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Adverse effects of transfusion

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Summary

Each blood product transfused carries a small risk of an acute or late adverse effect.

- Medical officers prescribing 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.
- Where possible the patient/parents should be informed of the possible adverse effects that may occur.
- Staff should follow hospital procedures for the collection of pretransfusion samples and for blood administration and adhere to all steps in the process.
- Patients should be monitored closely especially at the beginning of a transfusion.
- Any adverse reaction to the transfusion of blood or blood products should be reported to the patient's treating doctor and to the hospital blood bank as soon as possible. Speed is essential because of the possible life-threatening nature of acute transfusion reactions.

The most common immediate adverse reactions to transfusion are fever, chills and urticaria. The most potentially significant reactions include acute and delayed haemolytic transfusion reactions and bacterial contamination of blood products. During the early stages of a reaction it may be difficult to ascertain the cause.

Immediate nursing management comprises stopping the transfusion, reperforming the pretransfusion checklist, documenting observations, providing immediate patient care and contacting the treating medical officer.

In certain cases of mild urticarial reactions or the presence of repeated chill-fever reactions in multiply transfused patients, the medical officer may elect to restart the transfusion after evaluation and treatment of the patient.

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Immediate Management of a Suspected Transfusion Reaction

The following table appears on the reverse of the Blood Transfusion Record which accompanies each blood product. The table provides a summary of the main requirements for immediate management of a suspected transfusion reaction.

RECOGNISE	REACT	REPORT
• Fever • Chills • Hypotension/ Hypertension • Pain (along IV infusion line, chest or back) • Acute Respiratory Distress/stridor/ wheeze • Dark urine • Bleeding, oozing (DIC) • Urticaria (hives)	Immediate Nursing Management ***STOP transfusion*** (leave IV line in place), then • Provide emergency patient care • Arrange immediate medical review • Keep IV line open with N/saline (flush IV cannula or attach side arm) • Re-perform steps 1 to 4 of pre-transfusion check (above)	• Telephone Blood Bank (RCH Xn 5829, RWH Xn 2036) • Complete the Transfusion Reaction Report Form (if reaction requires investigation, see below) • Document reaction in medical record
Reviewing medical officer to determine if transfusion may recommence (consult with on-call-haematologist if required - contact via switchboard: RCH dial 91, RWH dial 92). If the transfusion is to be discontinued and the reaction investigated: 1. Disconnect pack from patient. 2. Complete Transfusion Reaction Report Form. 3. Obtain blood/urine samples as directed. 4. Send pack, Transfusion Reaction Report Form and samples to hospital Blood Bank. Definitive management including further transfusion support depends on the nature/cause of the reaction.		

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Investigation Requirements

- Completed Transfusion Reaction Report Form (PDF 143 KB)
- Blood pack
- Post reaction blood sample (EDTA)
- Post reaction urine sample (do not delay investigation while waiting for a urine sample)

Forward above to the hospital blood bank.

Additional samples sometimes required (as directed by haematologist-on-call)

- Blood cultures
- HLA or neutrophil antibodies (serum/gel)
- Anti-IgA antibodies (serum/gel)
- HLA typing (ACD)

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Immediate Adverse Effects of Transfusion

Febrile Reactions

***Cause*:** Fever and chills during transfusion are thought to be caused by recipient antibodies reacting with white cell antigens or white cell fragments in the blood product or due to cytokines which accumulate in the blood product during storage. Fever occurs more commonly with platelet transfusion (10-30%) than red cell transfusion (1-2%).

It is important to distinguish from fever due to the patient's underlying disease or infection (check pretransfusion temperature). Fever may be the initial symptom in a more serious reaction such as bacterial contamination or haemolytic reaction.

***Management*:** Symptomatic, paracetamol

***Investigation*:** Fever can be the initial sign in more severe transfusion reactions (haemolytic or bacterial sepsis) and should be taken seriously.

Follow the steps 'immediate management of an acute transfusion reaction'. For isolated fever or chills in some patients, the medical officer may elect to restart the transfusion. If the fever is accompanied by significant changes in blood pressure or other signs and symptoms, the transfusion should be ceased and investigated

Check for HLA antibodies in patients having repeated febrile reactions.

***Prevention*:** A proportion of patients who have febrile reactions will have similar reactions to subsequent transfusions. Many are prevented by leucocyte filtration (either bedside or pre-storage).

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Urticarial (Allergic) Reactions

***Cause*:** Seen in approximately 1% of recipients and caused by foreign plasma proteins. On rare occasions they may be associated with laryngeal oedema and bronchospasm.

