7.1: Transfusion in surgery

7.1.1: Red cell transfusion

Patient blood management should start in primary care at the time of referral for surgery; working closely with the preoperative assessment clinic at the hospital. It has three key strands:

Preoperative optimisation

- Anaemia (and other relevant health problems) should be identified and treated in a timely fashion before surgery.
- Patients at increased risk of bleeding, especially those on anticoagulants or antiplatelet drugs, should be recognised.
- The use of blood conservation techniques in appropriate patients should be planned in advance.

Minimising blood loss at surgery

- Drugs that increase bleeding risk should be withdrawn if safe to do so (discuss with prescribing clinician).
- Blood-sparing surgical and anaesthetic techniques should be used.
- Antifibrinolytic drugs, tissue sealants and intraoperative cell salvage procedures should be used when appropriate.

Avoiding unnecessary transfusion after surgery

- Use restrictive ‘transfusion triggers’, balancing safety and effectiveness in individual patients.
- Minimise blood loss from blood tests.
- Use postoperative red cell salvage and reinfusion where appropriate.
- Prescribe iron and other stimulants to red cell production as needed.

Alternatives to donor blood transfusion and blood conservation techniques are detailed in Chapter 6. For further useful information about transfusion alternatives see http://www.nataonline.com/ and http://www.transfusionguidelines.org.uk/.
7.1.1.1: Preoperative anaemia

Patients who are anaemic preoperatively (Hb <130 g/L in adult males and Hb <120 g/L in adult females) are more likely to be transfused and a number of retrospective studies have shown that preoperative anaemia is an independent risk factor for increased morbidity and mortality. Ideally, a full blood count is checked at least 6 weeks before planned surgery to allow time for investigation and treatment and reduce the risk of late cancellation.

Iron deficiency is the most common anaemia revealed by preoperative screening. In men and post-menopausal women iron deficiency may be an indicator of gastrointestinal bleeding from peptic disease or cancer and should always be investigated. The speed of response to oral iron depends on the Hb deficit and the presence of continued blood loss. At least 3 months of treatment after recovery of Hb is needed to restore body iron stores. Patients intolerant of full dose oral iron may tolerate a lower dose, albeit with slower response. Oral iron is ineffective in the early postoperative period because of the inhibitory effect of inflammation on red cell production. Intravenous iron preparations, which now have a very low incidence of severe allergic reactions, may be used in patients intolerant of oral iron and may also improve the Hb when administered postoperatively (see Chapter 6). Erythropoiesis stimulating agents (ESAs) such as recombinant erythropoietin are not cost-effective in this setting.

7.1.1.2: Red cell transfusion in surgery

Clinical factors, as well as the degree of anaemia, must always be considered when making the decision to transfuse. Peripheral blood Hb concentration gives only limited information about the delivery of oxygen to vital organs. Experience of surgical patients who decline red cell transfusion, such as Jehovah’s Witnesses, show that otherwise healthy individuals can have successful outcomes down to an Hb concentration as low as 50 g/L (haematocrit approximately 15%) with good supportive care. The ‘safe’ Hb concentration is likely to be higher in patients with heart or lung disease who are less able to compensate for anaemia.

A number of studies have shown that red cell transfusion is a significant predictor of mortality after cardiac surgery, although its significance in non-cardiac surgery is less clear. Randomised trials of red cell transfusion in haemodynamically stable surgical patients have shown no benefits for liberal transfusion policies in terms of mortality, length of hospital stay or postoperative mobilisation. There is up to a 40% reduction in exposure to donor transfusions when restrictive transfusion thresholds are employed (evidence for the management of more severely ill patients is discussed in section 7.2). Most experts now agree that:

- Transfusion should be considered if Hb below 80 g/L
- If the Hb is below 70 g/L transfusion is usually indicated
- The decision to transfuse should be based on the clinical condition of the patient (higher thresholds may be appropriate in individual cases).

The same ‘transfusion triggers’ are applicable to patients with asymptomatic cardiovascular disease. Many clinicians recommend using a higher Hb threshold in patients with acute coronary syndromes, but the evidence for this is limited and a recent systematic review actually showed a higher mortality in transfused patients.

