it is more difficult with increasing age, immobility and co-existing medical and surgical conditions. Age is not in itself a contraindication to PABD, which has been practised safely in elderly patients undergoing cardiac surgery.⁹⁵

- D** Preoperative autologous blood donation should be offered only when it is possible to guarantee admission and operative dates.

5.2.2 PABD APPLICATIONS

The degree to which PABD reduces a patient’s exposure to allogeneic blood was studied in a meta-analysis of six RCTs and nine well-conducted cohort studies.⁹⁵ Patients who predonated autologous blood were less likely to receive allogeneic blood in both the RCTs (933 patients, OR 0.17, 95% CI 0.08-0.32) and the cohort studies (2,351 patients, OR 0.19, 95% CI 0.14-0.26). However, the meta-analysis also showed that autologous donors were statistically more likely to undergo transfusion with allogeneic and/or autologous blood (OR 3.03, 95%CI 1.7-5.39).

1+

B PABD can be used to reduce allogeneic blood exposure, although it does increase the total number of transfusion episodes.

Any patient undergoing surgical procedures currently served by a Group & Screen policy is unsuitable for preoperative donation.

Patient enrolment to autologous blood programmes is reported as ranging from 54-65%⁷⁹⁻⁸² and has been reported as high as 100%,⁹⁶ possibly indicating that some studies are biased towards a fitter patient population. These cohort studies covered^{14,153} orthopaedic surgery patients with major comorbidities and with a mean age of 66 years, ranging from 19-92 years.

2+

C PABD can be used safely in elderly populations with diverse comorbidities.

A balance must be struck between collecting sufficient PABD units to minimise allogeneic exposure and over-collection, leading to a high discard rate. Observational studies indicate that PABD is unnecessary in primary joint surgery when the presenting haemoglobin is greater than 145 g/l.^{79,80} Limiting PABD collection to two units for total hip arthroplasty (THA) and one unit for total knee arthroplasty (TKA) was sufficient to avoid most allogeneic exposure without a high PABD discard rate.^{79,80}

2+

Patients undergoing primary hip and knee surgery with a presenting haemoglobin greater than 145 g/l should be discouraged from autologous donation.

When presenting haemoglobin is between 110-145 g/l in men and between 130-145 g/l in women, PABD has been shown to reduce the expected number of patients exposed to allogeneic blood to under 20% of the total number of patients. Women with a lower presenting haemoglobin (110-130 g/l) are likely to require additional transfusion support, for example, erythropoietin, to achieve a similar allogeneic transfusion rate.^{81,90}

2+

C PABD should be targeted to:

- men who present with haemoglobin 110-145 g/l
- women who present with haemoglobin 130-145 g/l.

5.3 ERYTHROPOIETIN

Human erythropoietin is a glycoprotein hormone that regulates erythropoiesis. Hypoxic or haemorrhagic stress results in the secretion of erythropoietin by the kidney. Erythropoietin is available as recombinant human erythropoietin (epoietin α and β) and has been widely used in the treatment of anaemia of chronic renal failure.

5.3.1 APPLICATIONS OF ERYTHROPOIETIN

The effect of erythropoietin in minimising allogeneic blood exposure compared to placebo has been studied in patients undergoing orthopaedic^{97,98} cardiac⁹⁷ or colon cancer surgery.^{99,100} The total number of patients randomised exceeds 1,100 and, with the exception of one study,⁹⁹ all showed a significant reduction in allogeneic transfusion (OR 0.36, 95% CI 0.24-0.56, $p < 0.0001$ in orthopaedic patients; OR 0.25, 95%, CI 0.06-1.04, $p < 0.06$ in cardiac patients). The postoperative transfusion rate fell from 40-60% in controls to 10-20% in erythropoietin-treated patients.

1+

The only published RCT showing no benefit from erythropoietin was a study of 102 cancer patients where more than half the patients only received erythropoietin for five preoperative days. This may have been insufficient time to allow a satisfactory response.⁹⁹

1-

There are six well conducted RCTs^{98,101-103,106,108} all using transfusion protocols specifying that every effort should be made not to transfuse patients with Hb levels greater than 90 g/l, except where clinical symptoms warranted this. Despite this, allogeneic transfusion rates in the control groups ranged from 30% to 70%. In addition there was a consistent and statistically significant rise in preoperative Hb of between 10 g/l and 20 g/l in those randomised to erythropoietin.

1+

De Andrade¹⁰⁸ stratified 316 orthopaedic patients into those with presenting baseline haemoglobin above and below 130 g/l. The allogeneic transfusion rate fell in the erythropoietin treated group from 45% to 16% in those with Hb < 130 g/l ($p=0.024$) and fell from 13% to 9% in those with levels > 130 g/l, a non-significant change.

Subgroup analysis has confirmed this finding in other studies.^{103,104} Erythropoietin also has a significant role when preparing patients with objections to allogeneic transfusion (for example Jehovah's Witnesses) for surgery that involves major blood loss.¹⁰⁵

2+

B Erythropoietin use should be targeted to patients aged under 70 years who are scheduled for major blood losing surgery and who have a presenting haemoglobin <130 g/l.

D Erythropoietin can be used to prepare patients with objections to allogeneic transfusion for surgery that involves major blood loss.

5.3.2 DOSE OF ERYTHROPOIETIN

The optimal dose of erythropoietin is not known. The two dosing schedules most widely used are:

- 300 u/kg subcutaneously for 14 days beginning 10 days preoperatively (approximately £2600/course/80 kg)
- or
- 600 u/kg subcutaneously three times weekly and on day of surgery (approximately £1,600/course/80 kg)

Both regimens are of proven benefit and seem equivalent in safety and efficacy.¹⁰⁶ Erythropoietin treatment has always been accompanied by oral or intravenous iron therapy but an optimal iron support schedule has not been defined.

