

CME Article

Ministry of Health Clinical Practice Guidelines: Clinical Blood Transfusion

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ABSTRACT

The Health Sciences Authority (HSA) and the Ministry of Health (MOH) publish clinical practice guidelines on Clinical Blood Transfusion to provide doctors and patients in Singapore with evidence-based guidance for blood transfusion. This article reproduces the introduction and executive summary (with recommendations from the guidelines) from the HSA-MOH clinical practice guidelines on Clinical Blood Transfusion, for the information of readers of the Singapore Medical Journal. Chapters and page numbers mentioned in the reproduced extract refer to the full text of the guidelines, which are available from the Ministry of Health website (<http://www.moh.gov.sg/mohcorp/publications.aspx?id=25700>). The recommendations should be used with reference to the full text of the guidelines. Following this article are multiple choice questions based on the full text of the guidelines.

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INTRODUCTION**1.1 Guideline objectives and target groups**

Blood transfusion is often a necessary and crucial component of patient care across all medical, surgical, and paediatric disciplines. This evidence-based transfusion clinical practice guidelines are intended to assist medical practitioners in the appropriate and rational use of blood and blood components.

Although the administration of blood transfusion is restricted to hospitals and some specialist ambulatory centres, general practitioners and primary health care physicians should also find this set of guidelines useful in determining the thresholds for transfusion and assessing patients for urgent referrals to hospitals. Nurses will also find this useful, as the daily administration of blood products forms an integral component of their work.

This clinical practice guideline provides current evidence-based clinical practice recommendations on blood transfusion. These have been compared and cross-referenced to numerous other international published

guidelines on the same subject. The concordance of such guidelines aims to instil consistency and appropriateness of transfusion practice in Singapore as well as being comparable to international evidence-based practices.

This set of guidelines aim to increase awareness among clinicians and healthcare workers about the benefits and risks of blood component therapy. They are, however, not intended for rigid prescription of care.

1.2 Guideline development

This guideline was developed by a workgroup appointed by the Ministry of Health. Its members comprised experts in their individual fields from the personnel involved in the production and availability of the blood components to clinical haematologists and major end users represented by surgeons and obstetricians. In addition, as much of red cell transfusion is based on the principle of restoring physiological carriage of oxygen, an expert in anaesthesiology also formed part of the workgroup. The nursing and primary health care sectors were also represented.

The workgroup formulated this clinical practice guideline by reviewing published international guidelines and current evidence available in the research and clinical practice literature. Specific recommendations intrinsic to the local situation and context have also been considered (for example, refer to the Rhesus negative section).

1.3 Assessing the evidence

In assessing the evidence, different study designs were considered, including randomised controlled trials, cohort studies, case control studies, uncontrolled clinical trials and expert opinions. Best practice guidelines important in transfusion medicine were also included.

1.4 Scope of guidelines

Recommendations have purposely been made broad and are applicable across general patient groups. Infants, children and patients in special clinical settings (e.g. liver transplantation, thalassaemias) are beyond the scope of this set of guidelines.

Principles guiding the decision to administer blood

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Haem-Onc Clinic Pte Ltd
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KK Women's and Children's Hospital
National University Health System
National University Hospital
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products for children above four months of age are largely similar to those for adults, bearing in mind that younger children below two years of age may have lower normal Hb values.

The practical aspects and actual administration of blood products are not covered in this set of guidelines. Each institution should have its own policies of checking blood and patient identity to ensure safety as well as the requisite monitoring of patients when receiving any blood product. These would usually come under the purview of the individual hospital transfusion committees.

Specific blood-derived products like human albumin, immunoglobulins and factor concentrates are also not covered in this set of guidelines.

1.5 Unique properties of blood

Blood and blood component therapy is an essential component in the life-saving management of patients. Advances in medical and surgical management have resulted in more lives being saved and in more complex procedures pioneered. Nonetheless, nearly all of these remain dependent on the prompt support of blood component therapy.

Blood component therapy (red cells, platelets, fresh frozen plasma and cryoprecipitate) is unique in that its supply and availability are still entirely dependent on the systematic collection, processing and testing of blood from voluntary, non-remunerated altruistic donors. Continuous worldwide efforts in looking for alternative sources like artificial blood have met with limited success, and healthy allogeneic donors' blood remains a scarce and precious source for most of the world.

Advances in technology and medical knowledge have enabled our blood supply to be safer than it has ever been. Nonetheless, each unit of blood and blood component does carry with it a small but significantly serious risk, infectious or immune-mediated.

The importance of this set of guidelines is to steer the physician into clinically appropriate, timely and rational use of blood products by maximising its life-saving potential and its ready availability to those who need it most. Non-evidenced-based, unwarranted blood transfusion only exposes patients to unnecessary risks as well as a wastage of a precious resource. This is the main basis why patient consent for transfusion is recommended and increasingly mandatory.

1.6 Review of guidelines

Evidence-based clinical practice guidelines are by nature constantly evolving. New, emerging evidence could always supersede these guidelines, and users need to be

aware of this. The workgroup advises that these guidelines be scheduled for review three years after publication, or if it is felt that new evidence is available that would require substantive amendments to the current set of guidelines.