***Management*:** If urticaria occurs in isolation (without fever and other signs), slow the rate or temporarily stop transfusion. If symptoms are bothersome, consider administering an antihistamine before restarting the transfusion. If associated with other symptoms, cease the transfusion and proceed with investigation.

***Investigation*:** In the case of mild urticarial reactions with no other signs or symptoms, it is not necessary to submit blood specimens for investigation. It is also usually possible to restart the transfusion. Such a decision should be made after assessment by the treating doctor.

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Severe Allergic (Anaphylactic) Reactions

Anaphylactic and anaphylactoid reactions have signs of cardiovascular instability including hypotension, tachycardia, loss of consciousness, cardiac arrhythmia, shock and cardiac arrest. Sometimes respiratory

involvement with dyspnoea and stridor are prominent.

***Cause*:** In some cases patients with IgA deficiency who have anti-IgA antibodies can have these reactions.

***Management*:** Immediately stop transfusion, supportive care including airway management may be required. Adrenaline may be indicated. Usually given as 1:1000 solution, 0.01mg/kg s.c./i.m. or slow i. v. Anaphylaxis

***Investigation*:** IgA levels and anti-IgA antibodies.

***Prevention*:** Patients with anti-IgA antibodies require special blood products such as washed red blood cells and plasma products prepared from IgA deficient donors. Manage further transfusion in consultation with the haematologist-on-call.

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Acute Haemolytic Reactions

***Cause*:** The majority of haemolytic reactions are caused by transfusion of ABO incompatible blood, eg group A, B or AB red cells to a group O patient. Most haemolytic reactions are the result of human error such as the transfusion of properly labelled blood to the wrong patient, or improper identification of pretransfusion blood samples.

Non-immune haemolysis of RBCs in the blood container or during administration can occur due to physical disruption (temperature changes, mechanical forces, non-isotonic fluid)

***Symptoms*:** Chills, fever, pain (along IV line, back, chest), hypotension, dark urine, uncontrolled bleeding due to DIC.

***Management*:** Immediately stop transfusion. Notify hospital blood bank urgently (another patient may also have been given the wrong blood!). These patients usually require ICU support and therapy includes vigorous treatment of hypotension and maintenance of renal blood flow.

***Prevention*:** Proper identification of the patient from sample collection through to blood administration, proper labelling of samples and products is essential. Prevention of non-immune haemolysis requires adherence to proper handling, storage and administration of blood products.

NOTE: ABO Haemolytic reactions are reported to DHS as a sentinal event

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Bacterial Contamination

***Cause*:** Bacteria may be introduced into the pack at the time of blood collection from sources such as donor skin, donor bacteraemia or equipment used during blood collection or processing. Bacteria may multiply during storage. Gram positive and Gram negative organisms have been implicated. Platelets are more frequently implicated than red cells.

***Symptoms*:** Very high fever, rigors, profound hypotension, nausea and/or diarrhoea.

***Management*:** Immediately stop the transfusion and notify the hospital blood bank. After initial supportive care, blood cultures should be taken and broad-spectrum antimicrobials commenced. Laboratory investigation will include culture of the blood pack.

***Prevention*:** Inspect blood products prior to transfusion. Some but not all bacterially contaminated products can be recognised (clots, clumps, or abnormal colour). Maintaining appropriate cold storage of red cells in a monitored blood bank refrigerator is important. Transfusions should not proceed beyond the recommended infusion time (4 hours).

Further information: **Medilink Newsletter ARCBS Volume 5 No 2 august 2002** (PDF)

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Transfusion-Related Acute Lung Injury

Transfusion Related acute Lung Injury (TRALI) is a clinical diagnosis of exclusion characterised by acute respiratory distress and bilaterally symmetrical pulmonary oedema with hypoxaemia developing within 2 to 8 hours after a transfusion. A CXR shows interstitial or alveolar infiltrates when no cardiogenic or other cause of pulmonary oedema exists.

***Cause*:** Pulmonary vascular effects are thought to occur secondary to cytokines in the transfused product or from interaction between patient white cell antigens and donor antibodies (or vice versa).

***Management*:** Symptomatic support for respiratory distress includes oxygen administration and may require intubation and mechanical ventilation. Symptoms generally resolve over 24-48 hours.

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Volume Overload

Cause: Patients with cardiopulmonary disease and infants are at risk of volume overload especially during rapid transfusion.

Management: Stop the transfusion, administer oxygen and diuretics as required.

Prevention: Avoid unnecessary fluids and use appropriate infusion rates.

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Hypothermia

Cause: Rapid infusion of large volumes of stored blood contributes to hypothermia. Infants are particularly at risk during exchange or massive transfusion.