5.3.3 COMPLICATIONS OF ERYTHROPOIETIN

Faught et al¹⁰⁷ found little evidence on the frequency and severity of side effects of short term erythropoietin use. However the number of patients treated with erythropoietin remains relatively small, especially in cardiac surgery. As yet no trial or meta-analysis is of sufficient power to detect important adverse effects at low incidence. In the de Andrade study¹⁰⁸ the risk of deep vein thrombosis (DVT) was increased in erythropoietin treated patients with baseline Hb above 130 g/l but was similar to controls when baseline Hb was 100-130 g/l. One study in cardiac patients found seven deaths (four thrombotic) in 126 erythropoietin treated patients, versus no deaths in 56 control patients.¹⁰⁹ This difference was not statistically significant and is comparable to mortality rates reported in the literature for cardiac bypass (CABG) surgery. Given the small numbers of cardiac patients studied in randomised trials of erythropoietin alone (224), it would seem wise to avoid its use without PABD in cardiac patients, especially when Hb exceeds 130 g/l. Concerns about thrombotic risk and hypertension have meant that trials of erythropoietin have very strict entry criteria, restricting recruitment to a small number of fit patients with a mean age of 65 years and few co-existent diseases. Even given these limitations, studies suggest that there is no increase in thrombotic complications or uncontrolled hypertension.¹⁰⁷

2+

- If erythropoietin brings about a >0.50 rise in the patient's haematocrit, a 500 ml venesection should be undertaken.
- Patients receiving erythropoietin should have weekly haematocrit checks.
- In order to monitor side effects, there should be a national register of all patients receiving erythropoietin perioperatively in Scotland.

5.4 COMBINATION OF PABD AND ERYTHROPOIETIN

The effect of erythropoietin plus PABD on the incidence of allogeneic transfusion has been studied in orthopaedic and cardiac surgery patients. A meta-analysis of 11 orthopaedic RCTs, enrolling 825 patients, found a statistically significant decrease in the proportion of patients transfused with allogeneic blood (OR 0.42, 95% CI 0.28-0.62, $p < 0.0001$).¹¹⁰ The mean volume of allogeneic blood saved was not large, at 0.14 units. In the five cardiac RCTs included in this meta-analysis, a statistically significant decrease in the proportion of patients transfused with allogeneic blood was also found (OR 0.25, 95% CI 0.08-0.82, $p = 0.02$), but the total number of cardiac patients studied was small, at 224.¹¹⁰

1+

B In fit patients undergoing major surgery, erythropoietin can be used in combination with autologous blood collection to reduce allogeneic transfusion.

In three small RCTs^{89,111,112} standard PABD was randomised against erythropoietin supported PABD. In a three-week preoperative period, 80% of patients treated with erythropoietin were able to donate significantly more units than the standard PABD group. The patients receiving erythropoietin also had a significantly higher day of surgery haemoglobin ($p < 0.0002$), a finding confirmed in other studies.^{113,114}

1+

Erythropoietin and PABD may be practical in young patients undergoing surgery with currently very large allogeneic requirements (e.g. spinal surgery or revision total hip surgery) and when used along with cell salvage, although there is little specific information on these indications.

B In fit patients undergoing major surgery, erythropoietin can be used to obtain multiple autologous red cell donations while maintaining an adequate day of surgery haemoglobin.

5.4.1 SIDE EFFECTS OF COMBINATION PABD AND ERYTHROPOIETIN

Mild side effects of erythropoietin and PABD, such as vasovagal episodes, were commonly reported, relating to the blood donation component.^{89,111-114} As the patients in these studies were young (mean ages 50-69 years) with minimal comorbidity, a similar multiple donation protocol could not be recommended for the more standard hip replacement/general surgical populations.

5.5 ACUTE NORMOVOLAEMIC HAEMODILUTION

Acute normovolaemic haemodilution (ANH) is the removal of whole blood and the restoration of blood volume with acellular fluid, shortly before anticipated significant surgical blood loss. In the context of elective surgery this may be performed prior to surgery or during the early part of the surgical procedure, if this period is associated with minimal anticipated blood loss. For example, during knee surgery blood may be withdrawn intraoperatively with reinfusion postoperatively. The maximum volume of blood that can be withdrawn during haemodilution depends on the preoperative haemoglobin, the lowest acceptable intraoperative haemoglobin and the estimated blood volume.^{85,115,116}

3

ANH is potentially most useful for a patient meeting all of the following criteria:

- a substantial anticipated blood loss
- a relatively low target haemoglobin (intraoperatively and postoperatively)
- a relatively high initial haemoglobin

Mathematical models have been developed that allow users to identify when a given combination of the above factors would save a unit of packed cells.¹¹⁵ Such models indicate that ANH is valuable for only a minority of patients, i.e. healthy adults in whom a low target haemoglobin is acceptable, with an anticipated surgical blood loss exceeding 50% of estimated blood volume and with a high initial haemoglobin.¹¹⁷ For example, modelling predicts a maximum saving of one unit, where a transfusion target of 90 g/l was used and where blood loss was estimated at two litres.

4

Any assessment of the benefit of ANH will depend on the surgical population being studied and on the haemoglobin concentration used as the ANH donation and transfusion threshold.

D ANH should be limited to patients with a haemoglobin level sufficiently high to allow 1,000 ml of blood to be removed, and in whom a relatively low target haemoglobin is deemed appropriate.

A meta-analysis of ANH trials¹¹⁸ found overall support for such mathematical predictions. The number of patients exposed to allogeneic transfusion was reduced when more than 1,000 ml of blood were withdrawn, though there was no reduction in the average volume of allogeneic blood transfused. Trials in which blood loss was in excess of 1,000 ml were associated with a significant reduction in the average number of allogeneic units transfused, though not in the number of patients exposed to allogeneic blood. No significant reduction was found where average blood loss was less than 1,000 ml. However, no benefit was identified when trials without a transfusion protocol were excluded.

1 -

In a more recent randomised study¹¹⁹ of ANH inpatients undergoing unilateral knee replacement, where measured perioperative blood loss was less than 1,000 ml, ANH was associated with a decreased total transfusion of allogeneic blood, but there was no reduction in the number of patients exposed to allogeneic blood. In all groups, allogeneic transfusion was administered without a transfusion protocol.

