GUIDELINES FOR MANAGEMENT OF ADVERSE TRANSFUSION REACTIONS

REACTION/CAUSE	SIGNS & SYMPTOMS	PREVENTION	MANAGEMENT
Febrile (non haemolytic) Transfusion Reaction (FNHTR) **Frequency:** 1-3:100 (higher in multi transfused recipients) • Common • Onset during or within 4 hours following transfusion ➢ Reaction induced by cytokines ➢ Other causes may exist	• **Mild:** unexplained fever ≥38°C and a temperature rise of at least 1°C but <1.5°C from pre-transfusion baseline, occurring in the absence of chills, rigors, respiratory distress and haemodynamic instability • **Moderate:** unexplained fever ≥38°C and a temperature rise of at least 1°C but not meeting criteria for either mild or severe FNHTR • **Severe:** unexplained fever >39°C and a temperature rise ≥2.0°C from pre-transfusion baseline and chills/rigors • Associated or secondary symptoms may be present: tachycardia, headache, nausea, flushing, anxiety, hypertension or occasionally hypotension • In severe cases: marked apprehension, loin pain, and/or angina	• Check for history of previous transfusion reactions. Consider pre-transfusion antipyretic Paracetamol 1g po where minor reactions occur and further transfusions are required • Consult TMS if recurrent reactions occur • Note: all blood components are leucocyte-depleted during production. Further leucodepletion at the bedside is not required	• Check label and recipient identity • Slow the transfusion if reaction is mild and MO elects to continue transfusion • Send Haemovigilance notification to Blood Bank • Antipyretic Paracetamol 1g po and monitor closely • Steroids are not appropriate treatment for minor reactions

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Allergic Reaction (minor) **Frequency:** 1:100 - 1:500 • More common with Plasma and Platelet Components • Onset: from commencement to 4 hours after transfusion ➢ Recipient may have an antibody reacting with an antigen in the transfused product	**Minor or localised reaction:** • Flushed skin • Morbilliform rash with itching • Urticaria (hives) • Angioedema • Periorbital itch, erythema and oedema • Conjunctival oedema • Minor oedema of lips, tongue and uvula	• For recurrent mild reactions prophylaxis with antihistamine to alleviate symptoms, eg Loratadine 10mg or Cetirizine 10mg po • Routine prophylaxis for all recipients before transfusion is not indicated	• Slow transfusion • Check label and recipient identity • Antihistamine, eg Loratadine 10mg or Cetirizine 10mg po if symptoms are troublesome • If symptoms mild and transient, transfusion may resume • Continue transfusion at a slower rate with increased monitoring, eg BP/TPR 15 – 30min • Send Haemovigilance notification to Blood Bank • If symptoms increase treat as a moderate or severe reaction
Allergic Reaction (moderate) **Frequency:** 1:500–1:5,000 • Onset usually within first 50-100 mL infused and within 4 hours of transfusion • Recipient may have an antibody reacting with a plasma protein or leucocyte antigen (HLA or other) in the transfused product	**Moderate or widespread reaction:** • Symptoms as for minor reactions, and - • Cough • Hypotension and tachycardia • Dyspnoea and oxygen desaturation are common • Chills and rigors • Loin pain and angina • Severe anxiety	• Discuss with TMS if recurrent. • Note: Prophylactic treatment with an antihistamine or hydrocortisone will not reliably prevent moderate and severe allergic reactions but may alleviate symptoms when present	• Stop transfusion • Check label and recipient identity • Replace IV set and give saline to keep vein open and/or maintain BP • Monitor closely and treat symptomatically as required with IV fluids, oxygen and antihistamine, eg Promethazine 25-50 mg IV (max rate 25 mg/min) or Loratadine 10mg or Cetirizine 10mg po. Hydrocortisone may be considered • Send Haemovigilance notification to Blood Bank • Discuss with TMS promptly if mod - severe reaction present