EXECUTIVE SUMMARY OF RECOMMENDATIONS

Details of recommendations can be found in the full text of the guidelines at the pages indicated. Details on the system of levels of evidence and grades of recommendations are also in the full text of the guidelines.

Red blood cell transfusion

D Patients should not be transfused so as to achieve a 'normal' haemoglobin (Hb) concentration (pg 26).

Grade D, Level 4

D In general, packed red cells should be provided for allogeneic transfusion (pg 26).

Grade D, Level 4

A When haemoglobin is >10 g/dL, there is usually very little indication for red cell transfusion (pg 27).

Grade A, Level 1+

C When haemoglobin is < 7 g/dL, red cell transfusion may be beneficial, particularly in symptomatic patients or when ongoing blood loss is expected (pg 27).

Grade C, Level 2+

C When haemoglobin is 7–10 g/dL, transfusion should be guided by clinical signs and symptoms, coexisting medical or surgical problems (e.g. > 65 years, cardiovascular disease, respiratory disease, ongoing blood loss, coagulopathy). In asymptomatic patients with chronic anaemia and where other specific treatment is available, the need for blood transfusion should be carefully weighed (pg 27).

Grade C, Level 2+

GPP The eventual decision for transfusion should be based on clinical judgement. Avoid transfusion if the indication is unclear, or if there is minimal or weak evidence for benefit (pg 27).

GPP

D Red cells should not be used as a volume expander, and initial volume replacement should be with colloids or crystalloids to ensure that the patient is euvolaemic (pg 28).

Grade D, Level 4

- D** In assessing the need for transfusion:
- For estimated volume loss (EVL) of < 15% of blood volume (< 750 ml in a 70 kg adult), fluid or blood replacement is usually unnecessary unless blood loss is superimposed on pre-existing anaemia or the patient is compromised by severe reduction in cardio-respiratory reserve.
 - For EVL between 15%–30% (750–1,500 ml in a 70 kg adult), replacement by crystalloids/colloids is needed, while red cell transfusion is generally unnecessary unless clinical assessment reveals reduced cardiorespiratory reserve or continuing blood loss.
 - For EVL of 30%–40% (1,500–2,000 ml in a 70 kg adult), red cell transfusion will probably be needed in addition to rapid volume replacement with crystalloids/colloids.
 - For EVL > 40% (> 2,000 ml in a 70 kg adult), both fluid and red cell replacement are needed (pg 28).
- Grade D, Level 4**
- GPP** Source of bleeding should be identified early, and appropriate action should be taken immediately, including endoscopic or surgical control of bleeding (pg 28).
- GPP**
- D** Where possible, preoperative evaluation should be done well in advance to correct or plan for the management of risk factors associated with transfusions (pg 29).
- Grade D, Level 4**
- GPP** Preoperative evaluation should include:
- Review of previous medical records
 - Interview of the patient or family
 - Physical examination of the patient
 - Review of laboratory test results, including haemoglobin and coagulation profiles (pg 29)
- GPP**
- D** If a patient admitted for elective surgery or an invasive procedure is found to have thrombocytopenia or an abnormal coagulation screen, the procedure should be postponed until the cause of the abnormality is identified (pg 29).
- Grade D, Level 4**
- D** Aspirin and clopidogrel should be discontinued at least seven days prior to planned surgery unless there is a strong contraindication for stopping it (pg 30).
- Grade D, Level 4**
- D** Vitamin K or another warfarin antagonist should be used for reversal of warfarin to potentially avoid transfusion of fresh frozen plasma (pg 30).
- Grade D, Level 4**
- D** The risk of thrombosis versus the risk of increased bleeding should be considered when altering the anti-coagulation status (pg 30).
- Grade D, Level 4**
- D** Administering pharmacologic agents prophylactically should be considered to promote coagulation and minimise blood loss (e.g. tranexamic acid) (pg 30).
- Grade D, Level 4**
- D** Specific attention should be paid to the detection, investigation and appropriate treatment of anaemia in advance of major elective surgery (pg 30).
- Grade D, Level 4**
- D** Correction of haemoglobin before surgery with measures other than red cell transfusion (e.g. iron replacement or erythropoietin) should be considered, where appropriate (pg 30).
- Grade D, Level 4**
- D** Erythropoietin may be administered in anaemic patients to reduce the need for allogeneic blood in selected patient populations (e.g. chronic renal insufficiency, anaemia of chronic disease, refusal of transfusion) (pg 31).
- Grade D, Level 4**
- D** Where suitable and indicated, autologous blood donation should be considered (pg 31).
- Grade D, Level 4**
- D** Liaise with Blood Bank to ensure that blood and blood components are available for patients when significant blood loss or transfusion is expected (pg 31).
- Grade D, Level 4**
- D** The cause of anaemia should be established before red cell transfusion (pg 32).
- Grade D, Level 4**
- D** Red cell transfusion should be reserved for patients with significant signs and symptoms requiring medical intervention. Even then, the patient should be transfused to a level just above that needed to ameliorate the symptoms of anaemia (pg 32).
- Grade D, Level 4**

D Where appropriate, specific pharmacological agents (iron, vitamin B₁₂, folate) should be used to correct the anaemia in order to reduce exposure to allogeneic transfusion (pg 32).