1 +

Much of the research into ANH has been done at a single American centre where trained anaesthetic technicians and nurses undertake the procedure.¹²⁰ A recent randomised study by this group compared ANH with preoperative autologous donation and found no difference in either calculated red cell saving (approximately one unit) or exposure to allogeneic transfusion.¹²¹ Surgical blood loss was approximately 1400 ml, with an allogeneic haematocrit transfusion threshold of 0.25. The authors suggest that ANH should be preferred to preoperative autologous blood donation (PABD) on the basis of lower cost and a lesser potential for transfusion errors. If ANH is to be used without a negative impact on theatre time, organisational issues must be dealt with.

2 ++

In summary, the evidence for the benefit of ANH is equivocal. The procedure can make a modest contribution to the avoidance of allogeneic exposure in prescribed circumstances, and where staff have received training in undertaking the procedure.

- ANH should only be implemented where the logistics of blood removal and replacement can be undertaken without detracting from patient care.
- Hospitals considering ANH must address organisational issues, including the provision of appropriate support to the anaesthetist.
- Autologous blood should be labelled and stored according to the British Committee for Standards in Haematology blood transfusion guideline,¹²² with particular care being taken where autologous blood transfusion is initiated postoperatively.

6 Cardiac surgery

6.1 OVERVIEW

Cardiac surgery has been identified as one of the major users of donor blood and blood products.⁴ In view of the increasing number of cardiac operations being undertaken, any procedure with the potential to safely reduce blood loss or transfusion requirements will have a significant impact on the available blood pool, in addition to reducing any risk from allogeneic transfusion. A variety of drugs may influence perioperative transfusion requirements in cardiac surgery. The principal therapies that should be considered include aprotinin and other antifibrinolytic drugs, which could have the potential to decrease blood loss, and aspirin and anticoagulant drugs, which could increase blood loss. Variation in the requirement for allogeneic transfusion during and following cardiopulmonary bypass (CPB)^{123,124} involves factors such as the transfusion threshold and the application of cell salvage strategies. Surgical factors such as the time to confirm complete surgical haemostasis are also important, as is the institution in which the surgery takes place.^{4,123}

Unit protocols setting a transfusion threshold should be encouraged.

6.2 APROTININ AND ANTIFIBRINOLYTIC DRUGS

Aprotinin is a serine proteinase inhibitor which preserves platelet function following CPB by a mechanism which may be independent of its potent antifibrinolytic activity. Its use was first described in 1987 in 84 patients undergoing repeat open heart surgery, when it was shown to significantly reduce blood transfusion in these high risk cases.¹²⁵

The dose of aprotinin used is the high dose schedule, unless otherwise stated, i.e.:

- 2 million Kallikrein Inactivator units pre-sternotomy
- 2 million Kallikrein Inactivator units in pump prime volume
- 500,000 Kallikrein Inactivator units/hour discontinued on return to ITU if no further significant bleeding.

A meta-analysis has evaluated the potent antifibrinolytic drugs, aprotinin, tranexamic acid and epsilon-aminocaproic acid (ϵ -ACA).¹¹⁰ End points included the need to transfuse one or more units of red cells, the mean transfusion requirement and the need to re-operate for bleeding. The majority of patients (5,808) were treated with aprotinin, which was found to significantly reduce allogeneic blood exposure (OR 0.44, 95% CI 0.27-0.73, $p=0.001$). This was independent of whether it was used for primary or repeat operation, or whether the patient was receiving preoperative aspirin therapy. Aprotinin use was also associated with a significantly reduced re-sternotomy rate for postoperative bleeding (OR 0.31, 95% CI 0.25-0.39, $p=0.0001$). Tranexamic acid decreased the proportion of patients transfused (OR 0.5, 95% CI 0.34-0.76, $p=0.0009$).¹¹⁰

Although overall patient numbers were low, the meta-analysis also found no difference in efficacy when aprotinin was compared with tranexamic acid; both drugs significantly reducing blood loss and transfusion requirements.¹¹⁰ An RCT focusing on patients at high risk of bleeding¹²⁶ (e.g. repeat cardiac operations, multiple valve replacements, thoracic aortic operations, procedures with long bypass times) found no major differences between the effects of aprotinin and tranexamic acid, although only aprotinin offered protection against blood loss associated with increased bypass duration.

The antifibrinolytic agent, ϵ -ACA did not demonstrate any significant reduction in the proportion of patients transfused following cardiac surgery (OR 0.2, 95% CI 0.04-1.12).¹¹⁰

6.2.1 MYOCARDIAL INFARCTION AND GRAFT PATENCY

It has been suggested that the use of aprotinin may lead to a heightened thrombotic state. In one frequently quoted placebo-controlled study,¹²⁷ Q-wave myocardial infarctions were found in 17.5% of patients receiving high dose aprotinin and in 8.9% of patients in the control arm, although this difference was not significant. Patients in the aprotinin arm of this study may have been inadequately anticoagulated.

In a meta analysis, the use of aprotinin was associated with a non-significant increase in perioperative myocardial infarction (8% versus 5.6%, OR 1.12, 95% CI 0.82-1.53).¹¹⁰ A second meta analysis¹²⁸ has shown that although there is an almost identical overall myocardial infarction rate, when the effect of high dose aprotinin is compared with that of low dose aprotinin, the MI rate is significantly higher (OR 2.15, 95% CI 1.12-4.11).

1++

A non-systematic review of six RCTs found wide variation in graft occlusion rates (between 0.7% and 12.7%). This probably reflects the differing methodologies and timing interventions used in all the six studies.¹⁰⁷

The International Multicentre Aprotinin Graft Patency Experience (IMAGE) trial¹²⁹ which investigated 870 patients undergoing first time myocardial revascularisation, found that patients treated with aprotinin had a significantly higher graft occlusion rate: 15.4% in comparison with 10.9% for patients in the control arm ($p=0.03$). Over the range of cardiac operations covered in this trial, the mean amount of blood saved per patient treated with aprotinin varied between 0.98 and 1.43 units. The value of such a saving in primary revascularisation would be more than offset by even a small real increase in graft occlusion, given that in the above trial overall mortality was not significantly different with or without aprotinin.

2+

At present there is insufficient high quality evidence to recommend the use of aprotinin in primary CABG.

In low risk primary CABG the routine use of aprotinin is not recommended.

B **The use of aprotinin or tranexamic acid is recommended for patients undergoing cardiac surgery which carries a high risk of transfusion** (e.g. repeat cardiac operations, multiple valve replacements, thoracic aortic operations, patients on preoperative aspirin therapy and procedures with anticipated long bypass times).

