



Clinical Blood Transfusion

HSA-MOH Clinical Practice Guidelines 1/2011



College of Family Physicians,
Singapore



College of
Anaesthesiologists,
Singapore



College of Surgeons,
Singapore



Academy of Medicine,
Singapore



MINISTRY OF HEALTH
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Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1 ⁺⁺	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.
1 ⁺	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1 ⁻	Meta-analyses, systematic reviews of RCTs, 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

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; or 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; or 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; or Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 ⁺
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Clinical Blood Transfusion

HSA – MOH Clinical Practice Guidelines 1/2011

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

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Foreword

Blood transfusion is an important and crucial component of adult and paediatric patient care across all medical and surgical disciplines. Errors from blood transfusion are potentially deadly and carry with them a high financial burden. In a landmark paper, Sazama and colleagues studied transfusion-related deaths reported to the US Food and Drug Administration (FDA) for 10 years¹ and identified 131 fatal ABO incompatible transfusions. The study showed that the most frequent error leading to a fatal outcome was administration to someone other than the intended recipient.

Overseas studies²⁻³ have shown that the incidence of inappropriate blood products transfusions can be as high as 43%. Red cells were used inappropriately most frequently in association with surgical procedures; fresh frozen plasma was most commonly inappropriately used as prophylaxis for abnormal coagulation tests or before procedures or surgery; for platelets, it was their use for bleeding.

This is the first guideline to be published by the Ministry of Health to address the issue of appropriate clinical blood transfusions. It covers red blood cells transfusion, platelet transfusion, fresh frozen plasma transfusion, cryoprecipitate transfusion, as well as safety issues and adverse reactions to transfusion. This guideline aims to guide the user on the international evidence-based practices for blood transfusion, thereby allowing a better understanding on the science in ensuring appropriate transfusion practices in Singapore.

I hope that all medical practitioners will find this set of guidelines useful in their management of patients that require transfusion of blood products.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES

¹ Sazama K. Reports of 355 transfusion-associated deaths: 1976 through 1985. *Transfusion*. 1990 Sep;30(7):583-90.

² Metz J, McGrath KM, Copperchini ML, Haeusler M, Haysom HE, Gibson PR, et al. Appropriateness of transfusions of red cells, platelets and fresh frozen plasma. An audit in a tertiary care teaching hospital. *Med J Aust*. 1995 Jun 5;162(11):572-3, 6-7.

³ Stanworth SJ, Grant-Casey J, Lowe D, Laffan M, New H, Murphy MF, et al. The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children. *Transfusion*. 2010 Aug 27.

Executive summary of key recommendations

Details of recommendations can be found in the main text at the pages indicated.

Red blood cells 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 >10g/dL – there is usually very little indication for red cell transfusion (pg 27).

Grade A, Level 1+

C When Haemoglobin <7g/dL – red cells transfusion may be beneficial particularly in symptomatic patients or ongoing blood loss is expected (pg 27).

Grade C, Level 2+

C When Haemoglobin is between 7-10g/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 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 euvolemic (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.
- EVL between 15-30% (750-1500 ml in a 70 kg adult), replacement by crystalloids / colloids is needed while red cell transfusion is generally unnecessary unless clinical assessment reveals reduced cardio-respiratory reserve or continuing blood loss.
- EVL of 30-40% (1500-2000 ml in a 70 kg adult), red cell transfusion will probably be needed in addition to rapid volume replacement with crystalloids/colloids.
- EVL > 40% (>2000 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 7 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 anticoagulation 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 anemic 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 thalasseмии and sickle cell disease, are treated according to specific disease-related protocols (pg 32).

Grade D, Level 4

A Maintaining haemoglobin level between 7-9g/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 rate of human leucocyte antigen (HLA) alloimmunisation
- non-hepatic solid transplant organ candidates to reduce 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
- human leucocyte antigen (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 that 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 become 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 the 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 will 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 counseled 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 6-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 towards:

- 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 < 1.5x reference value
- Fibrinogen : target value > 1.0g/L
- Platelets : target value > 50 x 10⁹/L
- Hb : target value > 7g/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 : 1.5x reference value
- Fibrinogen : 1.0 g/L
- Platelets : 50 x 10⁹/L
- Hb : 7g/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

Table 1 Summary of key recommendations on management of massive blood loss

[Source: BJH Guidelines on the management of massive blood loss (2006)] (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 	<p>Results may be affected by colloid infusion</p> <p>Ensure correct patient identification</p> <p>May need to give components before result available</p>

Goal	Procedure	Comments
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.

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 (of less or equal to 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 250IU 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 human leucocyte antigen (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

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

- Correct the hematocrit to >0.30 .
- Consider the use of desmopressin.
- Consider the use of dialysis, which also have hemostatic 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 $10 \times 10^9/L$ 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 $20 \times 10^9/L$ 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 $30 \times 10^9/L$ 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 $50 \times 10^9/L$ 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 ($100 \times 10^9/L$) (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 normalized 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 prothrombin time (PT)/international normalized ratio (INR) or activated partial thromboplastin time results should not be the sole reason 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 pre-operative screen for bleeding in surgical patients. In the event that pre-operative prothrombin time (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 (>1.5x midpoint of normal range) abnormalities in prothrombin time (PT) and activated partial thromboplastin time (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 factors 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 thrombotic thrombocytopenic purpura (TTP) and haemolytic uraemic syndrome (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 frozen plasma (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 fresh frozen plasma (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. Use of cryoprecipitate is considered **appropriate** when there is bleeding associated with hypofibrinogenaemia (fibrinogen level < 1.0gm/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, 1 unit/5 kg body weight - equivalent to 10 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 transfusion

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 human leucocyte antigen (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

Incidence/ Aetiology		Diagnostic Criteria/ Presentation		Management	
Type	Diagnosis	Criteria	Presentation	Testing	Management
Acute – within 24 hours of transfusion					
Allergic Reaction (Mild)/ Urticarial	<ul style="list-style-type: none"> Interaction of an allergen with preformed antibodies 	<ul style="list-style-type: none"> Morbiliform rash with or without pruritis Urticaria (hives) Flushing Localized angioedema 	N/A	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> Antibody to donor plasma protein (IgA, Haptoglobin, C4) 	<ul style="list-style-type: none"> Mucocutaneous symptoms Hypotension Respiratory signs and symptoms may be laryngeal (tightness in throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnoea, cough, wheezing, bronchospasm, hypoxemia) 	<ul style="list-style-type: none"> Rule out haemolysis 	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Incompatible blood transfusion results in antigen/antibody response with activation of complement and subsequent intravascular haemolysis 	<ul style="list-style-type: none"> Chills/rigors Fever Back/flank pain Hypotension Haemoglobinuria Oliguria / anuria Disseminated intravascular coagulation Pain or oozing at IV site 	<ul style="list-style-type: none"> Clerical Check Check for Haemolysis <ul style="list-style-type: none"> Direct Coombs test Visual inspection Repeat patient ABO, pre and post sample Further tests to detect haemolysis (LDH, Bilirubin, etc.) 	<ul style="list-style-type: none"> 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 	
Febriile Non Haemolytic Transfusion Reaction	<ul style="list-style-type: none"> Cytokines Antibody to donor white cells 	<ul style="list-style-type: none"> Fever ($\geq 38C$ or a change of $\geq 1C$ from pre transfusion value) Chills / Rigors Headache Vomiting 	<ul style="list-style-type: none"> Rule out haemolysis Rule out Bacterial contamination 	<ul style="list-style-type: none"> Initiate transfusion reaction workup; inform Blood Bank Leucoreduced components Premedication with antipyretics 	
Transfusion Associated Acute Lung Injury (TRALI)	<ul style="list-style-type: none"> Anti-human leucocyte antigen (HLA) and anti-HNA antibodies in donor (occasionally in recipients) 	<ul style="list-style-type: none"> Acute respiratory distress within six hours of transfusion Bilateral pulmonary infiltrates on chest xray Hypoxemia ($02 sat \leq 90\%$ on room air or $PaO2 \leq 300$ mm Hg) No evidence of circulatory overload Hypotension (some cases hypertension) Fever Transient Leucopenia 	<ul style="list-style-type: none"> Rule out haemolysis Rule out cardiogenic oedema Human leucocyte antigen (HLA) antibody screen Chest Xray 	<ul style="list-style-type: none"> Maintain airway; provide oxygen and ventilatory support Treat Hypotension Supportive care Initiate transfusion reaction workup; inform Blood Bank 	