Grade D, Level 4

A Erythropoietin should be considered when it is indicated, e.g. chronic renal failure, anaemia of chronic illness, haematologic malignancies (pg 32).

Grade A, Level 1++

D Congenital haemoglobinopathies, such as thalassaemias and sickle cell disease, are treated according to specific disease-related protocols (pg 32).

Grade D, Level 4

A Maintaining haemoglobin level between 7–9 g/dL is recommended in critically ill patients (pg 33).

Grade A, Level 1++

B Leucodepleted red cells transfusion is recommended in the following situations:

- Patients who require multiple transfusions to reduce the rate of human leucocyte antigen (HLA) alloimmunisation
- Non-hepatic solid transplant organ candidates to reduce the rate of HLA alloimmunisation
- Patients experiencing two or more non-haemolytic febrile transfusion reactions
- As a means of reducing cytomegalovirus (CMV) transmission and CMV disease in immunocompromised patients (pg 33)

Grade B, Level 2++

B Irradiated blood components are required in the following situations:

- Blood components from 1st and 2nd degree relatives
- HLA-compatible blood components
- Intra-uterine transfusions
- Neonatal exchange transfusions subsequent to intra-uterine transfusions
- Congenital T-cell immunodeficiency defects
- Autologous or allogeneic stem cell transplant patients
- Patients treated with fludarabine or related purine analogue
- All granulocyte products (pg 34)

Grade B, Level 2++

B Irradiated blood components are recommended in the following situations provided it does not cause a clinically significant delay:

- Neonatal exchange transfusions (no prior intra-uterine transfusion)
- Hodgkin’s disease patients (pg 34)

Grade B, Level 2++

D Blood group typing and antibody screening is recommended for patients undergoing major surgery and also during the antenatal workup. This is to prevent delays in obtaining blood should transfusion becomes necessary (pg 34).

Grade D, Level 4

GPP Due to stock availability, in clinical practice, ABO-compatible red cell rather than ABO-identical units may be transfused (pg 35).

GPP

D Non-identical but compatible packed red cells can be used for transfusion, e.g. group O donor packed cells to group A, B or AB recipient (refer to table below) (pg 35).

Grade D, Level 4

Patient ABO Group	Compatible Donor Red Cells
O	Only group O whole blood and red cells.
A	Group A whole blood and red cells. Group O red cells if group A blood not available.
B	Group B whole blood and red cells. Group O red cells if group B blood not available.
AB	Group AB whole blood and red cells. Group A or B red cells if group AB blood not available. Group O red cells as a last alternative.

GPP In the rare event that whole blood is to be transfused, it must be ABO group identical with the recipient (pg 35).

GPP

GPP In a rare event or emergency setting, when the patient’s ABO group cannot be determined, group O red cells must be selected (pg 36).

GPP

GPP All donor and recipient blood must be ABO and Rhesus D typed (pg 36).

GPP

D D negative whole blood and red cells must be given to all D negative patients with anti-D present or who have previously been demonstrated to have anti-D (pg 37).

Grade D, Level 3

D When two or more units of D positive blood have been transfused, a red cell exchange transfusion should be considered to reduce the load of D positive red cells in circulation (pg 37).

Grade D, Level 3

D D negative whole blood and red cells should be considered in D negative patients who receive repeated transfusions, or are likely to become transfusion-dependant, e.g. patients with haemoglobinopathies, aplastic anaemia, myelodysplasia (pg 37).

Grade D, Level 3

GPP D negative patients who have been or will be transfused with D positive blood and blood components must be informed and counselled regarding the implications of possible alloimmunisation (pg 37).

GPP

D Where there will be subsequent interventions, such as anti-D immunoglobulin and red cell exchange, the patient must also be informed of the implications of such treatment (pg 37).

Grade D, Level 4

C D negative whole blood and red cells must be given to D negative females with child-bearing potential. Where there has been inadvertent transfusion of D positive blood to D negative females with child-bearing potential, anti-D immunoglobulin should be given at the appropriate dose (pg 38).

Grade C, Level 2+

C Where D positive platelet concentrates are transfused to a D negative patient of child-bearing potential, it is recommended that anti-D immunoglobulin should be given as prophylaxis against possible D alloimmunisation. A dose of 250 iu anti-D immunoglobulin will be sufficient to cover up to five adult therapeutic doses of D positive platelets within a six-week period (pg 38).

Grade C, Level 2+

D Intramuscular administration of anti-D should be

avoided in thrombocytopenic patients (pg 38).

Grade D, Level 4

D In females with no child-bearing potential and adult males in whom no anti-D is present, D positive whole blood and red cells may be used in large volume replacement or when D negative blood is in short supply (pg 38).

Grade D, Level 3

C D negative platelet concentrates should be given, where available, to D negative patients. Where this is not available or would cause unacceptable delay, it may be necessary to transfuse D positive platelet concentrates (pg 39).

Grade C, Level 2+

D It is not necessary to give D negative plasma products to D negative patients, provided that such products are free of red cells (pg 39).