6.2.2 OTHER COMPLICATIONS

Aprotinin is associated with a transient deterioration in renal function, indicated by an elevation of serum creatinine above baseline, which returns to normal post-surgery. The overall incidence of renal failure in cardiac surgery is not affected. Up to 6% of patients exposed to aprotinin for the second time develop significant allergic reactions. This incidence falls as the interval between aprotinin exposures increases.¹³⁰

6.3 ASPIRIN

The most commonly prescribed antiplatelet drug is aspirin and its importance in longterm graft patency following CABG is well recognised.

Aspirin increases blood loss in patients undergoing first time or repeat myocardial revascularisation.^{131,132}

1+

Aspirin is an irreversible inhibitor of cyclo-oxygenase, which platelets (unlike vascular endothelium) are unable to regenerate. Aspirin therapy should therefore, in theory, be discontinued for seven days (the life span of a platelet) prior to surgery. Concern has been expressed about the potential deleterious effects of withdrawing aspirin treatment prior to surgery, on the grounds that patients who have their aspirin therapy withheld may be more vulnerable to ischaemia in the aspirin-free period, and that this may be more hazardous than the consequences of bleeding in the immediate postoperative period.

Although aspirin increases postoperative bleeding,^{131,132} this is not always accompanied by an increased requirement for allogeneic transfusion.^{133,134} Re-operation for control of continuing non-surgical haemorrhage is more common in those patients who receive preoperative aspirin.¹³⁵ However, a case control study of 8,641 patients found significantly higher mortality in the group of patients whose aspirin had been stopped.¹³⁶

If aspirin is not discontinued prior to surgery, consideration may be given to the use of pharmacological agents to reduce blood loss, aprotinin has been demonstrated to reduce bleeding in those patients on preoperative aspirin therapy.^{137,138}

Desmopressin (DDAVP) is not of benefit to all patients but may have a role in patients on preoperative aspirin therapy.¹²⁸ A reduction in the use of blood and blood products has been shown in patients on aspirin who are given desmopressin perioperatively. It should be noted that there was a high use of blood and blood components in the control group of one of the studies reviewed and there was a significantly increased risk of MI in the treated group (OR 2.39, CI 1.02-5.60).¹²⁸

6.4 CELL SALVAGE

Cell salvage has been used to minimise the requirement for allogeneic transfusion in cardiac surgery. Intraoperative cell salvage during the period of heparinisation simply involves the re-transfusion of any "spilt" blood from the operative field. A sucker returns blood to the bypass reservoir and following filtration to remove particulate debris, it is re-transfused. At the end of the bypass run, the contents of the cardiotomy reservoir may be returned to the patient and additional protamine administered to cover this heparinised autologous blood transfusion.

Prior to heparinisation, salvage may be undertaken using a conventional cell salvage device and this may also be utilised following reversal of heparin with protamine. Blood from chest drains may be re-transfused following filtration in the immediate postoperative period.

In a meta-analysis of 2,061 patients, where one primary end-point was the proportion of patients receiving at least one unit of allogeneic packed red cells, collection and re-infusion of unwashed shed mediastinal blood after bypass decreased allogeneic exposure (RR 0.85, 95% CI 0.79-0.92). Cell salvage alone also reduced exposure to allogeneic blood (RR 0.84, 95% CI 0.77-0.93).⁸⁸ This meta-analysis did not include trials of shed **washed** mediastinal blood and may therefore underestimate the value of re-infusion of shed mediastinal blood, since washing salvaged blood may prevent an induced coagulopathy.¹³⁹

1+

A retrospective analysis of autologous blood salvage in cardiac surgery, involving over 3,000 patients, noted that more blood products were given to patients who received salvaged autologous blood, although this may have been a marker for more complex cases.¹⁴⁰

In a small randomised trial of 38 patients, allogeneic transfusion requirements were compared in patients whose collected red cells were either washed or discarded. There was a significant reduction in transfusion of allogeneic RBCs and platelets in the washed group.¹⁴¹

2+

C Reinfusion of washed shed mediastinal blood may be used to reduce allogeneic transfusion in cardiac surgery.

An economic evaluation of using shed washed mediastinal salvage would be helpful, as in many studies, insufficient blood is salvaged to make processing worthwhile.

7 Orthopaedic surgery

7.1 OVERVIEW

The orthopaedic procedures most frequently requiring blood transfusion are primary and revision joint arthroplasties. Factors that may contribute to reducing allogeneic transfusion following routine orthopaedic surgery include:

- use of lower haemoglobin thresholds in transfusion protocols
- increased use of perioperative red cell salvage
- use of hypotensive techniques and regional anaesthesia.

Predonation of red cells has not been widely used in Scotland and the potential impact of developments such as the use of drugs to reduce blood loss, the use of tissue sealants, and the use of blood substitutes have not yet been fully evaluated. However, the gradually increasing number of bilateral and revision procedures will continue to make considerable demands on SNBTS.

7.2 APROTININ

Aprotinin has been shown to reduce blood loss in cardiac and liver surgery.¹⁴² Its use in orthopaedic surgery also raises concerns about side effects, namely:

- inadvertent re-exposure of a patient to aprotinin, with a high risk of an anaphylactic reaction
- a possible increase in thrombosis using a drug with anti-fibrinolytic properties.

7.2.1 DOSE

The dose required for a significant effect on blood loss appears to be high, with the majority of studies using a loading dose of 2 million units followed by 0.5 million units/hour during surgery. A smaller dose of 20,000 units/kg was not shown to be effective in one large study.¹⁴³

2+

7.2.2 APPLICATIONS

In view of the relatively high blood loss that may be associated with elective orthopaedic surgery, aprotinin has been investigated for hip replacements – unilateral,¹⁴⁴⁻¹⁴⁶ bilateral,¹⁴⁷ and revision¹⁴⁷ – as well as in knee replacement,¹⁴⁸ spinal surgery,¹⁴⁹ septic prosthesis removal, and tumour surgery.¹⁵⁰ These studies show a reduction in blood loss of 25-60%, with a more marked reduction seen in patients undergoing procedures associated with higher blood loss. The reduction in blood loss correlates with a reduction in the total number of units of blood transfused, but there is limited evidence of any significant reduction in the number of patients requiring transfusion. Though the quality of these randomised controlled trials is high, the total number of patients taking part is less than 1,000, which along with concerns over an enhanced thrombotic effect in surgical circumstances of high thrombotic risk, suggests its application should be restricted.