Type	Incidence/ Aetiology	Diagnostic Criteria/ Presentation	Diagnostic testing	Management
Acute – within 24 hours of transfusion				
Transfusion Associated Circulatory Overload (TACO)	<ul style="list-style-type: none"> Volume overload 	<ul style="list-style-type: none"> Acute respiratory distress (dyspnea, orthopnea, cough) Tachycardia Hypertension Evidence of left sided heart failure 	<ul style="list-style-type: none"> Rule out TRALI Chest Xray 	<ul style="list-style-type: none"> Maintain airway; provide oxygen and ventilatory support Diuretics Initiate transfusion reaction workup; inform Blood Bank
Transfusion Associated Sepsis (Bacterial Contamination)	<ul style="list-style-type: none"> Sepsis is the result of transfusion of disseminated blood components The bacteria locally originate from the blood donor or elute from the blood donor or enter from venipuncture (e.g. Staphylococcus, Streptococcus) or mislabeled bacteremia (e.g. Yersinia) but may also result from donor unit processing 	<ul style="list-style-type: none"> Fever; often $\geq 2C$ rise from baseline Chills / Rigors Hypotension Shock Renal failure Unexplained bleeding from mucocutaneous or infusion sites 	<ul style="list-style-type: none"> Rule out haemolysis Gram stain Component culture Blood culture on patient 	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Anamnestic immune response to red cell antigens 	<ul style="list-style-type: none"> Decrease in haemoglobin Fever Jaundice (Mild) Patient may be asymptomatic 	<ul style="list-style-type: none"> Antibody screen and identification Direct Coombs test Elution Test for haemolysis 	<ul style="list-style-type: none"> Initiate Delayed transfusion reaction workup; Inform Blood Bank Transfuse AHG crossmatch compatible blood; antigen negative if indicated
Graft Versus Host Disease (GVHD)	<ul style="list-style-type: none"> Donor lymphocytes engraft in recipient and mount attack on host tissues 	<ul style="list-style-type: none"> Fever Gastrointestinal symptoms Rash Hepatitis Pancytopenia 	<ul style="list-style-type: none"> Skin biopsy Human leucocyte antigen (HLA) typing Molecular Analysis for Chimerism 	<ul style="list-style-type: none"> Immunosuppressive agents Irradiation of blood components for patients at risk

(pgs 67-68)

Grade D, Level 3

1 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 amongst 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 products for children above 4 months of age are largely similar to adults, bearing in mind that younger children below 2 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 is 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 has 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 maximizing 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 wasting 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 in 3 years after publication or if it was felt that new evidence was available that would require substantive amendments to the current set of guidelines.

2 Red blood cells transfusion

2.1 Principles

The aim of red cell transfusion is to increase oxygen carrying capacity of blood by increasing haemoglobin concentration in patients with acute or chronic anaemia. There are significant risks associated with any transfusion and thus a transfusion should only be given when benefit outweighs risks.

The decision to transfuse should always be carefully weighed on a case-by-case basis taking into consideration clinical evaluation of symptoms and haemodynamic status as well as laboratory parameters such as haemoglobin level. The rate of development of anaemia is also an important factor. It is more relevant to consider the goal of red cell transfusion as the avoidance of tissue hypoxia.

D Patients should not be transfused so as to achieve a ‘normal’ haemoglobin (Hb) concentration.¹⁻²

Grade D, Level 4

D In general, packed red cells should be provided for allogeneic transfusion.³⁻⁴

Grade D, Level 4

The volume of one unit of packed cells is approximately 200ml. In the absence of ongoing blood loss or haemolysis, one unit of red cells should raise the haemoglobin in an average size adult by approximately 1g/dL or haematocrit by 3%.³⁻⁴

2.2 Trigger for red cell transfusion

There is no fixed transfusion trigger. The risks of transfusion should always be weighed against the perceived benefits (see section 6.3) as there are risks to transfusions, e.g. errors from transfusing incorrect blood product, bacterial contamination of blood products.

The following transfusion triggers based on haemoglobin levels should always be evaluated in the context of a multiplicity of factors including rate and amount of blood loss, cardiopulmonary reserve.^{1-2,5-7}

A When Haemoglobin >10g/dL – there is usually very little indication for red cell transfusion.⁶⁻⁷

Grade A, Level 1+

C When Haemoglobin <7g/dL – red cells transfusion may be beneficial particularly in symptomatic patients or ongoing blood loss is expected.^{1-2,5-8}

Grade C, Level 2+

C When Haemoglobin is between 7-10g/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.^{1-2,5-8}

Grade C, Level 2+

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

GPP

2.3 Management of transfusion needs during acute blood loss (including trauma and gastrointestinal bleeding)

Measurement of Hb level may be misleading in view of haemoconcentration and therefore, should not be used as the sole indicator of the amount and severity of blood loss. The clinical decision for blood transfusion depends on the estimation of blood loss, the rate of ongoing blood loss, the haemoglobin level prior to bleeding, evidence of end organ dysfunction and the risk of coronary artery disease.

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 euvolemic.^{1,7,9}

Grade D, Level 4

D In assessing the need for transfusion:⁹

- 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.
- EVL between 15-30% (750-1500 ml in a 70 kg adult), replacement by crystalloids / colloids is needed while red cell transfusion is generally unnecessary unless clinical assessment reveals reduced cardio-respiratory reserve or continuing blood loss.
- EVL of 30-40% (1500-2000 ml in a 70 kg adult), red cell transfusion will probably be needed in addition to rapid volume replacement with crystalloids/colloids.
- EVL > 40% (>2000 ml in a 70 kg adult), both fluid and red cell replacement are needed.

Grade D, Level 4

The treatment of ongoing bleeding is not blood transfusions but haemostasis by the most expedient means available.

GPP Source of bleeding should be identified early and appropriate action should be taken immediately, including endoscopic or surgical control of bleeding.

GPP

Massive blood transfusion constitutes a medical emergency and is dealt with in detail in section 2.11.

2.4 Red cell transfusion in the peri-operative setting

I. Preoperative evaluation

D Where possible, preoperative evaluation should be done well in advance to correct or plan for the management of risk factors associated with transfusions.¹⁰⁻¹³

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

GPP

The aim is to identify risk factors:

- Organ ischemia (e.g. cardiorespiratory disease), which may influence the ultimate transfusion trigger for red blood cells (e.g. haemoglobin level)
- Coagulopathy (e.g. use of warfarin, clopidogrel, aspirin), which may influence transfusion of non-red blood cell components
- History of congenital or acquired blood disorders e.g. haemophilia, ITP, liver cirrhosis
- The use of vitamins or herbal supplements that may affect coagulation.

II. Preoperative preparation

Preoperative patient preparation includes optimisation of haemostatic function (including discontinuation of antiplatelet drugs and management of patients on oral anticoagulation) to prevent perioperative bleeding.