Prevention and Management: Appropriately maintained blood warmers should be used during massive or exchange transfusion. Additional measures include warming of other intravenous fluids and the use of devices to maintain patient body temperature.

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Citrate toxicity

***Cause*:** Citrate is the anticoagulant used in blood products. It is usually rapidly metabolised by the liver. Rapid administration of large quantities of stored blood may cause hypocalcaemia and hypomagnesaemia when citrate binds calcium and magnesium. This can result in myocardial depression or coagulopathy. Patients most at risk are those with liver dysfunction or neonates with immature liver function having rapid large volume transfusion.

***Management*:** Slowing or temporarily stopping the transfusion allows citrate to be metabolised. Replacement therapy may be required for symptomatic hypocalcaemia or hypomagnesaemia.

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Potassium Effects

Cause: Stored red cells leak potassium proportionately throughout their storage life. Irradiation of red cells increases the rate of potassium leakage. Clinically significant hyperkalaemia can occur during rapid, large volume transfusion of older red cell units in small infants and children.

Prevention: At RCH red cells are irradiated just prior to issue. Blood less than 7 days old is generally used for rapid large volume transfusion in small infants (eg cardiac surgery, ECMO, exchange transfusion)

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Summary table 'Immediate adverse effects of transfusion and their management'

Category 1: Mild Reactions			
Signs	Symptoms	Possible Cause	Immediate Management
Urticaria/rash	Pruritis (itching)	Allergic	1. Stop transfusion 2. Assess patient 3. An antihistamine may be required 4. Transfusion may be restarted if no other signs/ symptoms are present 5. If signs/symptoms worsen treat as Category 2.
Category 2: Moderately severe reactions			
Signs	Symptoms	Possible cause	Immediate Management
Flushing Urticaria Rigors Fever Restlessness Tachycardia	Anxiety Pruritis Palpitations Mild dyspnoea Headache	Allergic (moderately-severe) • antibodies to proteins including IgA • possible contamination with pyrogens and /or bacteria Febrile non-haemolytic transfusion reaction:- antibodies to white cells or platelets	1. Stop transfusion and maintain IV line with NSaline 2. Contact Medical Officer 3. Patient may require antihistamine and/or paracetamol 4. Further investigation and management according to clinical features 5. If investigation required: complete Transfusion Reaction Form and send blood pack, form and samples to blood bank
Category 3: Life threatening reactions			
Signs	Symptoms	Possible cause	Immediate Management

Rigors
Fever
Restlessness
Hypotension
Tachycardia
Dark Urine
Unexplained bleeding (DIC)
	Anxiety
	Chest pain
	Pain at infusion site
	Respiratory distress
	Loin/back pain
	Headache
	Dyspnoea
		Acute intravascular haemolysis (wrong blood)
		Bacterial contamination and septic shock
		Fluid overload
		Anaphylaxis
		Transfusion related acute lung injury (TRALI)
			1. Stop transfusion and maintain IV line with NSaline
			2. Contact Medical Officer (RCH MET call if appropriate)
			3. Manage immediate needs:
			  1. fluid for hypotension
			  2. oxygen
			  3. adrenaline for anaphylaxis
			  4. diuretic for fluid overload
			4. Complete Transfusion Reaction Form and send blood pack, form and samples to blood bank
			5. Further management according to likely cause

Delayed and Long Term Averse Effects of Transfusion

Delayed Haemolysis

Cause: Patients may develop antibodies to red cell antigens. Antibodies can occur naturally, or may arise as a consequence of previous transfusion or pregnancy. A delayed haemolytic reaction occurs when a patient develops an antibody directed against an antigen on transfused red cells. The antibody may cause shortened red cell survival, with clinical features of fever, jaundice and lower than expected haemoglobin following transfusion. Most delayed haemolytic reactions produce few symptoms and may go unrecognised, however there are reports of serious consequences in critically ill patients.

Prevention: An antibody screen is performed as part of pre-transfusion testing. When an antibody is detected, it is identified and appropriate antigen negative blood is provided. Sometimes antibodies fall below detectable limits and may not be detected by pretransfusion testing.

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Alloimmunisation

Red Blood Cells

Patients experiencing alloantibody formation are asymptomatic. The alloantibody is discovered at the time of pretransfusion testing. Appropriate antigen negative blood will be supplied.

Prevention**:** alloimmunisation to the D and K (Kell) antigens is prevented by the provision of Rh(D) negative and Kell negative blood for Rh(D) negative, Kell negative patients. This is important for females with child-bearing potential as these antibodies can cause severe haemolytic disease of the newborn during pregnancy.