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Anaphylactic / Anaphylactoid Allergic Reaction (severe) **Frequency:** 1:20,000 – 1:50,000 • Rapid onset ➢ May be due to an antibody in the recipient reacting with a plasma protein in a blood component ○ IgA ○ Haptoglobin ○ Other plasma protein	**Life-threatening reaction:** • Symptoms as for moderate reactions, and - • Severe hypotension, shock and tachycardia • Widespread urticaria with skin flushing and itching • Wheezing, stridor, change in voice • Severe anxiety • Note: Respiratory symptoms may dominate in anaesthetised recipients	Discuss with TMS before requesting: • IgA deficient blood/blood products may be appropriate if recipient is known to have absolute IgA deficiency or to have anti-IgA • Washed cellular components may be indicated where the cause of the reaction is not identified	• Stop transfusion • Check label and recipient identity • Follow Anaphylaxis Guidelines: ○ Adrenalin 1:1000 IM and repeat at 5-10 min intervals if required: - Adult: 0.5mg / 0.5 mL - Children 0.01mg/kg IM; min dose 0.1mL, max dose 0.5mL ○ Replace IV set and give rapid IV colloid or saline, eg adults 2 L, children 20 mL/kg, until SBP>90 mmHg, then titrate ○ Consider Hydrocortisone 4mg/kg (200-400 mg IV) ○ Consider H1-antihistamine, eg Loratadine or Cetirizine 10 mg po for itch or angioedema. ○ H2-antihistamine, eg Ranitidine may be added for severe reactions. ○ Note: Sedating antihistamines, eg Promethazine contraindicated • CPAP ventilation, chest X-ray • ICU liaison • Follow NZRC Guidelines if no pulse present and for symptoms that persist after initial treatment • Collect serum tryptase sample within 1-2 h if anaphylaxis may be present (returns to normal within 6-8 h) • Send Haemovigilance notification to Blood Bank • Discuss severe reactions with TMS

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Hypotensive Reaction **Frequency:** 1-2:1,000 ➢ Often idiosyncratic reaction	• Hypotension – fall in systolic BP >30 mm Hg during or within 1 h of completing transfusion **and** systolic BP ≤80 mm Hg		• Stop transfusion • Replace the IV infusion set and infuse saline to manage BP • Symptomatic management until resolved • Send Haemovigilance notification to Blood Bank
Acute Haemolytic Reaction **Frequency:** 1:12,000–1:100,000 • Onset within 24 hours, usually immediate ➢ ABO or other incompatible red cell transfusion reaction caused by complement-fixing antibodies ➢ Rarely ABO antibodies in a platelet or plasma component or ➢ Improper handling and storage of blood	*Some or all of –* • Unexplained fever >1°C • Chills, rigors • Pain up arm • Chest, abdominal or low back pain • Dyspnoea • Tachycardia • Hypotension, shock • Haemoglobinaemia and haemoglobinuria • Oliguria with dark urine or anuria • Nausea, vomiting • Diarrhoea • Pallor, jaundice • Bleeding (due to DIC)	• Meticulous checking of recipient's ID and labeling of pre-transfusion blood sample at recipient's side • Meticulous two-person checking of ID of intended recipient of blood component and component label • Careful monitoring of recipient for first 15 min of each unit transfused • Store and handle blood components within specifications	• Stop transfusion • Check label and recipient identify • Replace IV set and start normal saline • Treat shock and maintain blood pressure with IV saline infusion • Investigate possible DIC and treat if clinically significant bleeding • Diuretic, eg Frusemide 1-2 mg/kg IV and/or Mannitol, may help maintain urine flow • Hydrocortisone may be considered • Samples to assess renal and liver function, DIC and haemolysis, eg full blood count, unconjugated bilirubin, LDH and haptoglobin • Send Haemovigilance notification to Blood Bank