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.¹³⁻¹⁵

Grade D, Level 4

Preoperative preparation should include:

1. Discontinuation or modification of antiplatelet and anticoagulation therapies

D Aspirin and clopidogrel should be discontinued at least 7 days prior to planned surgery unless there is a strong contraindication for stopping it.¹³⁻¹⁴

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 (FFP).¹³⁻¹⁴

Grade D, Level 4

The effects of warfarin may last for several days depending on patient response and the administration of reversal agents (e.g. vitamin K, prothrombin complex concentrate, recombinant activated Factor VII, or FFP).¹⁴

D The risk of thrombosis versus the risk of increased bleeding should be considered when altering anticoagulation status.¹⁴

Grade D, Level 4

2. Administration of prophylactic pharmacologic agents

D Administering pharmacologic agents prophylactically should be considered to promote coagulation and minimise blood loss (e.g. tranexamic acid).¹⁴

Grade D, Level 4

Prevention or reduction of allogeneic transfusion requirements:

D Specific attention should be paid to the detection, investigation and appropriate treatment of anaemia in advance of major elective surgery.^{1, 5, 14-15}

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.^{1, 5, 14-15}

Grade D, Level 4

D Erythropoietin may be administered in anemic patients to reduce the need for allogeneic blood in selected patient populations (e.g. chronic renal insufficiency, anaemia of chronic disease, refusal of transfusion).^{1, 5, 14-15}

Grade D, Level 4

Pre-operative transfusion is rarely required when Hb > 10g/dL and no differences have been found between patients who received transfusions to maintain their Hb > 10g/dL and those who received transfusions only when symptomatic or if Hb fell below 8 g/dL.^{7, 10-11, 16-18}

D Where suitable and indicated, autologous blood donation should be considered.^{15, 19}

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.^{12, 14}

Grade D, Level 4

Other active ways to reduce the blood usage during surgery include intra-operative haemodilution and intra-operative cell salvage.¹⁴⁻¹⁵

The management of perioperative bleeding would otherwise follow the guidelines as for acute blood loss. In the event of unexpected, considerable, blood loss, this may be treated as major blood loss and managed as described above.

2.5 Red cell transfusion in chronic anaemia

In contrast to acute blood loss, the decision to treat and correct chronic anaemia with red cells might be less urgent due to compensatory mechanisms that usually have already come into effect due to its chronicity. This means that haemodynamic shifts present in acute anaemia due to fluid depletion are not present.

The following practice points are indicated:

D The cause of anaemia should be established before red cell transfusion.^{1,5}

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.^{1-2, 5-7, 15}

Grade D, Level 4

Many patients are well compensated at their level of anaemia and do not require red cell transfusion, especially at Hb > 7g/dL.^{1-2, 5-7, 15}

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.¹⁴

Grade D, Level 4

A Erythropoietin should be considered when it is indicated, e.g. chronic renal failure, anaemia of chronic illness, haematologic malignancies.^{15,20}

Grade A, Level 1++

Its safety and efficacy profile has been established including its role in reducing exposure to allogeneic blood and its attendant risks (see section 6.3).

However, reports of anti-erythropoietin antibodies have been described with subcutaneous administration of erythropoietin and although rare, are important as they can cause red cell aplasia.

D Congenital haemoglobinopathies, such as thalassaemias and sickle cell disease, are treated according to specific disease-related protocols.^{1,5}

Grade D, Level 4

2.6 Red cell transfusion in critical care setting

A Maintaining haemoglobin level between 7-9g/dL is recommended in critically ill patients.²¹⁻²³

Grade A, Level 1++

A multicentre randomized clinical trial showed that a restrictive strategy where haemoglobin was kept between 7-9g/dL is as effective as and possibly superior to a liberal strategy where haemoglobin level was kept between 10-12g/dL in critically ill patients.²⁰⁻²² There is no evidence to suggest that a higher haemoglobin level could reduce mortality at 30 days.

2.7 Transfusion of leucodepleted or irradiated blood products

I Leucocyte reduction of red cells

One unit of red blood cells contains $\geq 10^8$ white cells. The presence of leucocytes provides no benefit and is associated with various adverse effects such as non haemolytic febrile transfusion reactions, cytomegalovirus (CMV) transmission and human leucocyte antigen (HLA) alloimmunization:

B Leucodepleted red cells transfusion is recommended in the following situations:²⁴⁻²⁵

- patients who require multiple transfusions to reduce rate of human leucocyte antigen (HLA) alloimmunisation
- non-hepatic solid transplant organ candidates to reduce 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

Grade B, Level 2++

II Irradiation of blood components (red cells, platelets)

Transfusion-associated graft-versus-host disease is a rare but usually fatal complication of transfusion of any blood component with viable T lymphocytes. Due to multi-organ engraftment and proliferation of

donor T lymphocytes, an acute syndrome manifested by dysfunction of the skin, liver, gastrointestinal tract and bone marrow develops. This condition is preventable by gamma irradiation of cellular blood components.²⁵⁻²⁷

B Irradiated blood components are required in the following situations^{24, 28-32}:

- Blood components from 1st and 2nd degree relatives
- human leucocyte antigen (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

Grade B, Level 2++

B Irradiated blood components are recommended in the following situations provided that it does not cause a clinically significant delay^{24, 28-32}:

- Neonatal exchange transfusions (no prior intra-uterine transfusion)
- Hodgkin's disease patients

Grade B, Level 2++

2.8 Pre-transfusion compatibility testing

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 become necessary.³³⁻³⁴

Grade D, Level 4

2.9 Selection of ABO Rh(D) red cells

In transfusion practice, the ABO blood groups are the most important. There are four different ABO groups – O, A, B and AB. These are determined by the respective antigen carried on the individual's red cells i.e. A antigen, B antigen, both A and B antigens or neither. From

early childhood, normal healthy individuals, produce antibodies against the A or B antigens that are not expressed on their red cells. Neonates may not begin to manufacture these antibodies until after the first few months of life.^{1,24}

Blood Group	Antibody present in plasma
Group A	Intrinsic anti-B antibody
Group B	Intrinsic anti-A antibody
Group O	Intrinsic anti-A and anti-B antibodies
Group AB	Neither A nor B antibodies

The antibodies are able to haemolyse transfused red cells rapidly and thus it is important to ensure ABO compatible blood is transfused. Transfusion of red cells incompatible with patient's ABO type can lead to severe acute haemolytic transfusion with possible fatality.

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

GPP

Red cell provided as packed cell concentrates or with additive solutions added contain minimal residual plasma and therefore minimal anti-A and/or anti-B.

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).^{1,5,35}

Grade D, Level 4

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

GPP

In summary,

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 or emergency setting, when the patient's ABO group cannot be determined, Group O red cells must be selected.

GPP

GPP All donor and recipient blood must be ABO and Rhesus D typed.

GPP

There are many other antigens present on the red cells surface other than ABO and Rhesus D. These include the Cc, Ee, Kell and Duffy blood groups. In routine cases, only ABO and Rh(D) is important but further matching for other antigens may be necessary depending on the clinical circumstances and the presence of clinically significant allo-antibodies with the potential to cause haemolytic transfusion reactions or haemolytic disease of the newborn. This should be done in consultation with a transfusion specialist or haematologist.^{1, 33, 36}

2.10 Management of Rh(D) negative patients

Anti-D is a clinically significant antibody that is associated with haemolytic disease of the newborn and haemolytic transfusion reactions. The incidence of anti-D production is 70-90% in volunteers exposed to repeated immunization³⁷⁻⁴⁰; this is lower in hospitalised patients and immune compromised patients.⁴¹⁻⁴⁴

D negative blood and blood products are scarce in the Singapore blood supply, as less than 1% of Chinese and Malays and only 6% of Indians are D negative. The selection of blood and blood components to D negative patients must therefore take into consideration the patient profile, risk of immunisation to D, and the limited supply of D negative blood components available.

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.⁴⁵⁻⁴⁷

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.⁴⁸⁻⁵²

Grade D, Level 3

D D negative whole blood and red cells should be considered in D negative patients who will receive repeated transfusions, or are likely to become transfusion-dependant, e.g. patients with haemoglobinopathies, aplastic anaemia, myelodysplasia.^{44,53}

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 counseled regarding the implications of possible alloimmunisation.

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.⁴⁸

Grade D, Level 4

The top priority is to prevent immunisation in females of child-bearing potential to avoid the complications of haemolytic disease of the newborn.

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^{39, 48-49, 54-57}

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.⁵⁸⁻⁶¹ 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 6-week period.

Grade C, Level 2+

D Intramuscular administration of anti-D should be avoided in thrombocytopenic patients.^{48, 53, 62}

Grade D, Level 4

In other patients, the goal of therapy is to reduce dependence on D negative blood for future bleeding episodes. The aim of these guidelines is to ensure a continuous supply of D negative blood components for these patients.