Grade D, Level 4

D Where there is a significant degree of blood loss, measures should be taken toward:

- Identifying the source of haemorrhage and taking the necessary actions, including prompt surgical intervention
- Preserving haemostasis
- Maintaining an adequate Hb level (pg 39)

Grade D, Level 4

D Normothermia should be restored and coagulopathy should be corrected with judicious use of blood component therapy (pg 39).

Grade D, Level 4

D A full blood count (FBC) and coagulation profile (prothrombin time, activated partial thromboplastin time, fibrinogen) should be done and repeated to guide therapy and blood product replacement (pg 40).

Grade D, Level 4

B One should aim to maintain:

- Prothrombin time/activated partial thromboplastin time: target value $< 1.5 \times$ reference value
- Fibrinogen: target value > 1.0 g/L
- Platelets: target value $> 50 \times 10^9$ /L
- Hb: target value > 7 g/dL in otherwise fit individuals (pg 40)

Grade B, Level 2++

GPP Platelet transfusions as well as replacement of clotting factors and fibrinogen with fresh frozen plasma (FFP) and cryoprecipitate should be considered before the following values:

- Prothrombin time/activated partial thromboplastin time: $1.5 \times$ reference value
- Fibrinogen: 1.0 g/L
- Platelets: $50 \times 10^9/L$
- Hb: 7 g/dL in otherwise fit individuals (pg 40)

GPP

D Recombinant activated Factor VII (rFVIIa) transfusion under the guidance of transfusion specialist or haematologist may be considered in those who fail conventional therapy (pg 41).

Grade D, Level 3

D The principles of management of massive haemorrhage should be incorporated into an institutional algorithm that denotes a logical, sequential approach to resuscitation (pg 41).

Grade D, Level 4

Platelet transfusion

GPP Platelet transfusions should be given as close to the procedure as possible for the best haemostatic effect (pg 44).

GPP

D Platelet count levels should not be used as the only indicator for transfusion, and the bleeding time is not a good indicator for risk of bleeding (pg 44).

Grade D, Level 4

GPP The cause of thrombocytopenia should always be established before considering platelet transfusion unless there is life-threatening bleeding (pg 44).

GPP

D If platelet transfusion is administered in certain conditions such as heparin-induced thrombocytopenia, thrombotic thrombocytopenic purpura or haemolytic uraemic syndrome, there can be possible exacerbation of the clinical situation. In these conditions, platelet transfusion should only be given after the risks associated with transfusion have been considered and only when the benefits outweigh the risks (pg 45).

Grade D, Level 4

B As ABO antigens are present on platelets, it is preferable

to transfuse with ABO compatible platelets (pg 45).

Grade B, Level 2++

GPP ABO incompatible platelets may be administered only if ABO compatible platelets are not available and there is an urgent clinical need. In this situation, it is preferable to use Group A platelets for group B patients, and vice versa. Group O platelets are not advisable in other blood groups unless in an emergency (pg 46).

GPP

D For paediatric recipients (≤ 45 kg body weight), ABO specific platelets should be ensured whenever possible. Cross matching of platelets is not necessary (pg 46).

Grade D, Level 4

C The concomitant administration of at least 250 IU of anti-D is recommended in case of transfusion of Rh(D) positive platelets to a Rh(D) negative patient in order to prevent Rh(D) alloimmunisation (pg 46).

Grade C, Level 2+

B Apheresed platelets are recommended to prevent HLA alloimmunisation and platelet refractoriness in patients who require prolonged platelet support (pg 46).

Grade B, Level 1+

B For critically ill patients with thrombocytopenia who are bleeding and where thrombocytopenia is considered as a major contributing factor, platelet transfusion is indicated regardless of the platelet count (pg 46).

Grade B, Level 2++

C Platelet transfusion is indicated where platelet count is less than $50 \times 10^9/L$. In such patients, a higher platelet threshold should be considered if there is clinical evidence of microvascular haemorrhage (pg 47).

Grade C, Level 2+

D Platelet transfusion is indicated in patients undergoing cardiopulmonary bypass surgery where bleeding is associated with acquired platelet dysfunction secondary to the bypass surgery or the presence of anti-platelet agents such as aspirin, ticlopidine or clopidogrel (pg 47).

Grade D, Level 4

GPP Platelet transfusion should be given in the event of acute life-threatening bleeds or just before major surgery (pg 47).

GPP

Table. 1 Summary of key recommendations on management of massive blood loss [Adapted from British committee for standards in haematology guidelines on management of massive blood loss] (pgs 42-43).