The American Association of Blood Banks (AABB) guidelines, published in 2012 (http://www.aabb.org/resources), stress the importance of considering symptoms and expected surgical blood loss as well as the Hb concentration in making the decision to transfuse. The AABB recommendations for red cell transfusion after surgery are as follows:

- Adhere to a restrictive transfusion strategy.
- Consider transfusion if Hb 80 g/L or less.
- Transfuse if symptomatic of anaemia – chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure.
- The same thresholds can be safely applied to patients with stable cardiovascular disease.
Patients who are not actively bleeding should be transfused with a single unit of red cells and then reassessed before further blood is given.

7.1.1.3: Does the age of red cells affect outcome after surgery?

Retrospective observational studies have suggested that transfusing ‘older’ stored red cells may be associated with higher mortality in patients undergoing cardiac surgery and cardiopulmonary bypass. This is controversial because of confounding factors and conflicting results from other studies. Large randomised trials are in progress to answer this important question. Unless or until there is prospective trial evidence of benefit, specific selection of fresh red cells is not recommended.

7.1.2: Bleeding problems in surgical patients

Patients who report abnormal bleeding, especially after dental extractions or surgery, or give a family history of bleeding problems, should be investigated before surgery wherever possible. Patients with known or suspected congenital bleeding disorders should be managed in conjunction with a comprehensive haemophilia care centre (http://www.ukhcdo.org/HaemophiliaCentres/a-c.htm). Most invasive surgical procedures can be carried out safely with a platelet count above $50 \times 10^9/L$ or international normalised ratio (INR) below 2.0.

7.1.2.1: Low platelet count

Guidelines for platelet transfusion thresholds in thrombocytopenic surgical patients and patients undergoing invasive procedures are largely based on expert opinion and clinical experience.

Patients who also have impaired blood coagulation (e.g. liver disease, oral anticoagulants) or are on antiplatelet drugs, such as aspirin or clopidogrel, are at higher risk of perioperative bleeding and specialist advice should be sought if major surgery cannot be delayed. The template bleeding time is not a useful screening test for risk of surgical bleeding.

Consensus guidelines commonly used for thrombocytopenic patients requiring surgery are summarised in Table 7.1. When treatment is indicated, a single adult therapeutic dose (ATD) of platelets should be transfused shortly before the procedure and the post-transfusion count checked (10 minutes after transfusion gives a reliable indication).

Table 7.1 Platelet transfusion thresholds in surgery and invasive procedures
### Indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Transfusion threshold or target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most invasive surgery (including post-cardiopulmonary bypass)</td>
<td>$50 \times 10^9/L$</td>
</tr>
<tr>
<td>Neurosurgery or posterior eye surgery</td>
<td>$100 \times 10^9/L$</td>
</tr>
</tbody>
</table>
| Prevention of bleeding associated with invasive procedures                | Lumbar puncture $50 \times 10^9/L$  
                            | Central-line insertion $50 \times 10^9/L$   
                            | Liver, renal or transbronchial biopsy $50 \times 10^9/L$  
                            | Gastrointestinal endoscopy with biopsy $50 \times 10^9/L$ |
| Spinal anaesthesia                                                       | $50 \times 10^9/L$              |
| Epidural anaesthesia                                                     | $80 \times 10^9/L$              |

Bone marrow aspiration and trephine biopsy can be performed in patients with severe thrombocytopenia without platelet support if adequate local pressure is applied.

#### 7.1.2.2: Patients on anticoagulants or antiplatelet drugs

Many older patients scheduled for surgery are on oral anticoagulants or antiplatelet drugs. A decision to temporarily stop the drug or reduce the dose must balance the risk of surgical bleeding against the indication for anticoagulation and be made in collaboration with the prescribing specialist (see 2012 British Committee for Standards in Haematology (BCSH) Guideline on the Management of Bleeding in Patients on Antithrombotic Agents (https://b-s-h.org.uk/)).

#### 7.1.2.3: Warfarin

The current BCSH Guidelines on Oral Anticoagulation with Warfarin (https://b-s-h.org.uk/) provide detailed discussion of perioperative management. Minor dental procedures, joint aspiration, cataract surgery and gastrointestinal endoscopic procedures (including biopsy) can be safely carried out on warfarin if the INR is within the therapeutic range. More complex perioperative management should be guided by local protocols and specialist haematological advice. Management options are summarised in Table 7.2.