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.^{44, 63-66}

Grade D, Level 3

Although D antigens are not expressed on platelets, residual red cells are present in platelet concentrates and may immunise D negative patients who are transfused with D positive platelets concentrates.^{45, 67-70} Although frozen plasma components such as fresh frozen plasma and cryoprecipitate do not contain red cells, they may contain small amounts of stroma; however, sensitisation following transfusion of D positive stroma is rare as it is less immunogenic than red cells.⁴⁵

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.^{48, 53, 62}

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.⁷¹

Grade D, Level 4

2.11 Blood transfusion in major blood loss

The primary objective of transfusion therapy during a major blood loss is ensuring adequate tissue perfusion and the preservation of tissue oxygenation at a level consistent with avoidance of critical ischaemic organ damage and irreversible organ failure.

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

- Identifying the source of haemorrhage and taking the necessary actions, including prompt surgical intervention^{34, 72-73}
- Preserving haemostasis^{34, 36, 72-76}
- Maintaining an adequate Hb level^{7, 34, 36, 72-73, 75}

Grade D, Level 4

D Normothermia should be restored and coagulopathy should be corrected with judicious use of blood component therapy.^{34, 36, 72-73, 77}

Grade D, Level 4

Hypothermia from lower ambient temperature, large open wounds and infusion of fluids at lower temperature can result in the exacerbation of coagulation abnormalities and worsening of oxygen availability.^{34, 36, 72-73}

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.^{34, 36, 72-78}

Grade D, Level 4

B One should aim to maintain:^{21-23,42,66-68,114,118,127-128}

- prothrombin time/ activated partial thromboplastin time : target value < 1.5x reference value
- Fibrinogen : target value > 1.0g/L
- Platelets : target value > 50 x 10⁹/L
- Hb : target value > 7g/dL in otherwise fit individuals

Grade B, Level 2++

Coagulation abnormalities would be expected after >1.5x replacement of blood volume and a lowering of platelet count <50 x 10⁹/L after 2x blood volume replacement.

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 : 1.5x reference value
- Fibrinogen : 1.0 g/L
- Platelets : 50 x 10⁹/L
- Hb : 7g/dL in otherwise fit individuals

GPP

There is no fixed algorithm for replacement and transfusion of specific components is best guided by ongoing laboratory testing. It is also important in such situations to keep in close communication with the Blood Services Group (BSG), Health Sciences Authority or doctor on call.^{34, 36, 72-78}

Disseminated Intravascular Coagulation can complicate any major blood loss and should actively be borne in mind. This can be a consequence of delayed or inadequate resuscitation and manifest by the onset of microvascular bleeding and abnormalities in the coagulation screen. Haematological advice should be sought.^{34, 36, 72-74, 76, 78}

In exceptional circumstances, if blood is required immediately, emergency stock Group O blood will be issued.^{34,36-38} 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. In most instances however, it is usually possible to resuscitate the patient with crystalloids or colloids while waiting for crossmatched compatible blood. Blood Services Group, Health Sciences Authority should be notified beforehand and advice sought if emergency unmatched blood is to be used.

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

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.^{34, 72-73}

Grade D, Level 4

Table 2 Summary of key recommendations on management of massive blood loss

[Source: BJH Guidelines on the management of massive blood loss (2006)] (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 	<p>Results may be affected by colloid infusion</p> <p>Ensure correct patient identification</p> <p>May need to give components before result available</p>

Goal	Procedure	Comments
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.

3 Platelet transfusion

3.1 General considerations

Thrombocytopenia does not always correlate with abnormal bleeding, hence the decision for platelet transfusion should not be based on platelet counts alone but take into consideration the clinical situation of the patient and other risk factors for bleeding. These include fever or sepsis, the presence of other associated coagulopathies, coexistent medical conditions including liver disease and renal failure and the rapidity of fall of the platelet count.

There is no difference in the efficacy, post-transfusion yield, haemostatic efficacy and frequency of transfusion reactions between apheresis platelets and whole blood derived platelets provided the same quantity of platelets are given.⁷⁹ The major risk of platelet transfusion is bacterial contamination (1:10 000) There is also the risk of human leucocyte antigen (HLA) alloimmunization with platelet transfusion.^{60, 80}

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

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.⁸⁰

Grade D, Level 4

GPP The cause of thrombocytopenia should always be established before considering platelet transfusion unless there is life threatening bleeding

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.^{14, 60, 80} 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.

Grade D, Level 4

3.2 Platelet products

Apheresis platelet unit

This is prepared from a single donor and contains at least 3.0×10^{11} platelets suspended in 200 to 400ml of plasma. Platelets collected by apheresis are usually leucocyte depleted, with a residual leucocyte count of less than 5×10^6 in each pack. In general, if leucocyte depleted platelets are indicated, apheresed products will be provided.⁸¹⁻⁸²

Random donor platelet unit

This is prepared from units of whole blood collected from random donors and contains at least 5.5×10^{10} platelets suspended in 40 to 70 ml of plasma.⁸¹⁻⁸²

One unit of apheresis platelets is equivalent to 4-6 units of random donor platelet units.⁸¹⁻⁸²

An adult dose of platelets (1 unit of random donor platelet concentrate/10 kg body weight or one unit of apheresis platelets) should usually raise the platelet count by $20-40 \times 10^9$ /L, if there are no other concomitant factors.⁸²

3.3 Platelet compatibility

B As ABO antigens are present on platelets, it is preferable to transfuse with ABO compatible platelets.^{60, 83-85}

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.

GPP

D For paediatric recipients (of less or equal to 45 kg body weight), ABO specific platelets should be ensured whenever possible. Cross matching of platelets is not necessary.⁶⁰

Grade D, Level 4

Although Rhesus antigens are not present on platelets, residual red cells may be present in the platelet concentrates.

C The concomitant administration of at least 250IU 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) allo-immunisation.^{68-69, 86-87}

Grade C, Level 2+

B Apheresed platelets are recommended to prevent human leucocyte antigen (HLA) alloimmunisation and platelet refractoriness in patients who require prolonged platelet support.⁸⁸⁻⁹³

Grade B, Level 1+

3.4 Indications for therapeutic platelet transfusion

3.4.1 For Haemostasis

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.⁹⁴⁻⁹⁷

Grade B, Level 2++

Thrombocytopenia is commonly present in critically ill patients with massive blood transfusion.

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.^{64, 77, 98-99}

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.^{14, 60, 100}

Grade D, Level 4

3.4.2 For patients with platelet dysfunction

Platelet dysfunction can be caused by inherited conditions such as Glansmann's Thrombasthenia, Bernard Soulier Syndrome. It can also be acquired in renal failure and in use of antiplatelet drugs such as aspirin and clopidogrel.^{60, 101-103} In these situations, the platelet count is less useful and the decision to transfuse should be based on clinical circumstances.

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

GPP

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

- Correct the hematocrit to >0.30 .¹⁰⁴⁻¹⁰⁵
- Consider the use of desmopressin.^{60, 106-107}
- Consider the use of dialysis, which also have hemostatic benefits in this situation.¹⁰⁸⁻¹⁰⁹
- Only use platelet transfusions where the above methods are inappropriate or ineffective.⁶⁰

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.⁶⁰
- Consider platelet transfusion in acute bleeding situation.

Grade D, Level 4

3.5 Prophylactic platelet transfusion (to prevent bleeding)

Prophylactic platelet transfusion is recommended in the following conditions:

B In patients with impaired bone marrow function when platelet count is less than $10 \times 10^9/L$ and there are no other risk factors.^{60, 95, 110-114}

Grade B, Level 1+

C In patients with impaired bone marrow function when platelet count is less than $20 \times 10^9/L$ and there are concomitant risk factors (e.g. sepsis, rapid fall of platelet count or coagulation abnormalities).^{94, 114-122}

Grade C, Level 2+

In patients with dengue fever who experience a rapid fall in platelet count or in the presence of prolonged clotting times, are thought to demonstrate a haemorrhagic state.¹²³⁻¹²⁴

D More liberal approach to prophylactic platelet transfusion should be practised. A transfusion trigger at platelet count of $30 \times 10^9/L$ is acceptable. Consultation with the haematologist or transfusion specialist is advised in individual cases where bleeding is thought to be a major risk factor.¹²³⁻¹²⁴

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 $50 \times 10^9/L$ and there are no other associated coagulopathies.^{60, 125-130}

Grade C, Level 2+

D Neurosurgical and ophthalmic procedures may benefit from a higher prophylactic platelet transfusion threshold ($100 \times 10^9/L$).⁶⁰

Grade D, Level 4

3.6 Contraindications

B Platelet transfusion is contraindicated if the thrombocytopenia is due to platelet activation.¹³¹⁻¹³⁵

Grade B, Level 2++

Platelet activation or aggregation is a contributory factor in the pathogenesis of these conditions such as thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome¹³¹⁻¹³³ and heparin induced thrombocytopenia.^{60, 134-135} As such, administering platelet transfusion would only serve to aggravate the underlying condition.