Goal	Procedure	Comments
Restore circulating volume	<ul style="list-style-type: none"> Insert wide bore peripheral or central cannulae (Grade A, Level 1B) Give crystalloid or colloid as needed (Grade C, Level 4) Avoid hypotension or urine output <0.5 ml/kg/hr (Grade D, Level 4) 	<ul style="list-style-type: none"> Monitor central venous pressure Keep patient warm Concealed blood loss is often underestimated
Contact key personnel (Grade D, Level 4)	<ul style="list-style-type: none"> Clinician in charge Anaesthetists Blood bank staff Haematologist 	Arrange Intensive Care Unit bed (Grade D, Level 4)
Arrest bleeding (Grade D, Level 4)	Early surgical or obstetric intervention Interventional radiology	
Request laboratory investigations (Grade D, Level 4)	<ul style="list-style-type: none"> FBC, PT, APTT, Fibrinogen; Cross match sample, biochemical profile, blood gases and pulse oximetry Ensure correct sample identification Repeat tests after blood component infusion 	<ul style="list-style-type: none"> Results may be affected by colloid infusion Ensure correct patient identification May need to give components before result available
Maintain Hb >8 g/dl (Grade C, Level 4)	<ul style="list-style-type: none"> Assess degree of urgency Employ blood salvage to minimise allogeneic blood use Give red cells: <ul style="list-style-type: none"> If blood is required immediately until ABO & Rh (D) groups are known, emergency stock Group O blood will be issued. This can be Rhesus D positive in Chinese and Malay, but should be Rhesus D negative in Indians and other races, especially in women of child bearing age. ABO group specific when blood group known if this does not lead to delay in urgent transfusion Use blood warmer and/or rapid infusion device if flow rate >50 ml/kg/h in adult (Grade C, Level 4) 	<ul style="list-style-type: none"> Further serological crossmatch not required After 1 blood volume replacement ABO and Rh compatible blood to be given
Maintain platelet count > 50 x 10 ⁹ /l (Grade C, Level 4)	Anticipate platelet count <50 x 10 ⁹ /L after 2 times blood volume replacement	Keep platelet count >100 x 10 ⁹ /L if multiple trauma or CNS trauma or if platelet function abnormal
Maintain PT & APTT < 1.5 x mean control (Grade C, Level 4)	<ul style="list-style-type: none"> Give FFP 10-15ml/kg (1 L or four units for an adult) guided by tests Anticipate need for FFP after 1.0-1.5 times blood volume replacement 	<ul style="list-style-type: none"> PT/APTT >1.5 times mean normal value correlates with increased microvascular bleeding. Keep ionised Ca²⁺ > 1.13 mmol/l.
Maintain Fibrinogen > 1.0g/L (Grade C, Level 4)	If not corrected by FFP give cryoprecipitate (10 units of cryoprecipitate (pooled) for an adult)	
Avoid DIC (Grade D, Level 4)	Treat underlying cause (shock, hypothermia, acidosis)	

FBC, full blood count; PT, prothrombin time; APTT, activated partial thromboplastin time; FFP, fresh frozen plasma; DIC, disseminated intravascular coagulation.
Grading of evidence as from source.

C In renal failure and uraemia, the following recommendations should be implemented to avoid platelet transfusion, if possible:

- Correct the haematocrit to > 0.30
- Consider the use of desmopressin

- Consider the use of dialysis, which also have haemostatic benefits in this situation
- Only use platelet transfusions where the above methods are inappropriate or ineffective (pg 47)

Grade C, Level 2+

D In drug-induced platelet dysfunction such as use of aspirin, NSAIDs or antiplatelet drugs, the following recommendations should be followed:

- Discontinue drugs with anti-platelet activity, where possible
- Consider platelet transfusion in acute bleeding situation (pg 48)

Grade D, Level 4

Prophylactic platelet transfusion is recommended in the following conditions:

B In patients with impaired bone marrow function when platelet count is less than 10 × 10⁹/L and there are no other risk factors (pg 48).

Grade B, Level 1+

C In patients with impaired bone marrow function when platelet count is less than 20 × 10⁹/L and there are concomitant risk factors (e.g. sepsis, rapid fall of platelet count or coagulation abnormalities) (pg 48).

Grade C, Level 2+

D More liberal approach to prophylactic platelet transfusion should be practised. A transfusion trigger at platelet count of 30 × 10⁹/L is acceptable. Consultation with the haematologist or transfusion specialist is advised in individual cases where bleeding is thought to be a major risk factor (pg 48).

Grade D, Level 4

C For patients undergoing surgery or invasive procedures (e.g. epidural, lumbar puncture, renal biopsy, liver biopsy, central line insertion) when the platelet count is less than 50 × 10⁹/L and there are no other associated coagulopathies (pg 49).

Grade C, Level 2+

D Neurosurgical and ophthalmic procedures may benefit from a higher prophylactic platelet transfusion threshold (100 × 10⁹/L) (pg 49).

Grade D, Level 4

B Platelet transfusion is contraindicated if the thrombocytopenia is due to platelet activation (pg 49).

Grade B, Level 2++

D Platelet transfusion is usually not indicated when thrombocytopenia is related to immune-mediated platelet destruction, such as autoimmune thrombocytopenia, drug-induced thrombocytopenia and post transfusion purpura. Platelet transfusions are only indicated when there is significant and/or potentially life-threatening bleeding in such conditions (pg 49).

Grade D, Level 4

GPP Expert advice should be obtained before platelet transfusion is given in any of the contraindicated conditions (pg 49).

GPP

Fresh frozen plasma transfusion

D Routine and timely tests for coagulopathy such as the prothrombin time (PT) or international normalised ratio (INR), activated partial thromboplastin time (APTT), platelet counts and fibrinogen level as well as haemoglobin/haematocrit should be obtained to guide decisions on plasma transfusion. These results should be integrated with a thorough assessment of the patient's clinical condition and the presence or risk of bleeding (pg 50).