1+

B Aprotinin may be considered to reduce blood loss in hip and knee arthroplasties but its use should be restricted to:

- procedures with an increased risk of high blood loss (e.g. bilateral and revision)
- circumstances when other blood conservation techniques are not appropriate (e.g. treatment of Jehovah's Witnesses).

7.3 TRANEXAMIC ACID

Tranexamic acid inhibits fibrinolysis by blocking the lysine binding sites of plasminogen to fibrin.¹⁵¹ It has been used primarily in gynaecology to reduce menstrual blood loss. More recently it has also been shown to be effective in reducing bleeding in cardiac surgery.¹¹⁰ Its potential application in orthopaedic surgery relates mainly to patients undergoing knee replacement surgery, who usually do so under tourniquet control, significantly enhancing local fibrinolytic activity.¹⁵²⁻¹⁵⁴ This may lead to postoperative bleeding once the tourniquet is removed.

7.3.1 DOSE

Tranexamic acid has been used at 10-15 mg/kg prior to release of the tourniquet. As tranexamic acid has a half-life of two hours¹⁵⁵ there are theoretical advantages to administering further doses postoperatively. One study continued tranexamic acid eight hourly for three days, but the majority gave further treatment at either three, three and six hours, or as an infusion for 12 hours postoperatively.¹⁵⁴⁻¹⁵⁶

1+

There is no evidence suggesting any benefit from limiting the use of tranexamic acid to the postoperative period to control bleeding.¹⁶⁰

7.3.2 APPLICATIONS

Six randomised controlled trials¹⁵⁶⁻¹⁶¹ have investigated the effect of tranexamic acid, given prior to tourniquet release, on blood loss and blood transfusion requirement in patients undergoing knee surgery. These show a reduction in blood of between 43% and 54%, as well as a significant reduction in both the total number of units transfused and the number of patients exposed to allogeneic blood.

1+

As with aprotinin, the major concern with tranexamic acid is the potential risk of thrombosis.^{158,162} Only one small study was identified that had routinely screened patients for DVT and only by Doppler.¹⁵⁷ No increase in DVT was demonstrated. None of the other studies¹⁵⁶⁻¹⁶¹ reported an increase in clinically detected DVT, although one did show a trend to an increase in both clinically suspected and venographically proven DVT in the treated patients.¹⁵⁹ The introduction of tranexamic acid into routine practice must await larger and more comprehensive studies of its safety in orthopaedic patients.

B Tranexamic acid can be used to reduce blood loss and transfusion requirements in patients undergoing knee replacement surgery, when other blood conservation techniques are inappropriate and where major blood loss is anticipated.

7.4 DESMOPRESSIN

No evidence was identified to support the use of desmopressin (DDAVP) in routine orthopaedic surgery to reduce bleeding. It has a major role to play in patients with defined coagulopathies such as von Willebrand's disease and haemophilia, but these patients should be treated under the direction of an experienced haematologist in a recognised haemophilia centre.

7.5 CELL SALVAGE

Postoperative retransfusion of blood from wound drains uses unwashed blood which is filtered to eliminate larger cell aggregates but not bacteria.¹⁶³⁻¹⁶⁵ There have been some reports of coagulation disorders following reinfusion of large volumes.^{166,167} Duncan¹⁶⁸ recommended that no more than 1,500 ml of salvaged blood should be reinfused. Due to the risks of infective colonisation, salvaged blood should not normally be reinfused later than six hours following collection.

4

Some authors have questioned the use of this technique in unilateral arthroplasty due to the relatively small amounts of blood obtained.^{169,170}

D Unwashed postoperative salvage using drains should be considered in patients in whom a postoperative blood loss of between 750 ml and 1,500 ml is anticipated (e.g. bilateral joint replacement).

Another technique is the intraoperative collection of cells which are washed prior to retransfusion.¹⁷¹ In comparison with postoperative salvage, large volumes can be transfused without significant risk to the patient.¹⁷²

1+

High volume blood loss is relatively rare in orthopaedics, but intraoperative salvage could be useful in major pelvic surgery and revision surgery, particularly of the hip, provided infection has been excluded. There is considerable capital cost for the basic equipment needed to undertake washed cell salvage, although the costs of disposables are similar to those involved with retransfusion of unwashed red cells.

B **Washed intraoperative salvage should be considered in patients in whom an intraoperative blood loss of more than 1,500 ml is anticipated** (e.g. major pelvic, spinal or non-infected revision surgery).

The recent introduction of small battery powered red cell recovery and washing systems allows the same disposable equipment to be utilised during and after a procedure. This should allow relatively economical intra- and postoperative salvage.

A meta analysis⁸⁸ of the effectiveness of cell salvage in minimising perioperative allogeneic transfusion concluded that, in orthopaedic surgery, devices producing either washed or unwashed cells decreased the frequency of exposure to allogeneic blood to a similar degree when compared with a control.

1+

B **In orthopaedic surgery, cell salvage using either unwashed or washed red blood cells may be considered as a means of significantly reducing the risk of exposure to allogeneic blood.**

8 Implementation and audit

8.1 LOCAL IMPLEMENTATION

Implementation of national clinical guidelines is the responsibility of each NHS Trust and is an essential part of clinical governance. It is acknowledged that every Trust cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

Implementation of the guideline and compliance with the Scottish Office MEL Executive (1999)9 *Better Blood Transfusion*¹⁷³ depends not only on the commitment of clinicians but also the support of Trust and hospital managements to provide organisational resource to enable:

- preadmission assessments 3-6 weeks before operation
- patients to be given fixed admission dates if pre-donation or preoperative erythropoietin therapy has been agreed
- availability of erythropoietin for the limited number of patients in whom it is clearly indicated
- availability of blood salvage equipment where caseload is shown to justify its use
- availability of suitable anaesthetic support if ANH is being used
- adequate audit of transfusion practice locally through the hospital Blood Transfusion Committee
- adequate audit of transfusion practice nationally
- training of all staff involved in the transfusion process.