D Platelet transfusion is usually not indicated when thrombocytopenia is related to immune mediated platelet destruction,^{60, 136-138} such as autoimmune thrombocytopenia, drug-induced thrombocytopenia and post transfusion purpura¹³⁹. Platelet transfusions are only indicated when there is significant and/or potentially life threatening bleeding in such conditions.

Grade D, Level 4

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

GPP

4 Fresh frozen plasma transfusion

Fresh frozen plasma is prepared either from whole blood donations or from plasma collected by apheresis and contains near-normal plasma levels of coagulation factors, albumin and immunoglobulins.¹⁴⁰ Its use should be limited to the replacement of coagulation factors and there are limited situations where this becomes necessary.¹⁴¹

General considerations:

D Routine and timely tests for coagulopathy such as the prothrombin time (PT) or international normalized 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.⁶⁴ These results should be integrated with a thorough assessment of the patient's clinical condition and the presence or risk of bleeding.

Grade D, Level 4

B Abnormal prothrombin time (PT)/international normalized ratio (INR) or activated partial thromboplastin time (APTT) results should not be the sole reason 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.¹⁴²⁻¹⁴⁴

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.

GPP

GPP A comprehensive personal and family history of bleeding is the best pre-operative screen for bleeding in surgical patients. In the event that pre-operative prothrombin time (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.

GPP

4.1 Indications for fresh frozen plasma

Fresh frozen plasma is recommended for the following situations:

B Massive blood transfusion, especially with evidence of microvascular bleeding and associated with significant (>1.5x midpoint of normal range) abnormalities in prothrombin time (PT) and activated partial thromboplastin time (APTT).⁷⁴ When PT and APTT cannot be obtained in a timely fashion, it is **reasonable** to give fresh frozen plasma after replacement of one blood volume while waiting for results.¹⁴⁵

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.¹⁴⁶⁻¹⁴⁷

Grade B, Level 2++

C Acute disseminated intravascular coagulation (DIC) associated with microvascular bleeding and abnormal coagulation profile.^{71, 148}

Grade C, Level 2+

D Bleeding due to coagulopathy associated with chronic liver diseases.²

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.¹⁴⁹⁻¹⁵¹

Grade A, Level 1+

C Bleeding associated with clotting factors deficiency if no alternative processed products or specific factor concentrates are available.^{2, 71}

Grade C, Level 2+

Fresh frozen plasma is **not justified** in the following situations:

D As a volume expander in hypovolaemia.^{71, 152}

Grade D, Level 4

D As replacement for albumin or immunoglobulin.¹⁵²⁻¹⁵³ Specific albumin and immunoglobulin preparations are available.

Grade D, Level 4

D Replacement for any clotting factors unless processed and virally inactivated products are unavailable.^{71, 152}

Grade D, Level 4

B Reversal of warfarin effect in the absence of bleeding.^{71, 152} Oral or intravenous vitamin K should be the therapy of choice in this instance.^{71, 147, 154}

Grade B, Level 2++

C Plasma exchange procedures other than for thrombotic thrombocytopenic purpura (TTP)/haemolytic uraemic syndrome (HUS).^{71, 152, 155}

Grade C, Level 2++

D Treatment of immunodeficiency states.¹⁵²

Grade D, Level 4

D Nutritional support.¹⁵²

Grade D, Level 4

4.2 Dose and compatibility

D The recommended dose for fresh frozen plasma is 10-15 ml per kg body weight.^{71, 152-153} It is always useful to have fresh frozen plasma administration guided by coagulation screens. If necessary, these should be repeated and more fresh frozen plasma (FFP) given, depending on the clinical situation.^{71, 153}

Grade D, Level 4

Fresh frozen plasma (FFP) units are labelled with the donor ABO and Rh(D) group. ABO compatible FFP should be used although compatibility testing is not required.

Group O FFP should only be used for Group O recipients although the latter can also receive Group A and B FFP if Group O FFP is unavailable. (See table below).

Patient ABO Group	Donor FFP ABO Group
O	O, A, B or AB
A	A or AB
B	B or AB
AB	AB

B Although small amounts of red cell stroma may be present in fresh frozen plasma (FFP), it is less immunogenic than intact red cells and sensitisation following Rh(D) positive FFP to Rh(D) negative patients is unlikely.¹⁵⁶ FFP of any Rh type may be given regardless of Rh status of the patient.

Grade B, Level 2++

5 Cryoprecipitate transfusion

5.1 Indications for cryoprecipitate

C Cryoprecipitate is rich in Factor VIII, von Willebrand factor, Factor XIII and fibrinogen. Use of cryoprecipitate is considered **appropriate** when there is bleeding associated with hypofibrinogenaemia (fibrinogen level < 1.0gm/L) in the following conditions:^{71, 157-158}

- 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

Grade C, Level 2+

D Cryoprecipitate may be used during bleeding in congenital Factor XIII deficiency when Factor XIII concentrate is not available.¹⁵⁹

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.¹²³

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.¹⁵⁹

Grade D, Level 4

5.2 Dose and compatibility

C In the management of hypofibrinogenaemia, 1 unit/5 kg body weight - equivalent to 10 units for an average size adult - should be administered. Further therapy should be guided by fibrinogen levels.⁷¹

157-159

Grade C, Level 2+

As far as possible, group compatible cryoprecipitate will be provided. However, the issue of compatibility is less crucial in cryoprecipitate due to the small volumes of plasma present.⁷¹

6 Safety issues related to blood and blood component transfusion

6.1 Blood safety

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.

GPP

The current criteria for blood donation are:

- Age:
16 to 60 years
(16 & 17 year-olds can donate with parental / guardian consent)
- Weight:
At least 45 kg (100 lbs) for both males and females
- Well being:
In generally good health and feeling well that day. Not having colds, coughs or flu in the last one week. No fever (temperature $>38^{\circ}\text{C}$) in the last 3 weeks.
- Haemoglobin level:
At least 12.5g/dL for both males and females

Up-to-date information on eligibility for blood donation can be found on the **website www.hsa.gov.sg/donationcriteria**.

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).

GPP

6.2 Ensuring safe blood

C Blood donations should be collected from the safest possible donors, namely regular voluntary donors.^{25,160-161}

Grade C, Level 2+

The first and most important line of defence against transfusion-transmitted infection is the collection of blood from the safest possible donors. Evidence from around the world demonstrates that patients who receive blood from regular voluntary donors are at the lowest risk of contracting blood-borne pathogens from the transfusion.¹⁶²⁻¹⁶⁵ These donors are motivated solely by altruism and have no reason to conceal why their blood may be unsafe.

C Replacement or directed donations should be avoided as far as possible.¹⁶⁶⁻¹⁶⁸

Grade C, Level 2+

Experience in Singapore between 1990 and 1996, and internationally have shown that family replacement donors have a higher probability of transfusion transmissible infections among these donors due to psychological pressure placed on them to donate.¹⁶⁶⁻¹⁶⁸

Neither the system of individual replacement or directed donations are practised by Blood Services Group, Health Sciences Authority. Family and friends of patients may be encouraged to donate blood for the general blood inventory, as part of community responsibility. Distribution of blood and provision of blood to patients is strictly dependant on clinical need, and never influenced by the provision of replacement donors.

Directed donation is not practised except where there is specific medical indication. This includes the selection of specific donors to provide patient-specific products in cases of multiple red cell antibodies, platelet refractoriness, or neonatal alloimmune thrombocytopenia.