At risk groups: Patients with sickle cell disease or major haemoglobinopathy syndromes who are chronically transfused are at greatest risk of alloantibody formation. Prior to commencing transfusion, patients with these condition should have extended red cell phenotyping performed (EDTA sample). Blood matched for the patient's Rhesus and Kell antigens is usually supplied for transfusion

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Platelets

When thrombocytopenic patients do not achieve the expected post-transfusion platelet count increment they are said to be refractory. This usually occurs in patients receiving frequent platelet transfusions. There are clinical and immunological causes of platelet refractoriness. Clinical causes include; sepsis, DIC, bleeding, fever, some drugs, and enlarged spleen.

Cause: Immunological causes include the development of antibodies to human leucocyte antigens (HLA) or human platelet antigens (HPA).

***Management*:** Immunological refractoriness can be managed by the provision of HLA or HPA matched platelets.

***Prevention*:** Leucocyte reduction of blood products to levels less than 10^6/unit reduces the likelihood of alloimmunisation. This can be achieved through the use of prestorage or bedside leucocyte reduced blood products.

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Transfusion associated Graft Versus-Host Disease (Ta-GVHD)

***Cause*:** Ta-GVHD occurs when donor lymphocytes in cellular blood products engraft in a susceptible transfusion recipient. These donor lymphocytes proliferate and damage target organs especially bone marrow, skin, liver and gastrointestinal tract. The clinical syndrome comprises fever, skin rash, pancytopenia, abnormal liver function and diarrhoea and is fatal in over 80% of cases. The usual onset is 8-10 days post transfusion, with a longer interval between transfusion and onset of symptoms in infants.

The most commonly reported setting for Ta-GVHD is immunocompetent recipients of blood from biologically related (directed) or HLA identical donors. The disease is also reported in immunologically compromised patients.

***Prevention*:** Gamma irradiation of cellular blood products (whole blood, red blood cells, platelets, granulocytes) for at risk patients.

At risk groups:

- Recipients of blood from biologically related (directed) or HLA matched donors'
- Intrauterine and all subsequent transfusion and exchange transfusion recipients
- Patients with congenital cellular immunodeficiency
- Patients receiving granulocyte transfusions
- Patients with Hodgkin's Disease
- Allogeneic and autologous Peripheral Blood Stem Cell (PBSC) and bone marrow transplant recipients
- Patients with Aplastic Anaemia receiving immunosuppression
- Patients treated with purine analogue drugs

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Immunomodulatory effects

Some studies suggest a link between blood transfusion and increased risk of infection and cancer recurrence. However this is currently considered unproven.

Cause: Unknown, possibly mediated by donor white cells or plasma.

Management and Prevention: Not known, possibly leucocyte depletion of blood products.

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Iron accumulation

Cause: Iron accumulation is a predictable consequence of chronic RBC transfusion. Organ toxicity begins when reticuloendothelial sites of iron storage become saturated. Liver and endocrine dysfunction creates significant morbidity and the most serious complication is cardiotoxicity which causes arrhythmias, and congestive heart failure. Patients receiving chronic transfusion usually have their iron status monitored and managed by their physician.

Management and Prevention: Iron chelation therapy is usually commenced early in the course of chronic transfusion therapy.

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Infectious Disease transmission

A variety of infectious agents may be transmitted by transfusion. Definitive evidence of transmission by transfusion requires demonstration of seroconversion or new infection in the recipient and isolation of an agent with genomic identity from both the recipient and the implicated donor. Strong presumptive evidence of transfusion transmission includes recipient seroconversion within an appropriate interval after transfusion, the recognition of appropriate infectious markers in an implicated donor on follow-up investigation, or both. Transfusion transmitted disease should be reported to the Australian Red Cross Blood Service.

Suspected transfusion-transmitted bacterial or parasitic infection (malaria) should be reported urgently in order to recall other potentially infectious blood products from the same donation.

Estimated risk of transfusion transmitted infection from Medilink, ARCBS October 2004.

Point estimates for risk of transfusion transmitted viral infection from ARCBS donations calculated using data from July 2000 to June 2003.

Virus and testing standard	Window Period (Days)	Point estimate of residual risk 'per unit'
HIV 1 and 2 antibody only	22	1 in 2,404,000
HIV antibody + NAT	9	1 in 7,299,000
HCV antibody only	66	1 in 330,000
HCV antibody + NAT	7	1 in 3,663,000
HBV	45	1 in 1,339,000
HTLV I & II	51	Considerably less than 1 in 1,000,000
vCJD		Possible. Not yet reported in Australia

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Transfusion Reaction Report Form (PDF 108 KB)

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