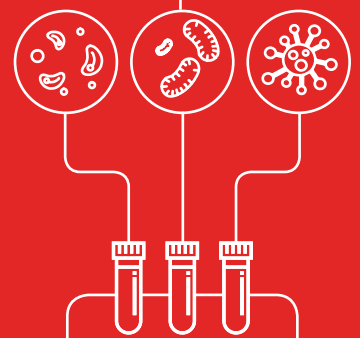
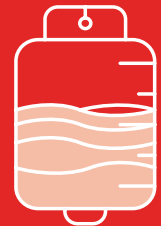


CLINICAL GUIDELINES FOR

THE USE OF BLOOD AND BLOOD PRODUCTS IN SOUTH AFRICA





Contents



Introduction / Foreword	3
Patient Blood Management	4
Legal Aspects of Blood Transfusion	11
Ordering and Administration of Blood	15
Red Cell Components	22
Platelet Product Transfusion	35
Plasma Components and Derivatives	43
Leucocyte Depletion and Irradiation of Blood Components	57
Haemovigilance, Risks and Adverse Reactions Associated with Blood Transfusions	63
Abbreviation List	71



This edition of the *Clinical Guidelines for the Use of Blood and Blood Products in South Africa* has been updated to reflect the evolution of blood transfusion medicine, which continues to develop based on numerous scientific-research advances and widely agreed principles.

With Patient Blood Management (PBM) gaining traction worldwide, including in South Africa, these Guidelines now include a chapter devoted to PBM and an increasing number of surgical specialties are also publishing discipline-specific PBM guidelines. All clinicians are encouraged to consider PBM principles in their management of patients, as these are associated with improved clinical outcomes.

Clinicians are also urged to take note of Chapter 2, *Legal Aspects of Blood Transfusion*, particularly with reference to informed consent. The blood supply in South Africa is safe, but blood transfusion is not without risks. Legal aspects to be considered include adverse transfusion reactions and transfusion-transmissible infections. Medico-legal issues may be avoided by ensuring patients are made fully aware of the risks and benefits of transfusion therapies, as well as the risks and benefits of alternatives to blood transfusion.

Clinicians are also advised to stay up to date with developments in transfusion medicine, such as the indications for specific products, PBM and haemovigilance.

The 6th Edition is once again the collaborative effort of the South African National Blood Service and the Western Cape Blood Service and the National Bioproducts Institute contributed to Chapter 6, Plasma Components and Derivatives.

The content of these Guidelines has been updated in line with recent peer-reviewed and authoritative publications. While every effort has been made to ensure they are accurate, the blood services, contributors and publishers cannot be held responsible for any errors or omissions contained within this publication.

The Guidelines are also available on the South African National Blood Service and Western Cape Blood Service websites: www.sanbs.org.za and www.wcbs.org.za.

Finally, we wish to thank Adcock Ingram Critical Care for sponsoring the publication and distribution of these Guidelines.



CONTRIBUTORS



- Dr Greg Bellairs
- Dr Thabiso Rapodile
- Dr Caroline Hilton
- Dr Karin van den Berg
- Dr Petro-Lize Wessels
- Dr Tanya Glatt
- Dr Ute Jentsch
- Dr Solomuzi Ngcobo
- Dr Jeh-Han Omarjee
- Mr Leith Kwaan
- Dr Colwyn Poole

Chapter 1:

PATIENT BLOOD MANAGEMENT



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

PATIENT BLOOD MANAGEMENT

Blood and blood products remain a life-saving intervention for the patient who requires a transfusion. The aim of informing the reader on Patient Blood Management (PBM) is to ensure an appropriate, step-wise, multidisciplinary

approach to the management of patients so that blood and blood products are used appropriately and patient outcomes are optimised.

BACKGROUND

In 2010, the 63rd World Health Assembly adopted Resolution WHA63.12 on *Availability, safety and quality of blood products*. The Director General of the World Health Organization (WHO) was requested 'to provide guidance, training and support to Member States on safe and rational use of blood products ... and patient blood management'.

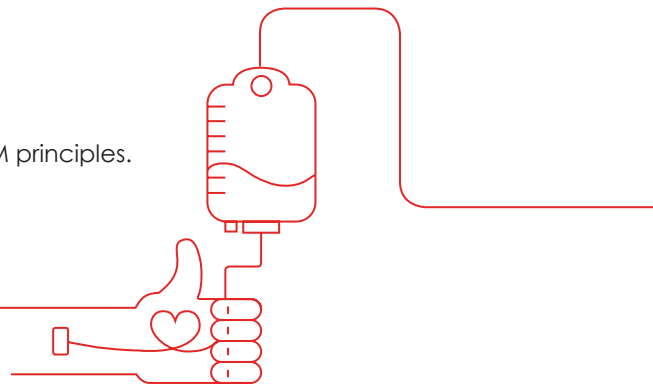
PBM remained a focus point for WHO, culminating in Strategic Objective 4 of the *WHO Action Framework to Advance Universal Access to Safe, Effective and Quality Assured Blood Products 2020 – 2023* being *Effective implementation of patient blood management to optimize clinical practice of transfusion*.