D Irradiated blood components are indicated in bone marrow/stem cell auto- or allo- grafting, and transfusions from relatives or human leucocyte antigen (HLA)-selected platelet donors.^{29, 169}

Grade D, Level 3

There is a higher risk of fatal transfusion associated graft versus host disease.^{8,9,170} when using blood from first degree relative or human leucocyte antigen (HLA)-selected platelet donors which is not irradiated.

6.3 Infectious and non-infectious risks for blood transfusion

The risk of blood transfusion can be divided into infectious and non infectious risks. These range from common to rare but nevertheless, when it happens, can be life threatening and have severe consequences. Table 1 illustrates the infectious risk and their estimated frequencies in some developed countries. These are internationally quoted figures and although may not accurately reflect the situation in Singapore, it nonetheless provides a rough estimation for the infectious risk in blood transfusion.

In the local context, there have been no documented and proven cases of HIV, Hepatitis B or Hepatitis C infection in the past 6 years. Locally, HTLV is not a problem (results from an in-house study) and hence testing is not mandatory.

Table 2 summarises the local experience from the haemovigilance programme intended to capture the local hazards of clinical transfusion.

This haemovigilance programme has been in place since 2002 and relies on a voluntary, anonymous and non punitive mode of reporting from the hospitals. Thus far, all hospitals in Singapore have participated in this programme.

The 3 transfusion transmitted infections involve bacteria in one instance, dengue and a possible hepatitis B which could not be confirmed.

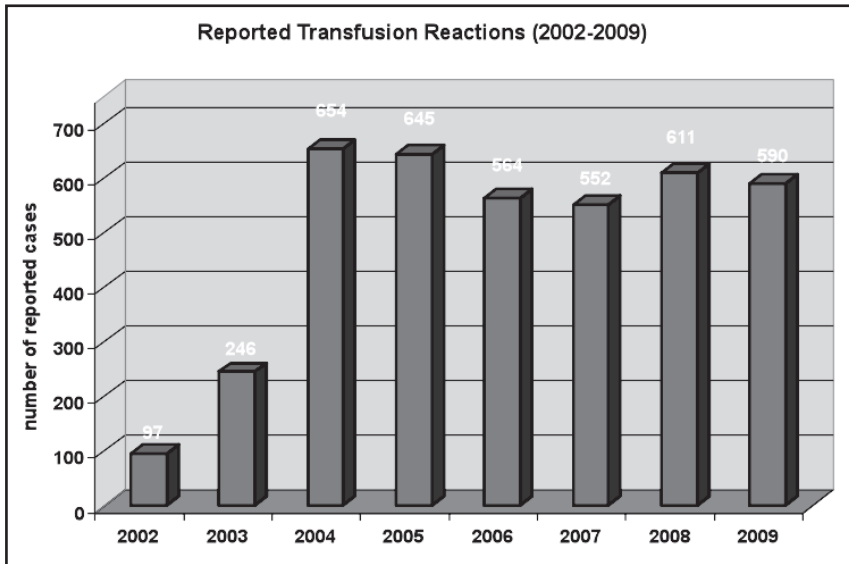
The data demonstrates that incorrect blood (ICBT) including ABO incompatible transfusion still occurs.

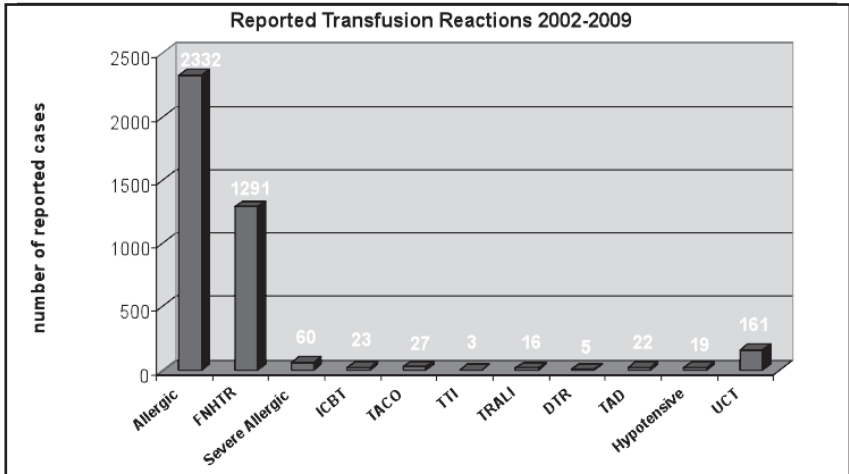
A recent report from Serious Hazards of Transfusion (SHOT) from United Kingdom has demonstrated that serious complications (e.g. intravascular haemolysis, transfusion-induced coagulopathy, renal impairment and failure, admission to intensive care, persistent viral infection, and death) occur at a rate of 1 in 67,000; deaths related to blood transfusion occur at a rate of about 1 in 250,000 to 300,000 (47 deaths in 12 millions blood components).

Table 1 Estimated Risk of Transfusion Transmitted Infections (TTI)^{26,171}

TTI	Estimated risk per unit	References
HIV	1 / 493,000 (pre-NAT) >1 / 2,000,000 to 9,000,000 (post-NAT)	Schreiber (1996), Wylie (2001), Holland (2001)
Hepatitis B	1 in 400,000 - 66,000 (pre-NAT)	Schreiber (1996), Wylie (2001), Muller (2001), Dodd (2001)
Hepatitis C	1 / 125,000 (pre-NAT) 1 / 1,000,000 - 277,500 (post-NAT)	Schreiber (1996), Holland (2001), Wylie(2001)
Hepatitis A	1/1,000,000	Dodd (1994)
HTLV types 1 and II	1/641,000 1 in 24,000 - 3,300	Schreiber (1996) Luban (1994)
Parvovirus B19	Red cell : 1 in 500,000 - 65,000	Theakston (1997), CDC report (1997), SHOT report (1999)
Bacteria contamination	Platelet : 1 in 20,000 - 10,000	Dodd (1994)

Table 2





Allergic – Mild to Moderate Allergic Reactions

Severe Allergic – Anaphylactic Reaction

Hypotensive reactions

FNHTR - Febrile Non Haemolytic Transfusion Reaction

TACO - Transfusion Associated Circulatory Overload

TAD - Transfusion Associated Dyspnea

TRALI - Transfusion Related Acute Lung Injury

DTR - Delayed Transfusion reactions (Haemolytic and Serologic)

TTI - Transfusion Transmitted Infections (including septic transfusion reactions)

ICBT - Incorrect Blood Transfused

UCT - Unclassifiable Complications of Transfusion

7 Adverse reactions to transfusion

An **adverse reaction** to transfusion is defined as an undesirable response or effect in a patient temporally associated with the administration of blood or blood component.¹⁷² It may be the result of an incident or of interaction between a recipient and blood, a biologically active product.

Each blood or blood component transfused carries a risk of an acute or delayed effect and for this reason; physicians prescribing the transfusion should carefully select patients who will benefit from transfusion therapy according to established criteria. The indication for transfusion should be documented in the medical record.

The aim of this guideline is to provide the hospital doctor, with the necessary tools to recognize transfusion reactions and to concentrate on their immediate management. When an adverse transfusion reaction occurs, medical and nursing personnel must be prepared to recognize both acute (immediate) and delayed reactions, and be ready to provide the immediate management. Because the signs and symptoms of different types of adverse reactions overlap and their severity can vary considerably, all transfusions must be carefully monitored and stopped as soon as symptoms of a reaction appear. Early recognition is the key to minimizing serious complications.