Grade D, Level 4

B Abnormal PT/INR or APTT results should not be the sole reasons for transfusing plasma, as they do not correlate well with bleeding risk and only a small proportion of patients with abnormal results will experience bleeding manifestations (pg 50).

Grade B, Level 2++

GPP All attempts must be made to identify the underlying cause of a coagulopathy and manage this appropriately, together with efforts to correct such abnormality with plasma transfusion, if necessary (pg 50).

GPP

GPP A comprehensive personal and family history of bleeding is the best preoperative screen for bleeding in surgical patients. In the event that preoperative PT and partial thromboplastin time (PTT) tests are performed and found to be abnormal, its significance should be carefully considered and if necessary, further discussed with a haematologist (pg 50).

GPP

Fresh frozen plasma is recommended for the following situations:

B Massive blood transfusion, especially with evidence of microvascular bleeding and associated with significant ($> 1.5 \times$ midpoint of normal range) abnormalities in PT and APTT. When PT and APTT cannot be obtained in a timely fashion, it is reasonable to give fresh frozen plasma (FFP) after replacement of one blood volume while waiting for results (pg 51).

Grade B, Level 2++

B If immediate reversal of warfarin effect is required. Intravenous vitamin K should be concurrently given for sustained reversal of warfarin effect (pg 51).

Grade B, Level 2++

C Acute disseminated intravascular coagulation (DIC) associated with microvascular bleeding and abnormal coagulation profile (pg 51).

Grade C, Level 2+

D Bleeding due to coagulopathy associated with chronic liver diseases (pg 51).

Grade D, Level 4

A Plasma exchange for thrombotic thrombocytopenic purpura (TTP) and haemolytic uraemic syndrome (HUS). Cryosupernatant may also be considered as an alternative (pg 51).

Grade A, Level 1+

C Bleeding associated with clotting factor deficiency if no alternative processed products or specific factor concentrates are available (pg 51).

Grade C, Level 2+

Fresh frozen plasma is not justified in the following situations:

D As a volume expander in hypovolaemia (pg 52).

Grade D, Level 4

D As replacement for albumin or immunoglobulin. Specific albumin and immunoglobulin preparations are available (pg 52).

Grade D, Level 4

D Replacement for any clotting factors unless processed and virally inactivated products are unavailable (pg 52).

Grade D, Level 4

B Reversal of warfarin effect in the absence of bleeding. Oral or intravenous vitamin K should be the therapy of

choice in this instance (pg 52).

Grade B, Level 2++

- C** Plasma exchange procedures other than for TTP and HUS (pg 52).

Grade C, Level 2++

- D** Treatment of immunodeficiency states (pg 52).

Grade D, Level 4

- D** Nutritional support (pg 52).

Grade D, Level 4

- D** The recommended dose for fresh FFP is 10–15 ml per kg body weight. It is always useful to have FFP administration guided by coagulation screens. If necessary, these should be repeated and more FFP given, depending on the clinical situation (pg 52).

Grade D, Level 4

- B** Although small amounts of red cell stroma may be present in FFP, it is less immunogenic than intact red cells and sensitisation following Rh(D) positive FFP to Rh(D) negative patients is unlikely. FFP of any Rh type may be given regardless of Rh status of the patient (pg 53).

Grade B, Level 2++

Cryoprecipitate transfusion

- C** Cryoprecipitate is rich in Factor VIII, von Willebrand factor, Factor XIII and fibrinogen. The use of cryoprecipitate is considered appropriate when there is bleeding associated with hypofibrinogenaemia (fibrinogen level < 1.0 gm/L) in the following conditions:

- Massive blood transfusion
- Disseminated intravascular coagulation
- Obstetric emergencies
- Open heart surgery
- Congenital hypofibrinogenaemia or documented dysfibrinogenaemia
- Advanced liver disease associated with low fibrinogen
- Bleeding associated with thrombolytic therapy (pg 54)

Grade C, Level 2+

- D** Cryoprecipitate may be used during bleeding in congenital Factor XIII deficiency when Factor XIII concentrate is not available (pg 54).

Grade D, Level 4

Cryoprecipitate is not recommended:

- D** For clotting factor deficiency or von Willebrand disease unless processed, virally inactivated products are not readily available (pg 54).

Grade D, Level 4

- D** For preparation of fibrin glue with commercial sources of thrombin. Factor V inhibitors have been reported following exposure to such preparations. Commercially produced fibrin sealants containing human thrombin is preferred (pg 54).

Grade D, Level 4

- C** In the management of hypofibrinogenaemia, one unit/5 kg body weight, equivalent to ten units for an average size adult, should be administered. Further therapy should be guided by fibrinogen levels (pg 55).

Grade C, Level 2+

Safety issues related to blood and blood component transfusions

- GPP** Before making a donation, the blood donor should be made aware that he or she needs to ensure that the donated blood is safe to be used (pg 56).

GPP

- GPP** Every unit of donated blood or apheresis component needs to be tested for evidence of the following infections: hepatitis B, hepatitis C, treponema palladium, and human immunodeficiency (HIV) (pg 56).

GPP

- C** Blood donations should be collected from the safest possible donors, namely regular voluntary donors (pg 57).

Grade C, Level 2+

- C** Replacement or directed donations should be avoided as far as possible (pg 57).