WHAT IS PBM?

PBM is a multidisciplinary, patient-centric approach that aims to improve patient outcomes. PBM-based rationales should be applied to both surgical and non-surgical patients to:

- Ensure the appropriate use of blood and blood products
- Minimise risk
- Optimise patient outcomes

Any transfusion decision-making process should show cognisance of PBM principles.



Despite different definitions being used for PBM, the core focus points are similar:

- Timely optimisation of the patient's own red cell mass (**Note: Diagnose and treat anaemia**)
- Control/minimise blood loss and bleeding
- Optimise and harness the patient's physiological reserve/tolerance to anaemia
- Patient empowerment and participation in the decision-making process
- Multidisciplinary approach

In addition, it is imperative to acknowledge the need to apply PBM principles in all phases of a patient's treatment programme:

- Pre-operative
- Intra-operative
- Post-operative

WHY DO WE NEED TO IMPLEMENT PBM?

There are several well-documented reasons why the implementation of PBM should receive attention – and even be fast-tracked – in South Africa.

♥ Anaemia

The global burden of anaemia in 2015 was estimated at ~ 2.4 billion, with iron deficiency anaemia accounting for ~ 1.5 billion of these cases. The negative impact on quality of life due to iron deficiency is well described in the literature and the negative impact on pregnancy outcomes and the cognitive development of children is receiving increasing attention.

In South Africa, at least 2 studies have demonstrated the high prevalence of anaemia in elective surgery (47.8%) and pregnant patients (42.7%). The presence of pre-operative anaemia was also independently linked to poorer patient outcomes (increased morbidity and mortality) in both the South African and several other studies.

Correcting pre-operative anaemia should be a priority, according to the South African Society of Anaesthesiologists as well as several international sources.

♥ Mitigate Transfusion Risks

While an appropriate transfusion still remains a life-saving intervention, no transfusion is without risk. Transfusion risks are per product transfused, rather than per transfusion episode.

The adverse events related to transfusion, their negative impact on clinical outcomes in certain patient populations and the association between negative clinical outcomes and high-dose transfusions are well described in the literature. Clinically inappropriate transfusions should be avoided at all times.

♥ Improved Patient Outcomes

Several publications have shown improved outcomes (15% – 31% improvement) when implementing effective PBM programmes. Outcomes include:

- Decreased exposure to allogeneic red cells
- Decreased transfusion-related adverse events (TRAEs)
- Decreased length of hospital stay
- Decreased intensive care unit (ICU) admissions
- Decreased serious morbidity, e.g. infectious and thrombotic complications
- Decreased in-hospital mortality

By applying PBM principles to our daily decision-making processes, we will ensure that the right product reaches the right patient at the right time for the right reason – resulting in optimal patient outcomes.

♥ Cost-Effective Healthcare

Delivering cost-effective healthcare is imperative for all role-players in a resource-constrained setting. PBM can be a valuable tool to achieve this goal in South Africa as the implementation of effective PBM programmes has been demonstrated to reduce not only the “blood bill”, but also overall transfusion-associated costs.

The cost of PBM interventions (cell salvage, iron supplementation, etc.), can be off-set against the lower transfusion rates, with literature showing that improved patient safety can be achieved in a cost-effective manner.