8.2 KEY POINTS FOR AUDIT

8.2.1 NATIONAL AUDIT

- National, consistent method for collecting information on blood use.
- A national audit of blood requirements in cardiac and orthopaedic surgery.
- Blood requirements for revision hip in Scotland.
- The variation in the use of blood between hospitals and between operating teams.
- Establish a national transfusion register recording:
 - use of Erythropoietin
 - adverse effects of autologous transfusion.

8.2.2 LOCAL AUDIT

- Amount of blood used per surgeon per operation:
 - grade of surgeon
 - type of operation.
- Cross-matched to transfusion ratio.
- Preoperative Hb.
- Postoperative/target Hb.
- Prospective audit of discharge haemoglobin in patients undergoing major blood losing surgery.
- Performance and timing of preoperative Hb check.
- Wristband check compliance.
- Staff training in safe transfusion practice.

8.3 RECOMMENDATIONS FOR FURTHER RESEARCH

1. Development of improved computer programmes for routine hospital blood banks, allowing blood use for given surgical operations to be measured.
2. Prospective study of the effect of haemoglobin/anaemia on the rate of recovery and length of hospital stay after operation.
3. Large randomised controlled studies comparing different blood conservation strategies, including economic assessments.
4. A large prospective randomised control trial of the use of aprotinin with mortality, myocardial infarction and transfusion as primary outcomes.
5. A prospective controlled trial evaluating the therapeutic effect of increasing haemoglobin preoperatively in anaemic patients.
6. A randomised controlled trial examining the safety aspects and potential benefits of tranexamic acid used as part of an overall blood conservation package in orthopaedic surgery.
7. Prospective assessment of near-patient haemoglobin techniques in the operative and immediate postoperative period.

8.4 KEY MESSAGES FOR PATIENTS AND THE PUBLIC

These key messages are not intended for direct dissemination to patients, but are provided for possible use by clinicians in discussing treatment options with patients who are at risk of requiring transfusion. They may be incorporated into local patient information materials.

- The risks from blood transfusion have never been lower, the risk of any adverse outcome is very small, at 1 in 12,000, less than the risk of being killed in a road traffic accident or of dying from flu.
- No transmission of variant Creutzfeldt-Jakob disease by transfusion has yet been documented and the risk of contracting HBV, HCV or HIV from blood transfusion is minimal.
- Blood transfusion remains essential for the continued safe performance of major surgery. Over 300,000 units of blood are issued for use in Scotland every year.
- "Bloodless surgery" does not imply safer surgery. The fact that profound anaemia can be tolerated perioperatively does not mean that it is advisable or acceptable.
- In a healthy patient, mild degrees of anaemia are well tolerated and transfusion can be avoided.
- Autologous donation is only appropriate for surgical patients undergoing major blood losing operations, where there is a likelihood that it will be used. If a patient's haemoglobin level is greater than 145 g/l then for most common operations autologous blood should not be collected, as 90% would only be discarded.
- Improvements in the quality of transfused blood, by, for example, the removal of white blood cells, eliminate the theoretical risk that transfusion might lead to cancer recurrence or postoperative infection.

9 Development of the guideline

9.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other health care professionals, and patient organisations, funded by the Clinical Resource and Audit Group (CRAG) of the Scottish Executive Health Department. SIGN guidelines are developed by multidisciplinary groups using a standard methodology, based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in *SIGN 50: A guideline developer's handbook*, available at www.sign.ac.uk.

9.2 THE GUIDELINE DEVELOPMENT GROUP

Dr Pat Tansey (Chairman)	Consultant Haematologist, Victoria Infirmary, Glasgow
Dr Brian McClelland (Methodologist)	Regional Director of Transfusion Medicine, Edinburgh Royal Infirmary
Mrs Pauline Cumming	Practice Development Nurse, Ninewells Hospital, Dundee
Mrs Sandra Gray	Project Manager, Scottish National Blood Transfusion Service, Edinburgh
Dr Rachel Green	Regional Director, Glasgow & West of Scotland Blood Transfusion Service, Carlisle
Mr William Hadden	Consultant Orthopaedic Surgeon, Perth Royal Infirmary
Mr Robin Harbour	Information Manager, SIGN
Dr Cameron Howie	Consultant Anaesthetist, Victoria Infirmary, Glasgow
Mr Robert Jeffrey	Consultant Cardiac Surgeon, Aberdeen Royal Infirmary
Dr Martin Lees	Consultant in Obstetrics and Gynaecology, Edinburgh Royal Infirmary
Dr Allan Merry	General Practitioner, Ardrossan
Mr Robert Murdoch	Consultant General Surgeon, Perth Royal Infirmary
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Dr Safia Qureshi	Senior Programme Manager, SIGN
Dr Steve Rogers	Consultant Haematologist, Victoria Hospital, Kirkcaldy
Dr Colin Sinclair	Consultant Anaesthetist, Edinburgh Royal Infirmary
Mr John Taylor	Patient representative, Innerleithen
Mr George Welch	Consultant Vascular Surgeon, Southern General Hospital, Glasgow

9.3 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Manager in collaboration with members of the guideline development group. Searches were restricted to systematic reviews, meta-analyses, and randomised controlled trials. Material relating to children; blood plasma, leukocyte, or platelet transfusions; emergency surgery; surgical techniques; and national strategies for transfusion services was specifically excluded from the searches. Internet searches were carried out on the Web sites of the Canadian Practice Guidelines Infobase, the New Zealand Guidelines Programme, and US National Guidelines Clearinghouse. Searches were also carried out on the search engines Northern Light and OMNI, and all suitable links followed up. Database searches were carried out on Cochrane Library, Embase, Healthstar, and Medline from 1985 - May 1999. A number of ancillary searches were carried out on specific subtopics during the guideline development process. The Medline version of the main search strategy and notes on the coverage of ancillary searches can be found on the SIGN website, in the section covering supplementary guideline material. The main searches were supplemented by material identified by individual members of the development group. All selected papers were evaluated using standard methodological checklists before conclusions were considered as evidence.