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Delayed Haemolytic Reaction **Frequency:** Estimated 1:5,000 but recognized and reported events 1:35,000 • Onset usually 1-7 days post transfusion but may be up to 28 days ➢ Recipient has previously been immunised to a blood group antigen, usually by transfusion or pregnancy. Transfusion with red cells expressing the relevant antigen produces a secondary immune response and results in haemolysis of transfused antigen-positive red cells	• Worsening anaemia and jaundice from destruction of red cells • Often asymptomatic but rarely splenomegaly, haemoglobinaemia and haemoglobinuria • Renal impairment may occur in severe cases • Blood screen shows unexpected anaemia and spherocytes may be present on film	• Blood group antibodies are recorded on the NZ Blood Service national database so that compatible red cell components can be provided for future transfusions Note. Delay may occur when providing compatible red cells for transfusion	Investigate haemolysis: • Full blood count with film comment • Direct antiglobulin test (may be negative when most red cells cleared) • Blood group antibody screen (may be negative until red cells cleared) • Liver function tests • Haptoglobin concentration falls while haemolysis is occurring • LDH • Send Haemovigilance notification to Blood Bank if reaction is suspected
Bacterial Sepsis **Frequency:** Platelet components: <1:10,000 Red cell components: <1:250,000 • Rapid onset ➢ Blood component contains bacteria that have grown to a high concentration ➢ Most commonly affects platelet components; rarely affects red cells ➢ If gram negative bacteria are present, endotoxin levels may be very high	• Rigor, chills, fever • Shock, usually within minutes of starting transfusion • Respiratory distress, wheezing and oxygen desaturation • Pain up arm • Chest and back / loin pain • Nausea, vomiting • Explosive diarrhoea may occur with *Yersinia enterocolitica* sepsis • Most common infecting agents: staphylococcal species (platelet components), gram negative species (red cell components)	• Collect, store and handle blood components within specifications • Inspect products for any visual abnormality or defect in unit container before transfusing: ○ a visibly clumped platelet component ○ an unusually dark red cell component ○ punctured or leaking bag	• Stop transfusion • Replace IV set; give saline to maintain BP and/or keep vein open • Send Haemovigilance notification to Blood Bank • Notify Blood Bank by phone and contact TMS urgently • Obtain blood cultures from recipient if sepsis suspected • Give antibiotics: a broad-spectrum penicillin or cephalosporin and gentamicin 5mg/kg • Note: Blood Bank will arrange urgent Gram stain and cultures on blood component and report any positive findings

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TACO: Transfusion Associated Circulatory Overload **Frequency**: 1:100-1:1,000 red cell transfusion episodes • Rapid onset after infusion of a volume of fluid that is clinically significant for the affected recipient. ➢ Main risk factors: ○ Elderly recipient with impaired cardiovascular state or renal impairment ○ Infusion too rapid for recipient ○ Volume infused too great, especially if normovolaemic	• Increased blood pressure • Rapid bounding pulse • Respiratory distress with raised resp. rate, dyspnoea, cough, pink frothy sputum, crepitations and oxygen desaturation consistent with pulmonary oedema • Raised JVP and CVP • Nausea • Acute or worsening pulmonary oedema on CXR • Restlessness, anxiety	• Restrictive transfusion practice • Monitor fluid balance esp. in elderly and children, and recipients with cardiovascular or renal disease • Transfuse at a rate appropriate for recipient • Give a diuretic immediately **prior** to a transfusion if cardiovascular reserve is impaired or a large transfusion is required • Avoid elective transfusions at night • Always prescribe paediatric transfusion dose in mL, **not** in Units.	• Stop transfusion • Seek urgent medical assessment • Sit recipient upright with legs over side of bed, administer oxygen, diuretic (Frusemide 1-2 mg/kg IV), CPAP ventilation • Phlebotomy may be necessary • Demonstration of raised BNP may help to distinguish from TRALI • Send Haemovigilance notification to Blood Bank
Post Transfusion Purpura **Frequency:** <1:100,000 (mostly occurs in women who have been pregnant) • Onset about 5-12 days after transfusion of cellular blood components ➢ Recipient has produced an antibody to an HPA (human platelet-specific) antigen. The antibody forms immune complexes with transfused platelet antigens resulting in clearance of most circulating platelets	• Severe thrombocytopenia often with purpura and possibly other bleeding • Thrombocytopenia will persist for 1-2 weeks	• Restrictive transfusion practice • Notify Blood Bank and TMS promptly so that relevant investigations can be initiated. Further transfusions will require selected components. • Note: Delay may occur for supply of cellular blood products.	• Consult Transfusion Medicine Specialist or Haematologist if a recipient of cellular blood components develops an unexpected severe thrombocytopenia in the following 1-2 weeks • Test for HPA antibodies • If not bleeding – monitor • If clinically significant bleeding – intravenous immunoglobulin and/or plasma exchange are recognised treatments • Avoid random-donor platelet transfusion • If life-threatening bleeding – platelet components lacking the relevant HPA antigen are desirable