**Table 7.2 Perioperative management of warfarin anticoagulation** (adapted from BCSH Guidelines on Oral Anticoagulation with Warfarin – 4th edition, 2011, with permission)
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<table>
<thead>
<tr>
<th>Scenario</th>
<th>Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate/high risk of surgical haemorrhage, low risk of thrombosis</td>
<td>Stop warfarin 5 days preoperatively.</td>
</tr>
<tr>
<td>(e.g. lone atrial fibrillation)</td>
<td>Check INR on day before surgery:</td>
</tr>
<tr>
<td></td>
<td>• If INR &lt;1.5, proceed</td>
</tr>
<tr>
<td></td>
<td>• INR 1.5 or above, give intravenous vitamin K 1–3 mg</td>
</tr>
<tr>
<td></td>
<td>Restart maintenance dose of warfarin on evening of surgery if haemostasis secured.</td>
</tr>
<tr>
<td>Moderate/high risk of surgical haemorrhage, high risk of thrombosis</td>
<td>Stop warfarin 5 days preoperatively and give ‘bridging therapy’ with low molecular weight heparin (LMWH) according to BCSH guideline.</td>
</tr>
<tr>
<td>(e.g. mechanical heart valve – especially mitral, venous thromboembolism within last 3 months)</td>
<td>Last dose of LMWH 24 hours preoperatively.</td>
</tr>
<tr>
<td></td>
<td>Restart LMWH when haemostasis secure (at least 48 hours in high bleeding risk surgery).</td>
</tr>
<tr>
<td></td>
<td>Restart maintenance dose of warfarin when oral intake possible and continue LMWH until INR in</td>
</tr>
<tr>
<td></td>
<td>therapeutic range.</td>
</tr>
<tr>
<td>Semi-urgent surgery (within 6–12 hours)</td>
<td>Stop warfarin and give intravenous vitamin K 1–3 mg.</td>
</tr>
<tr>
<td></td>
<td>Significant correction of INR within 6–8 hours.</td>
</tr>
<tr>
<td>Emergency surgery or life-threatening bleeding</td>
<td>Stop warfarin.</td>
</tr>
<tr>
<td></td>
<td>Give 25–50 IU/kg of four factor prothrombin complex concentrate (PCC) and 5 mg intravenous vitamin K.</td>
</tr>
<tr>
<td></td>
<td>(Fresh frozen plasma produces suboptimal anticoagulation reversal and should only be used if PCC is not available.)</td>
</tr>
</tbody>
</table>

### 7.1.3: Newer oral anticoagulants

In recent years a number of new oral anticoagulant drugs have been licensed. These include direct oral thrombin inhibitors, such as dabigatran, and direct oral Factor Xa inhibitors, such as rivaroxaban and apixaban. These drugs have no specific antidote. Their half-life is relatively short but can be prolonged in patients with reduced renal function. Wherever possible, treatment should be stopped at least 24 hours before surgery, longer if renal function is impaired (see Summary of Product Characteristics for each drug).

Management of bleeding involves stopping the drug, applying local pressure and administration of antifibrinolytic agents such as tranexamic acid. Fresh frozen plasma (FFP) does not reduce bleeding...
caused by these drugs. Recombinant activated Factor VII (rFVIIa, NovoSeven™), prothrombin complex
concentrate (PCC) and activated PCC (FEIBA™) have been used as a treatment of last resort in
uncontrollable bleeding but may increase the risk of thrombosis.

7.1.4: Heparins

Unfractionated heparins (UFHs) have a short plasma half-life, but this is increased in the presence of renal
dysfunction. They can be administered by intravenous infusion or subcutaneous injection and therapeutic
dosing is usually adjusted by comparison of the activated partial thromboplastin time with that of normal
pooled plasma (APTT ratio). The anticoagulant effect can be rapidly reversed by injected protamine
sulphate (1 mg reverses 80–100 units of UFH, maximum recommended dose 50 mg). Protamine can cause
severe allergic reactions and, in most situations, simply discontinuing the UFH is all that is necessary.

Low molecular weight heparins (LMWHs) have a longer half-life, around 3 to 4 hours, which is significantly
increased in renal dysfunction. The duration of anticoagulant effect depends on the particular LMWH and is
only partially reversible by protamine. LMWHs have a more ‘targeted’ anticoagulant effect (mainly anti-Xa)
than UFH, which may reduce the risk of bleeding, and a lower risk of heparin-induced thrombocytopenia
(HIT) and osteopenia. Administration is by subcutaneous injection once or twice daily. They can be
prescribed in a fixed or weight-related dose without monitoring in many clinical situations and are
convenient for self-administration. Consequently, LMWHs have largely replaced UFH for many routine
indications, including thromboprophylaxis for surgery. Perioperative management of patients on heparins is
summarised in Table 7.3.