9.4 CONSULTATION AND PEER REVIEW

9.4.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents their draft recommendations for the first time. The national open meeting for this guideline was held at the Royal College of Physicians of Edinburgh on 30th May 2000. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

9.4.2 SPECIALIST REVIEW

The guideline was reviewed in draft form by a panel of independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. SIGN is very grateful to all of these experts for their contribution to this guideline.

Professor James AuBuchon	<i>Professor of Pathology, Dartmouth-Hitchcock Medical Centre, New Hampshire, USA</i>
Dr James Beattie	<i>General Practitioner, Inverurie</i>
Mr Ivan Brenkel	<i>Consultant Orthopaedic Surgeon, Queen Margaret Hospital, Dunfermline</i>
Dr Alex Colquhoun	<i>Consultant Anaesthetist, Glasgow Royal Infirmary</i>
Dr John Colvin	<i>Consultant Anaesthetist, Ninewells Hospital, Dundee</i>
Dr Michael Desmond	<i>Consultant Anaesthetist, Liverpool NHS Trust, Liverpool</i>
Mr Alan Faichney	<i>Consultant Cardiac Surgeon, Western Infirmary, Glasgow</i>
Mr Eric Gardener	<i>Consultant Orthopaedic Surgeon, Victoria Infirmary, Glasgow</i>
Professor Tim Goodnough	<i>Professor of Medicine in Pathology, Washington University School of Medicine, USA</i>
Professor Michael Greaves	<i>Professor of Haematology, University of Aberdeen</i>
Dr Mike Higgins	<i>British Heart Foundation Senior Lecturer in Cardiac Surgery and Honorary Consultant Anaesthetist, Glasgow Royal Infirmary</i>
Mr Richard Holdsworth	<i>Consultant Vascular Surgeon, Stirling Royal Infirmary</i>
Dr Paul Kelsey	<i>Consultant Haematologist, Victoria Hospital, Blackpool</i>
Dr Harry MacFarlane	<i>Consultant Anaesthetist, Aberdeen Royal Infirmary</i>
Mr Ian McLean	<i>Consultant Orthopaedic Surgeon, Dumfries & Galloway Royal Infirmary</i>
Mr John Martin	<i>Senior Assistant Editor, British National Formulary</i>
Mr John Newman	<i>Consultant Orthopaedic Surgeon, Bristol Royal Infirmary</i>
Professor Martin Pippard	<i>Professor of Haematology, Ninewells Hospital & Medical School, Dundee</i>
Dr Lorna Williamson	<i>Consultant in Transfusion Medicine, East Anglia Blood Centre, Cambridge</i>

9.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an Editorial Group comprising the relevant specialty representatives on SIGN Council to ensure that the peer reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The Editorial Group for this guideline was as follows:

Dr Douglas Adamson	<i>Junior Doctor representative</i>
Dr Doreen Campbell	<i>CRAG Secretariat, Scottish Executive Department of Health</i>
Dr Patricia Donald	<i>Primary Care Adviser to SIGN</i>
Mr Douglas Harper	<i>Royal College of Surgeons of Edinburgh</i>
Dr Grahame Howard	<i>Acting Chairman of SIGN</i>
Ms Juliet Miller	<i>Director of SIGN, Editor</i>
Mr Ian Stother	<i>Royal College of Physicians and Surgeons Glasgow</i>

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Abbreviations

ε-ACA	Epsilon-aminocaproic acid
ANH	Acute normovolaemic haemodilution
CABG	Coronary artery bypass surgery
CI	Confidence interval
CPB	Cardiopulmonary bypass
CRC	Concentrated red cells
ECG	Electrocardiogram
Hb	Haemoglobin
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HTLV	Human T-lymphocytic virus
ICU	Intensive care unit
MI	Myocardial infarction
MSBOS	Maximum surgical blood ordering schedule
NHS	National Health Service
OR	Odds ratio
PABD	Preoperative autologous blood donation
RBC	Red blood cells
RCT	Randomised controlled trial
RR	Relative risk
SHOT	Serious Hazards of Transfusion
SIGN	Scottish Intercollegiate Guidelines Network
SNBTS	Scottish National Blood Transfusion Service
THA	Total hip arthroplasty
TKA	Total knee arthroplasty
TTI	Transfusion transmitted infection
UK	United Kingdom
US	United States
vCJD	Variant Creutzfeldt-Jakob disease

BLOOD SPARING STRATEGIES

Blood sparing strategies should be considered for all patients who may require a transfusion and who have consented to transfusion.

- All patients undergoing major blood losing surgery, and who have consented to transfusion, must have as a minimum provision a blood specimen grouped and screened by their hospital bank.

PREOPERATIVE AUTOLOGOUS BLOOD DONATION

B Preoperative autologous blood donation (PABD) can be used to reduce allogeneic blood exposure, although it does increase the total number of transfusion episodes.

D Preoperative autologous blood donation should be offered only when it is possible to guarantee admission and operative dates.

C PABD should be targeted to:

- men who present with haemoglobin 110-145 g/l
- women who present with haemoglobin 130-145 g/l.

C PABD can be used safely in elderly populations with diverse comorbidities.

- Any patient undergoing surgical procedures currently served by a Group and Screen policy is unsuitable for preoperative donation.

- Patients undergoing primary hip and knee surgery with a presenting haemoglobin > 145 g/l should be discouraged from autologous donation.

ERYTHROPOIETIN

B Erythropoietin use should be targeted to patients aged under 70 years who are scheduled for major blood losing surgery and who have a presenting haemoglobin < 130 g/l.

D Erythropoietin can be used to prepare patients with objections to allogeneic transfusion for surgery that involves major blood loss.

- If erythropoietin brings about a >0.50 rise in the patient's haematocrit, a 500 ml venesection should be undertaken.

COMBINING PABD & ERYTHROPOIETIN

B In fit patients undergoing major surgery, erythropoietin can be used:

- in combination with autologous blood collection to reduce allogeneic transfusion
- to obtain multiple autologous red cell donations while maintaining an adequate day of surgery haemoglobin.

ACUTE NORMOVOLAEMIC HAEMODILUTION (ANH)

ANH is potentially most useful for a patient meeting all of the following criteria:

- a substantial anticipated blood loss
- a relatively low target haemoglobin (intraoperatively and postoperatively)
- a relatively high initial haemoglobin.