Grade C, Level 2+

- D** Irradiated blood components are indicated in bone marrow/stem cell auto- or allo-grafting, and transfusions from relatives or HLA-selected platelet donors (pg 58).

Grade D, Level 3

Adverse reactions to transfusion

- GPP** It is advisable that a policy be in place in each hospital for the management and reporting of adverse events following transfusion of blood and blood components. This should be regularly

reviewed by the hospital transfusion committee with an aim to improving transfusion practice (pg 65).

GPP

GPP Institutional policies may vary regarding the initial steps in managing an adverse reaction but the following key elements should be followed:

1. The transfusion of on-going unit should be discontinued immediately.
2. Immediately do a clerical check at bedside to detect any misidentification and major ABO mismatch.
3. Monitor patient's vital signs.

4. The intravenous access should be kept open for treatment if necessary.
5. The adverse reaction should be reported to the blood bank immediately.
6. Coordinate with the blood bank regarding the collecting of samples for transfusion reaction investigation workup.
7. Continue to observe and monitor the patient.
8. Do not initiate another transfusion without blood bank consultation.
9. Document all events on appropriate forms and in the patient's chart (pgs 65-66).

GPP

D Categories and management of acute and delayed adverse reactions to transfusion (pgs 67-68).

Type	Incidence/ Aetiology	Diagnostic Criteria/ Presentation	Diagnostic testing	Management
Acute – within 24 hours of transfusion				
Allergic Reaction (Mild)/ Urticarial	• Interaction of an allergen with preformed antibodies	• Morbilliform rash with or without pruritis • Urticaria (hives) • Flushing • Localized angioedema	• N/A	• Diphenhydramine • Transfusion can be restarted if the symptoms and signs have subsided provided the incomplete unit can be completed within 4 hours of issuance • Monitor closely for other signs and symptoms
Anaphylactoid Anaphylaxis (Severe)	• Antibody to donor plasma protein (IgA, Haptoglobin, C4)	• Mucocutaneous symptoms • Hypotension • Respiratory signs and symptoms may be laryngeal (tightness in throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing, bronchospasm, hypoxemia)	• Rule out haemolysis	• Maintain airway; provide oxygen and ventilatory support • Treat hypotension with fluids, dopamine if unresponsive • Initiate transfusion reaction workup • Do not initiate another transfusion without blood bank consultation • Premedicate with diphenhydramine and/or steroids • Use of washed red cells (and platelets) in severe anaphylaxis
Haemolytic Reaction	• Incompatible blood transfusion results in antigen/antibody response with activation of complement and subsequent intravascular haemolysis	• Chills/rigors • Fever • Back/flank pain • Hypotension • Haemoglobinuria • Oliguria / anuria • Disseminated intravascular coagulation • Pain or oozing at IV site	• Clerical Check • Check for Haemolysis - Direct Coombs test - Visual inspection - Repeat patient ABO, pre and post sample - Further tests to detect haemolysis (LDH, Bilirubin, etc.)	• Maintain airway; provide oxygen and ventilatory support • Hydration to maintain urinary output • Diuretics to promote renal perfusion • Cardiovascular support with pressor agents if needed • Treatment of disseminated intravascular coagulation • Initiate transfusion reaction workup; inform Blood Bank
Febrile Non Haemolytic Transfusion Reaction	• Cytokines • Antibody to donor white cells	• Fever (≥38C or a change of ≥1C from pre transfusion value) • Chills / Rigors • Headache • Vomiting	• Rule out haemolysis • Rule out Bacterial contamination	• Initiate transfusion reaction workup; inform Blood Bank • Leucoreduced components • Premedication with antipyretics
Transfusion Associated Acute Lung Injury (TRALI)	• Anti- human leucocyte antigen (HLA) and anti-HNA antibodies in donor (occasionally in recipients)	• Acute respiratory distress within six hours of transfusion • Bilateral pulmonary infiltrates on chest xray • Hypoxemia (O2 sat ≤ 90% on room air or PaO2 ≤ 300 mm Hg) • No evidence of circulatory overload • Hypotension (some cases hypertension) • Fever • Transient Leucopenia	• Rule out haemolysis • Rule out cardiogenic oedema • Human leucocyte antigen (HLA) antibody screen • Chest Xray	• Maintain airway; provide oxygen and ventilatory support • Treat Hypotension • Supportive care • Initiate transfusion reaction workup; inform Blood Bank
Acute – within 24 hours of transfusion				
Transfusion Associated Circulatory Overload (TACO)	• Volume overload	• Acute respiratory distress (dyspnea, orthopnea, cough) • Tachycardia • Hypertension • Evidence of left sided heart failure	• Rule out TRALI • Chest Xray	• Maintain airway; provide oxygen and ventilatory support • Diuretics • Initiate transfusion reaction workup; inform Blood Bank
Transfusion Associated Sepsis (Bacterial Contamination)	• Sepsis is the result of transfusion of contaminated blood components • The bacteria usually originate from the blood donor either from venipuncture (e.g. Staphylococcus, Streptococcus) or unsuspected bacteremia (e.g. Yersinia) but may also result from donor unit processing	• Fever, often ≥ 2C rise from baseline • Chills / Rigors • Hypotension • Shock • Renal failure • Unexplained bleeding from mucocutaneous or infusion sites	• Rule out haemolysis • Gram stain • Component culture • Blood culture on patient	• Maintain airway; provide oxygen and ventilatory support • Hydration to maintain urinary output • Diuretics to promote renal perfusion • Broad Spectrum Antibiotics • Cardiovascular support with pressor agents if needed • Treatment of disseminated intravascular coagulation • Initiate transfusion reaction workup; inform Blood Bank
Delayed –more than 24 hours from transfusion				
Delayed Haemolytic Transfusion Reaction	• Anamnestic immune response to red cell antigens	• Decrease in haemoglobin • Fever • Jaundice (Mild) • Patient may be asymptomatic	• Antibody screen and Identification • Direct Coombs test • Elution • Test for haemolysis	• Initiate Delayed transfusion reaction workup; inform Blood Bank • Transfuse AHG crossmatch compatible blood; antigen negative if indicated
Graft Versus Host Disease (GVHD)	• Donor lymphocytes engraft in recipient and mount attack on host tissues	• Fever • Gastrointestinal symptoms • Rash • Hepatitis • Pancytopenia	• Skin biopsy • Human leucocyte antigen (HLA) typing • Molecular Analysis for Chimerism	• Immunosuppressive agents • Irradiation of blood components for patients at risk