Adverse reactions to transfusion can be categorized into acute (immediate) and delayed. Acute (immediate) reaction usually presents within minutes to hours but usually within 24 hours of the transfusion. Acute reactions can be further divided into subgroups of presenting signs and symptoms: fever and or chills, hives or urticaria, dyspnea and hypotension.¹⁷³

Figure 1 An approach to diagnosing the type of likely transfusion related adverse event

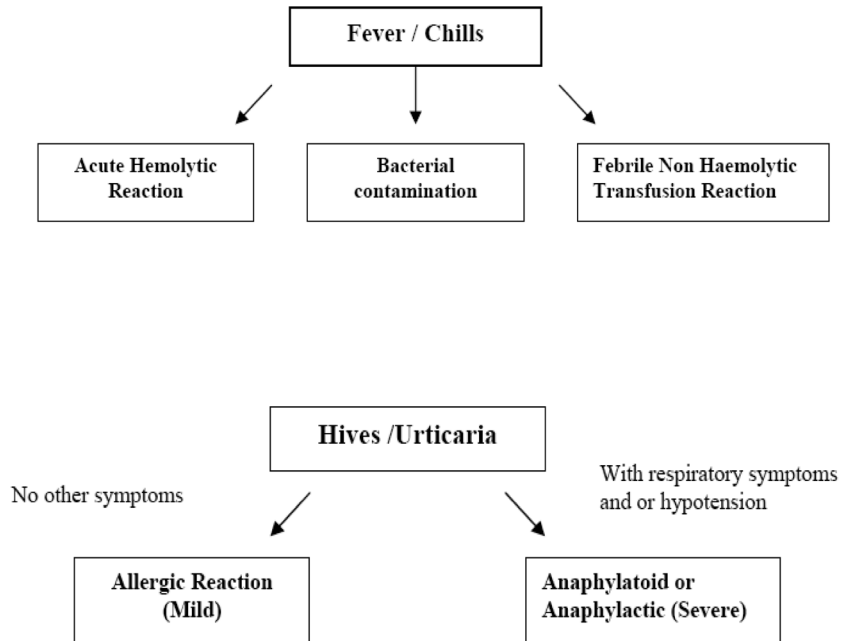
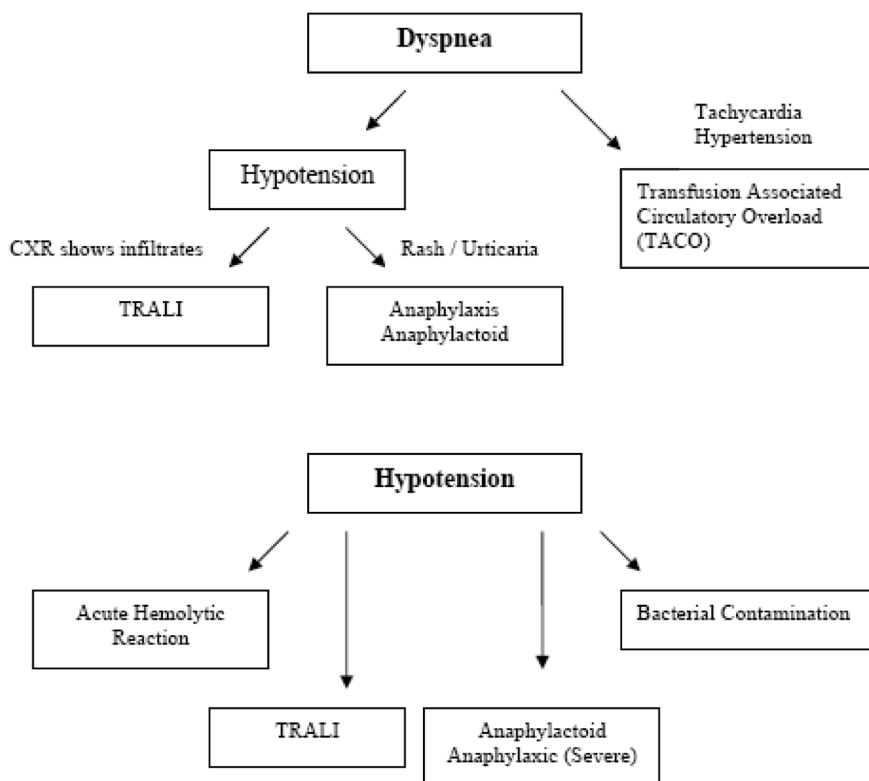


Figure 1 An approach to diagnosing the type of likely transfusion related adverse event (continuation)



Allergic reactions and febrile non haemolytic transfusion reactions are **common** but **less serious** whereas acute haemolytic reactions, bacterial contamination, Transfusion Related Acute Lung Injury and anaphylactic reactions are **less common** but **life threatening**.

Acute haemolytic reaction is commonly due to **misidentification** of the patient and therefore **positive identification of the patient at the bedside** when taking blood for crossmatch and before commencing transfusion is the Most Important step in the **prevention** of this complication.

Delayed transfusion reactions usually manifest **days or weeks** after the completion of blood transfusion. Recognition of signs and symptoms and correlation with an earlier transfusion can aid in the correct management of the patient and in some cases even reduce the potential complications.

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.

GPP

GPP Institutional policies may vary regarding the initial steps in managing an adverse reaction but the following key elements should be followed:¹⁷⁴

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.

GPP

D

Categories and management of acute and delayed adverse reactions to transfusion.^{25, 172, 175-176} Grade D, Level 3

Type	Incidence/ Aetiology	Diagnostic Criteria/ Presentation	Diagnostic testing	Management
<p>Acute – within 24 hours of transfusion</p> <p>Allergic Reaction (Mild)/ Urticarial</p> <ul style="list-style-type: none"> Interaction of an allergen with preformed antibodies 	<ul style="list-style-type: none"> Morbiliform rash with or without pruritis Urticaria (hives) Flushing Localized angioedema 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> 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 	
<p>Anaphylactoid Anaphylaxis (Severe)</p> <ul style="list-style-type: none"> Antibody to donor plasma protein (IgA, Haptoglobin, C4) 	<ul style="list-style-type: none"> Mucocutaneous symptoms Hypotension Respiratory signs and symptoms may be laryngeal (tightness in throat, dysphagia, dysphonia, hoarseness, stridor) or pulmonary (dyspnea, cough, wheezing, bronchospasm, hypoxemia) 	<ul style="list-style-type: none"> Rule out haemolysis 	<ul style="list-style-type: none"> 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 	
<p>Haemolytic Reaction</p> <ul style="list-style-type: none"> Incompatible blood transfusion results in antigen/antibody response with activation of complement and subsequent intravascular haemolysis 	<ul style="list-style-type: none"> Chills/rigors Fever Back/flank pain Hypotension Haemoglobinuria Oliguria / anuria Disseminated intravascular coagulation Pain or oozing at IV site 	<ul style="list-style-type: none"> Clerical Check Check for Haemolysis <ul style="list-style-type: none"> Direct Coombs test Visual inspection Repeat patient ABO, pre and post sample Further tests to detect haemolysis (LDH, Bilirubin, etc.) 	<ul style="list-style-type: none"> 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 	
<p>Febriile Non Haemolytic Transfusion Reaction</p> <ul style="list-style-type: none"> Cytokines Antibody to donor white cells 	<ul style="list-style-type: none"> Fever ($\geq 38^{\circ}\text{C}$ or a change of $\geq 1^{\circ}\text{C}$ from pre transfusion value) Chills / Rigors Headache Vomiting 	<ul style="list-style-type: none"> Rule out haemolysis Rule out bacterial contamination 	<ul style="list-style-type: none"> Initiate transfusion reaction workup; inform Blood Bank Leucoreduced components Premedication with antipyretics 	
<p>Transfusion Associated Acute Lung Injury (TRALI)¹⁷⁷</p> <ul style="list-style-type: none"> Anti-human leucocyte antigen (HLA) and anti-HNA antibodies in donor (occasionally in recipients) 	<ul style="list-style-type: none"> Acute respiratory distress within six hours of transfusion Bilateral pulmonary infiltrates on chest xray Hypoxemia ($\text{O}_2 \text{ sat} \leq 90\%$ on room air or $\text{PaO}_2 \leq 300 \text{ mm Hg}$) No evidence of circulatory overload Hypotension (some cases hypertension) Fever Transient Leucopenia 	<ul style="list-style-type: none"> Rule out haemolysis Rule out cardiogenic oedema Human leucocyte antigen (HLA) antibody screen Chest Xray 	<ul style="list-style-type: none"> Maintain airway; provide oxygen and ventilatory support Treat Hypotension Supportive care Initiate transfusion reaction workup; inform Blood Bank 	