Table 7.3 Perioperative management of patients on heparins (general guidance only, see Summary
of Product Characteristics for specific LMWH)

<table>
<thead>
<tr>
<th>Heparins</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfractionated heparins</td>
<td>Stop infusion 6 hours before surgery for full reversal (longer if renal dysfunction)</td>
</tr>
<tr>
<td>Low molecular weight heparins</td>
<td>Prophylactic dose: stop 12 hours before surgery</td>
</tr>
<tr>
<td></td>
<td>Therapeutic dose: stop 24 hours before surgery</td>
</tr>
</tbody>
</table>

7.1.5: Antiplatelet drugs

Aspirin and clopidogrel impair the function of platelets produced during exposure to the drug and the
antiplatelet effect takes around 5 days to wear off (varies between individuals). Platelet function analysis or
platelet mapping, if available, may give clinically useful information about residual antiplatelet activity.
Urgent surgery should not be delayed in patients on these drugs. Many international guidelines recommend
clopidogrel is stopped 3 to 5 days before elective surgery because of the risk of perioperative bleeding but
the balance of risks and benefits depends on the indication for clopidogrel therapy. Aspirin can be stopped
at the time of surgery in cardiac surgery and continued in many surgical procedures except in neurosurgery
or operations on the inner eye.

Non-steroidal anti-inflammatory drugs (NSAIDs) produce reversible platelet dysfunction and have a short
duration of action. Most guidelines suggest they are stopped at least 2 days before surgery associated with
significant bleeding risk. Studies in elective orthopaedic surgery (mainly hip replacement) show increased
blood loss and transfusion requirements in those who continue NSAID therapy to the time of surgery. The
optimum time to discontinue NSAIDs prior to orthopaedic surgery is uncertain. Some guidelines have
suggested a 2-week interval but acknowledge the evidence base for this is weak.
Inhibitors of platelet surface receptors GPIIb/IIIa may be used in patients with acute coronary syndromes. Abciximab inhibits platelet function for 12 to 24 hours after administration whereas eptifibatide and tirofiban have a short half-life of 1.5 to 2.5 hours. Invasive surgery should be delayed for 12–24 hours if possible. The drug effect is partially reversible by platelet transfusion.

7.1.6: Systemic fibrinolytic agents

‘Clot-busting’ drugs may be used in acute myocardial infarction, acute ischaemic stroke or massive pulmonary embolism. Streptokinase has a variable half-life, depending on the presence of anti-streptococcal antibodies, but can reduce fibrinogen and anti-plasmin levels for several days. With recombinant tissue plasminogen activator (e.g. alteplase) fibrinogen levels are only modestly reduced, usually returning to normal within 24 hours. Treatment for haemorrhage due to these drugs, or preparation for emergency surgery, may include antifibrinolytic agents (tranexamic acid or aprotinin—see Chapter 6), transfusion of FFP and cryoprecipitate or fibrinogen concentrate (not licensed for this indication) if the plasma fibrinogen is <1 g/L.

7.1.7: Cardiopulmonary bypass

Cardiopulmonary bypass (CPB) causes thrombocytopenia and platelet dysfunction that can increase the risk of haemorrhage. Prophylactic transfusion of platelets (or other blood components) is not beneficial but antifibrinolytic agents, such as aprotinin and tranexamic acid, may reduce blood loss. Thromboelastography (TEG) or rotational thromboelastometry (ROTEM), usually performed in the operating room, may be helpful in guiding blood component therapy when excess bleeding occurs.

7.1.8: Liver transplantation

Transfusion requirements for liver transplantation have fallen significantly, but substantial, complex blood component support may still be necessary. Problems include preoperative coagulopathy due to liver disease, difficult surgery with the risk of high blood losses and intraoperative coagulopathy and hyperfibrinolysis before the transplanted liver starts to function. Intraoperative red cell salvage is effective in reducing donor blood transfusion and TEG is often used to direct blood component transfusion with FFP and platelets. Antifibrinolytic therapy with tranexamic acid or aprotinin may be beneficial in individual cases.