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TRALI: Transfusion Associated Lung Injury **Frequency: <**1:5,000 • Onset within 6 hours following transfusion of plasma or plasma-containing cellular components ➢ A complex group of disorders indistinguishable clinically from ARDS ➢ One recognised mechanism involves a donor antibody reacting with recipient neutrophil- or HLA-antigens causing cell activation that results in acute severe microvascular lung injury ➢ Other contributing factors may exist	• Onset of severe dyspnoea and cyanosis proceeding to respiratory failure with bilateral infiltrates on CXR within 6 hours of transfusion • If the reaction occurs during anaesthesia the lungs become very stiff from rapidly developing pulmonary exudate • Absence of left atrial hypertension (circulatory overload) • Distinguish from: ○ cardiovascular overload (TACO) ○ other causes of acute respiratory distress syndrome (ARDS) or less severe acute lung injury (ALI)	• Restrictive transfusion practice • NZ case rate from FFP and platelet components has been reduced by supply of: ○ Male-only FFP ○ HLA-antibody testing of apheresis platelet donors ○ Pooled Platelets are suspended in platelet additive solution (PAS) and have minimal residual plasma • Notify Blood Bank so that donor(s) can be assessed for relevant antibodies and implicated donor(s) withdrawn from the active donor panel	• Intensive care management for respiratory failure • Diuretics are not usually helpful • Send Haemovigilance notification to Blood Bank • Notify Blood Bank by phone and contact TMS urgently • Tissue typing samples will be required
Transfusion associated Graft versus Host Disease (TA-GVHD) **Frequency:** Rare but fatal ➢ A risk for TA-GVHD exists with: ○ Congenital cellular immune deficiency ○ Intrauterine transfusion and neonatal exchange transfusion ○ Hodgkin lymphoma ○ Some chemotherapy agents, eg purine analogues, alemtuzamab ○ Transfusion of cellular components from near genetic relative ○ HLA-matched apheresis platelets ○ Severe immunodepression	• Clinical syndrome with fever, rash, liver dysfunction, diarrhoea and pancytopenia occurring 1-6 weeks following transfusion with no other apparent cause	• Irradiate cellular blood components to inactivate residual lymphocytes • When notified of a patient requiring irradiation of cellular components , NZBS attaches a protocol to the patient's transfusion record	• Consult with a Haematologist and Transfusion Medicine Specialist to investigate and establish diagnosis • Send Haemovigilance notification to Blood Bank

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Cooling **Frequency: no data** • Progressive onset during rapid infusion of large volumes of cold fluids, including blood products (more than 50 mL/kg/h in adults or 15 mL/kg/h in children)	• Reduced temperature • May be associated with cardiac rhythm irregularity and a negative inotropic effect • Impaired platelet function and coagulation	• Give large fluid infusions through a warmer designed for rapid infusion of blood components and follow the manufacturer's instructions • Equipment must be properly maintained and validated to ensure the correct temperature is achieved as excessive temperature will produce haemolysis	• Limit heat loss from the recipient and monitor BP/TPR • If further blood components required, infuse through a warmer • Note: Reliable determination of temperature requires core temperature measurement

TMS = Transfusion Medicine Specialist