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

Multiple Choice Questions (Code SMJ 201103B)

These questions are based on the full text of the guidelines which may be found at <http://www.moh.gov.sg/mohcorp/publications.aspx?id=25700>.

- | | True | False |
|---|--------------------------|--------------------------|
| Question 1. Regarding transfusion of red cells: | | |
| (a) One unit of packed cell has volume of approximately 400 ml. | <input type="checkbox"/> | <input type="checkbox"/> |
| (b) There should not be a fixed transfusion trigger to determine transfusion threshold. | <input type="checkbox"/> | <input type="checkbox"/> |
| (c) Preoperatively, patients should be transfused to Hb level of > 10 g/dl, where possible. | <input type="checkbox"/> | <input type="checkbox"/> |
| (d) All patients should be transfused when their Hb is < 7 g/dl. | <input type="checkbox"/> | <input type="checkbox"/> |
| Question 2. Regarding transfusion of red cells: | | |
| (a) Red cells are used mainly as volume expanders for acute blood loss. | <input type="checkbox"/> | <input type="checkbox"/> |
| (b) The main goal of red cell transfusion is to avoid tissue hypoxia and organ dysfunction rather than a normal Hb level. | <input type="checkbox"/> | <input type="checkbox"/> |
| (c) Measurement of Hb level is a reliable indicator for amount and severity of blood loss during acute blood loss. | <input type="checkbox"/> | <input type="checkbox"/> |
| (d) Leucodepleted red cells is recommended in non-hepatic solid transplantation organ candidates. | <input type="checkbox"/> | <input type="checkbox"/> |
| Question 3. For transfusion of plasma: | | |
| (a) Abnormal prothrombin time (PT) or activated partial thromboplastin time (APTT) results should not be the sole reason for transfusion. | <input type="checkbox"/> | <input type="checkbox"/> |
| (b) Fresh frozen plasma should never be given without PT and APTT results. | <input type="checkbox"/> | <input type="checkbox"/> |
| (c) Vitamin K should be given concurrently for sustained reversal of warfarin. | <input type="checkbox"/> | <input type="checkbox"/> |
| (d) Fresh frozen plasma must always be ABO and Rhesus compatible. | <input type="checkbox"/> | <input type="checkbox"/> |
| Question 4. For platelet transfusion: | | |
| (a) It is preferable to transfuse with ABO compatible platelets. | <input type="checkbox"/> | <input type="checkbox"/> |
| (b) All critically ill patients with thrombocytopenia and are actively bleeding must have platelet transfusion. | <input type="checkbox"/> | <input type="checkbox"/> |
| (c) Thrombocytopenia secondary to platelet activation is not a contraindication. | <input type="checkbox"/> | <input type="checkbox"/> |
| (d) There are no indications for prophylactic transfusion. | <input type="checkbox"/> | <input type="checkbox"/> |
| Question 5. Acute haemolytic reaction following red cell transfusion: | | |
| (a) The commonest cause for this complication is misidentification of the patient. | <input type="checkbox"/> | <input type="checkbox"/> |
| (b) Most important step to prevent this complication is to positively identify the patient at the bedside when taking blood for crossmatch and before commencing blood transfusion. | <input type="checkbox"/> | <input type="checkbox"/> |
| (c) Simple urticaria is the common presentation of this complication. | <input type="checkbox"/> | <input type="checkbox"/> |
| (d) Patient may complain of discomfort at the site of transfusion. | <input type="checkbox"/> | <input type="checkbox"/> |

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

SUBMISSION INSTRUCTIONS:

(1) Log on at the SMJ website: <http://www.sma.org.sg/cme/smj> and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

RESULTS:

(1) Answers will be published in the SMJ May 2011 issue. (2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 2 May 2011. (3) All online submissions will receive an automatic email acknowledgement. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

Deadline for submission: (March 2011 SMJ 3B CME programme): 12 noon, 25 April 2011.