Type	Incidence/Aetiology	Diagnostic Criteria/ Presentation	Diagnostic testing	Management
Acute – within 24 hours of transfusion				
Transfusion Associated Circulatory Overload (TACO)	<ul style="list-style-type: none"> Volume overload 	<ul style="list-style-type: none"> Acute respiratory distress (dyspnea, orthopnea, cough) Tachycardia Hypertension Evidence of left sided heart failure 	<ul style="list-style-type: none"> Rule out TRALI Chest Xray 	<ul style="list-style-type: none"> Maintain airway; provide oxygen and ventilatory support Diuretics Initiate transfusion reaction workup; inform Blood Bank
Transfusion Associated Sepsis (Bacterial Contamination)	<ul style="list-style-type: none"> Sepsis is the result of transfusion of disseminated blood components The bacteria may originate from the blood donor either from spontaneous (e.g. Staphylococcus, Streptococcus) or unsuspected bacteremia (e.g. Yersinia) but may also result from donor unit processing 	<ul style="list-style-type: none"> Fever, often $\geq 2^{\circ}\text{C}$ rise from baseline Chills / Rigors Hypotension Shock Renal failure Unexplained bleeding from mucocutaneous or infusion sites 	<ul style="list-style-type: none"> Rule out haemolysis Gram stain Component culture Blood culture on patient 	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Alloimmune immune response to red cell antigens 	<ul style="list-style-type: none"> Decrease in haemoglobin Fever Jaundice (Mild) Patient may be asymptomatic 	<ul style="list-style-type: none"> Antibody screen and Identification Direct Coombs test Elution Test for haemolysis 	<ul style="list-style-type: none"> Initiate Delayed transfusion reaction workup; inform Blood Bank Transfuse AHG crossmatch compatible blood; antigen negative if indicated
Graft Versus Host Disease (GVHD)	<ul style="list-style-type: none"> Donor lymphocytes engraft in recipient and mount attack on host tissues 	<ul style="list-style-type: none"> Fever Gastrointestinal symptoms Rash Hepatitis Pancytopenia 	<ul style="list-style-type: none"> Skin biopsy Human leucocyte antigen (HLA) typing Molecular Analysis for Chimerism 	<ul style="list-style-type: none"> Immunosuppressive agents Irradiation of blood components for patients at risk

8 Cost-effectiveness issues

In Singapore, blood donation is voluntary and blood donors donate freely to the community. However, there is a cost to the collection, processing, testing, storage and distribution of the blood and blood products. These constitute the *blood processing fee* for blood and blood components that is charged to hospitals.

Processing fees for blood and blood products are uniform across all hospitals in Singapore, and are regularly reviewed and updated. The government subsidises as much as 50% of the blood processing fee for Singaporeans. This is further subjected to the subsidy provided for the different class of wards in public hospitals.

The blood processing fee does not include other transfusion-related processes within the hospital – pre-transfusion compatibility tests performed in the hospital transfusion laboratory, maintaining the cold chain of blood components, management of transfusion reactions, clerical routines, informed consent procedures, administering and monitoring of the blood components.

From a societal perspective, the true cost of blood transfusion would also include cost incurred to donors (including transportation and donors' opportunity cost), cost of lost productivity, cost of managing and distributing national inventory, cost of emergency preparedness, and cost of organizing and maintaining nationwide haemovigilance.

The safety of blood transfusion in Singapore, as in other developed countries, is at a high level and at high costs. The addition of new strategies to expand current safety strategies further will continue to increase cost-utility ratios. In transfusion safety, the drive towards zero-risk blood transfusion means that the accepted threshold of costs per quality adjusted life year gained is sometimes exceeded by more than 100-times.

In addition to the rising costs associated with blood transfusion, there is also major concern in both developed and developing countries as to how long the blood donor base can be stretched before the demand for blood outstrips supply. It is therefore important to assess the effectiveness of the various interventions against competing therapies, and to balance the benefits against the impact of possible transfusion-related adverse outcomes.

The need for allogeneic transfusions can be significantly reduced or completely avoided in some patient populations. Strategies that can be utilized include pre-operative anaemia diagnosis and treatment with haematinics and erythropoiesis-stimulating agents, surgical techniques and devices combined with haemostatic agents and anaesthetic techniques to minimize blood loss, autologous blood recovery with acute normovolemic haemodilution and intra and postoperative cell salvage, and targeted fluid management crystalloid solutions.

In the long term, clinicians need to move away from blood transfusion as the default settings, into more intelligent strategies that are utilized in a patient-specific manner. This has the potential of improving the health and quality of life of patients in the future more cost effectively.

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning - Verifiable Self Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: <http://smj.sma.org.sg/cme/smj/index.html> (*the link will only be available once the March 2011 issue of the SMJ becomes available*). The answers will be published in the SMJ May 2011 issue and at the MOH webpage for these guidelines after the period for submitting the answers is over.

Instruction: Indicate whether each statement is True or False.

	True	False
1. Transfusion of red cells		
A) 1 unit of packed cell has volume of approx 400ml.	<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) Pre-operatively, patients should be transfused to Hb level of >10g/dl where possible.	<input type="checkbox"/>	<input type="checkbox"/>
D) All patients should be transfused when their Hb is <7g/dl.	<input type="checkbox"/>	<input type="checkbox"/>
2. 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 Haemoglobin 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"/>

		True	False
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 a 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) the fresh frozen plasma must always be ABO and Rhesus compatible.	<input type="checkbox"/>	<input type="checkbox"/>
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"/>
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 & 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"/>

Workgroup members

The members of the workgroup, who were appointed in their personal professional capacity, are:

Chairperson Dr Mickey Koh Boon Chai
Division Director
Patient Services
Blood Services Group
Health Sciences Authority;
Director
Stem Cell Transplant Programme
Senior Lecturer & Consultant
St George's Hospital & Medical School
London, United Kingdom

Members

Dr Diana Teo Lay Tin
Group Director &
Senior Consultant
Blood Services Group
Health Sciences Authority

Dr Tan Hwee Huang
Division Director
Blood Supply Division
Blood Services Group
Health Sciences Authority

A/Prof Lee Lai Heng
Head & Senior Consultant
Dept of Haematology
Singapore General Hospital;
Clinical Associate Professor
Yong Loo Lin School of
Medicine;
National University Singapore
Adjunct Associate Professor
Duke-NUS Graduate
Medical School

Dr Lim Lay Cheng
Senior Consultant
Dept of Haematology
Singapore General Hospital

Dr Ting Wen Chang
Haematologist
Haem-Onc Clinic Pte Ltd

Dr Ng Heng Joo
Senior Consultant
Dept of Haematology
Singapore General Hospital

SNM Chong Lai Ling
Senior Nurse Manager
Ward 72
Singapore General Hospital

Dr Tan Lip Kun
Senior Consultant
Dept of Haematology Oncology
National University Health System

Members

A/Prof P. Kuperan
Head & Senior Consultant
Dept of Haematology
Tan Tock Seng Hospital

A/Prof Tay Kiang Hiong
Head & Senior Consultant
Dept of Diagnostic Radiology
Singapore General Hospital

Prof Alex Sia
Head & Senior Consultant
Dept of Women's Anaesthesia
KK Women's & Children's
Hospital

Dr Philip Iau
Senior Consultant
Dept of Surgery
National University Hospital

Dr Yong Tze Tein
Senior Consultant
Obstetrics & Gynaecology
Singapore General Hospital

A/Prof Goh Lee Gan
Associate Professor
Head, Division of Family Medicine
University Medicine Cluster
National University Health System;
President
College of Family Physicians
Singapore

Subsidiary editors:

Dr Pwee Keng Ho
Deputy Director (Health Technology Assessment)
Health Services Research & Evaluation Division
Ministry of Health

Dr Jeff Loke
Medical Officer
Health Services Research & Evaluation Division
Ministry of Health

Acknowledgement:



Dr Edwin Chan Shih-Yen
Head, Epidemiology
Singapore Clinical Research Institute
Assoc Professor, Duke-NUS Graduate Medical School, Singapore
Director, Singapore Branch, Australasian Cochrane Centre;
Head (Evidence-based Medicine)
Health Services Research & Evaluation Division
Ministry of Health

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Ministry of Health, Singapore

College of Medicine Building

16 College Road

Singapore 169854

TEL (65) 6325 9220

FAX (65) 6224 1677

WEB www.moh.gov.sg

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