D ANH should be limited to patients with a haemoglobin level sufficiently high to allow 1,000 ml of blood to be removed, and in whom a relatively low target haemoglobin is deemed appropriate.

- ANH should only be implemented where the logistics of blood removal and replacement can be undertaken without detracting from patient care.
- Hospitals considering ANH must address organisational issues, including the provision of appropriate support to the anaesthetist.
- Autologous blood should be labelled and stored according to the British Committee for Standards in Haematology blood transfusion guideline, with particular care being taken where autologous blood transfusion is initiated postoperatively.



CARDIAC & ORTHOPAEDIC SURGERY

APROTININ & ANTIFIBRINOLYTICS

B

- The use of aprotinin or tranexamic acid is recommended for patients undergoing cardiac surgery which carries a high risk of transfusion (e.g. repeat cardiac operations, multiple valve replacements, thoracic aortic operations, patients on preoperative aspirin therapy and procedures with anticipated long bypass times).
- Aprotinin may be considered to reduce blood loss in hip and knee arthroplasties but its use should be restricted to:
 - procedures with an increased risk of high blood loss (e.g. bilateral and revision)
 - circumstances when other blood conservation techniques are not appropriate (e.g. treatment of Jehovah's Witnesses).
- Tranexamic acid can be used to reduce blood loss and transfusion requirements in patients undergoing knee replacement surgery, when other blood conservation techniques are inappropriate and where major blood loss is anticipated.

CELL SALVAGE

C Reinfusion of washed shed mediastinal blood may be used to reduce allogeneic transfusion in cardiac surgery.

D In orthopaedic surgery, unwashed postoperative salvage using drains should be considered in patients in whom a postoperative blood loss of between 750 ml and 1,500 ml is expected (e.g. bilateral joint replacement).

B In orthopaedic surgery, washed intraoperative salvage should be considered in patients in whom an intraoperative blood loss of more than 1,500 ml is anticipated (e.g. major pelvic, spinal or uninfected revision surgery).
Cell salvage using either unwashed or washed red blood cells may be considered as a means of significantly reducing the risk of exposure to allogeneic blood.

KEY

A B C D Grade of recommendation

Good practice point

DECIDING WHETHER OR NOT TO TRANSFUSE

The decision to transfuse any patient for a given indication must balance the risks of not transfusing, influenced for example by disease prognosis, against the risks of transfusion, influenced for example by the probable duration of patient survival and the incubation time of known infective agents.

D Given the potential risks, however small, each allogeneic transfusion must have a valid, defined and justifiable indication.

- The indication for each transfusion should be documented in the patient's records.
- In a haemodynamically stable patient, one unit of concentrated red cells should be transfused at a time, allowing the benefit of each to be assessed at 24 hourly intervals.

B Transfusion of leucodepleted allogeneic blood should not be limited by concerns over increased cancer recurrence or perioperative infection.

D All surgical and anaesthetic units should have protocols:

- to prepare anticoagulated patients for all types of surgery
- for deep vein thrombosis prophylaxis in the preoperative period.

AVOIDING PROCEDURAL ERROR

D The British Committee for Standards in Haematology collaborative guideline for the administration of blood and blood components and management of transfused patients should be implemented in all Scottish hospitals where transfusion takes place.

- A final check of the patient's wrist identity band against the identity given on the blood component to be transfused is essential for safe practice.

HAEMOGLOBIN TRANSFUSION THRESHOLDS

The transfusion threshold is the haemoglobin value at which transfusion will normally be indicated, under stable conditions, and in the absence of other clinical signs or symptoms of anaemia.

- A transfusion threshold should be defined as part of an overall strategy to provide optimal patient management.
- The transfusion threshold should be viewed as the haemoglobin value below which the patient should not fall during the perioperative period, particularly in the context of ongoing or anticipated blood loss.

PREOPERATIVE THRESHOLDS

- All patients undergoing major elective surgery should have a full blood count performed prior to surgery, to avoid short-term cancellation and to allow those patients presenting with anaemia to be investigated and treated appropriately (e.g. iron therapy).

C Where possible, anaemia should be corrected prior to major surgery, to reduce exposure to allogeneic transfusion.

INTRAOPERATIVE THRESHOLDS

There is no indication that thresholds should differ during this period but the use of intraoperative transfusion must reflect the ongoing rate of surgical blood loss, continued haemodynamic instability, and anticipated postoperative bleeding.

POSTOPERATIVE THRESHOLDS

- D** ■ Transfusion is required at haemoglobin values < 70 g/l.
- C** ■ Patients with cardiovascular disease, or those expected to have a high incidence of covert cardiovascular disease (e.g. elderly patients or those with peripheral vascular disease) are likely to benefit from transfusion when their haemoglobin level falls below 90 g/l.
- D** ■ Transfusion is unjustified at haemoglobin values > 100 g/l.

PREDICTING THE NEED FOR TRANSFUSION

Nine risk factors which predict the need for allogeneic transfusion have been defined:

- low preoperative haemoglobin/haematocrit, either before intervention or on day of surgery
- low weight
- small height
- female sex
- age over 65 years
- availability of preoperative autologous blood donation (PABD)
- estimated surgical blood loss
- type of surgery
- primary or revision surgery.

BLOOD ORDERING EQUATIONS

Blood ordering schedules relate the ordering of blood to the likelihood that a transfusion will be required, taking into account the type of operation and an individual patient's risk factors.

- C** ■ All hospitals should use a maximum surgical blood ordering schedule to provide concentrated red cells.
- When ordering blood, all nine factors determining the risk and degree of transfusion should be taken into account, for example by using Mercuriali's formula.

MERCURIALI'S FORMULA

$$\text{Expected blood loss} = \text{Preoperative red cell volume} - \text{Postoperative red cell volume} + \text{Red cells transfused}$$

- *preoperative red cell volume* is influenced by preoperative haemoglobin, weight, height, sex
- *postoperative red cell volume* is influenced by postoperative target haemoglobin, weight, height, sex, age, medical history
- *red cells transfused* is partly determined by the potential use of blood sparing strategies such as salvage, PABD, ANH