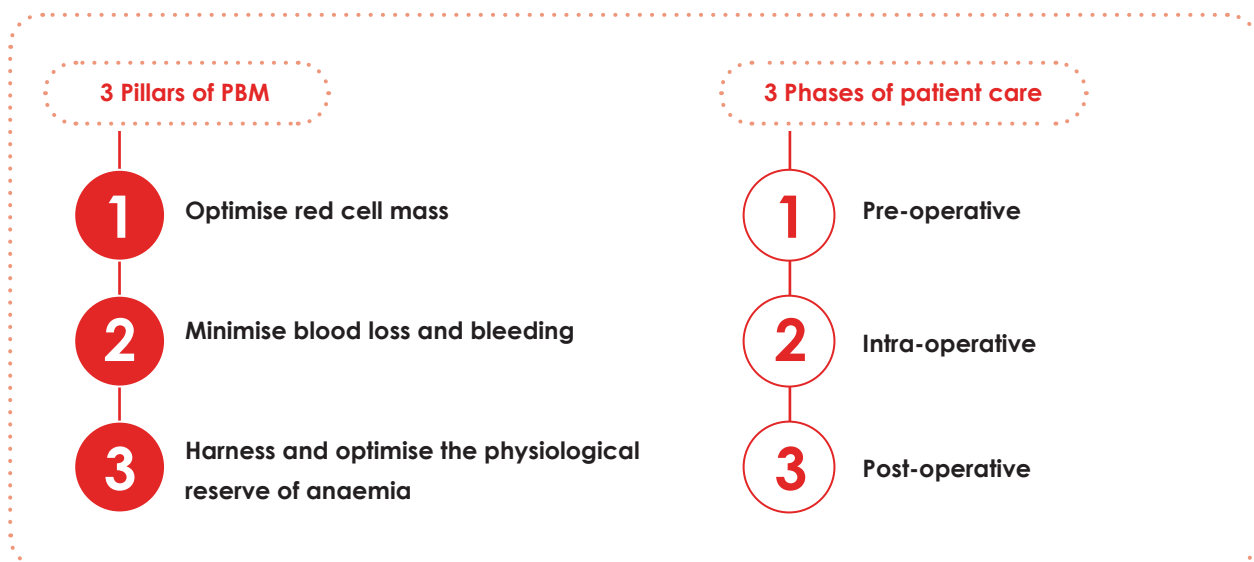
HOW TO GET STARTED WITH PBM

Several toolkits and guiding documents exist to assist clinicians, healthcare management and funders with PBM implementation, and on-line PBM courses for healthcare workers are now freely available. In 2011, WHO published priorities for action for stakeholders at different levels, which can guide our attempts.

A practical starting point with the perioperative patient is to revert back to the 3 pillars of PBM and apply these to the 3 phases of patient care.

A practical starting point with the perioperative patient is to revert back to the 3 pillars of PBM and apply these to the 3 phases of patient care.

Table 1.1



A patient-specific plan, with the individual's underlying condition/s fully documented, should be developed. One size does not fit all. This patient-specific plan should then be communicated to all role-players and be continuously changed and adjusted throughout the patient's treatment as required.

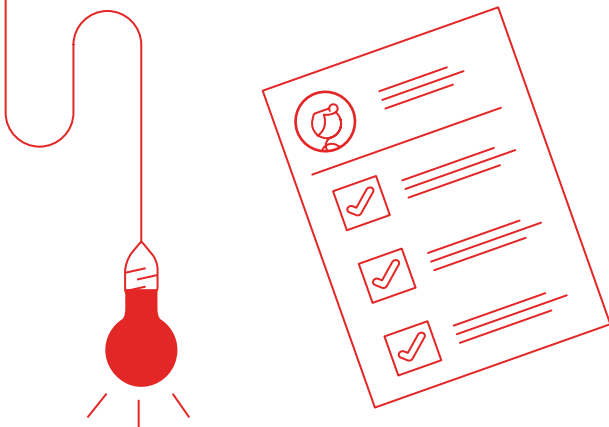


Table 1.2

Pillar 1: Optimise red cell mass	Pillar 2: Minimise blood loss and bleeding	Pillar 3: Harness and optimise the physiological reserve of anaemia
Pre-operative phase		
<ul style="list-style-type: none"> • Detect anaemia • Identify the underlying disorder/s causing anaemia • Manage disorder/s • Refer for further evaluation if necessary • Treat suboptimal iron stores/iron deficiency/anaemia of chronic disease/iron-restricted erythropoiesis • Treat other haematinic deficiencies <p>Note: Anaemia is a contra-indication for elective surgery</p>	<ul style="list-style-type: none"> • Identify and manage bleeding risk • Minimise iatrogenic blood loss • Plan and rehearse procedure 	<ul style="list-style-type: none"> • Assess/optimize patients' physiological reserve and risk factors • Compare estimated blood loss with patient-specific tolerable blood loss • Formulate patient-specific management plan using appropriate blood-conservation modalities to minimise blood loss, optimise red cell mass and manage anaemia
Intra-operative phase		
<ul style="list-style-type: none"> • Time surgery with haematological optimisation 	<ul style="list-style-type: none"> • Employ meticulous haemostasis and surgical techniques • Use blood-sparing surgical device/s • Use anaesthetic blood-conserving strategies • Choose autologous blood options • Maintain normothermia • Use pharmacological/haemostatic agents 	<ul style="list-style-type: none"> • Optimise cardiac output • Optimise ventilation and oxygenation
Post-operative phase		
<ul style="list-style-type: none"> • Optimise erythropoiesis • Be aware of drug interactions that can increase anaemia 	<ul style="list-style-type: none"> • Vigilantly monitor and manage post-operative bleeding • Avoid secondary haemorrhage • Employ rapid warming/maintain normothermia (unless hypothermia is specifically indicated) • Employ autologous blood salvage • Minimise iatrogenic blood loss • Manage haemostasis/anticoagulation • Employ prophylaxis of upper gastrointestinal (GI) haemorrhage • Avoid infections or treat promptly • Be aware of adverse effects of medication 	

Given the importance of anaemia screening, diagnosis and treatment in a successful PBM programme, the value of the primary healthcare level/general practitioners should not be underestimated, nor should they be excluded from the PBM plan.

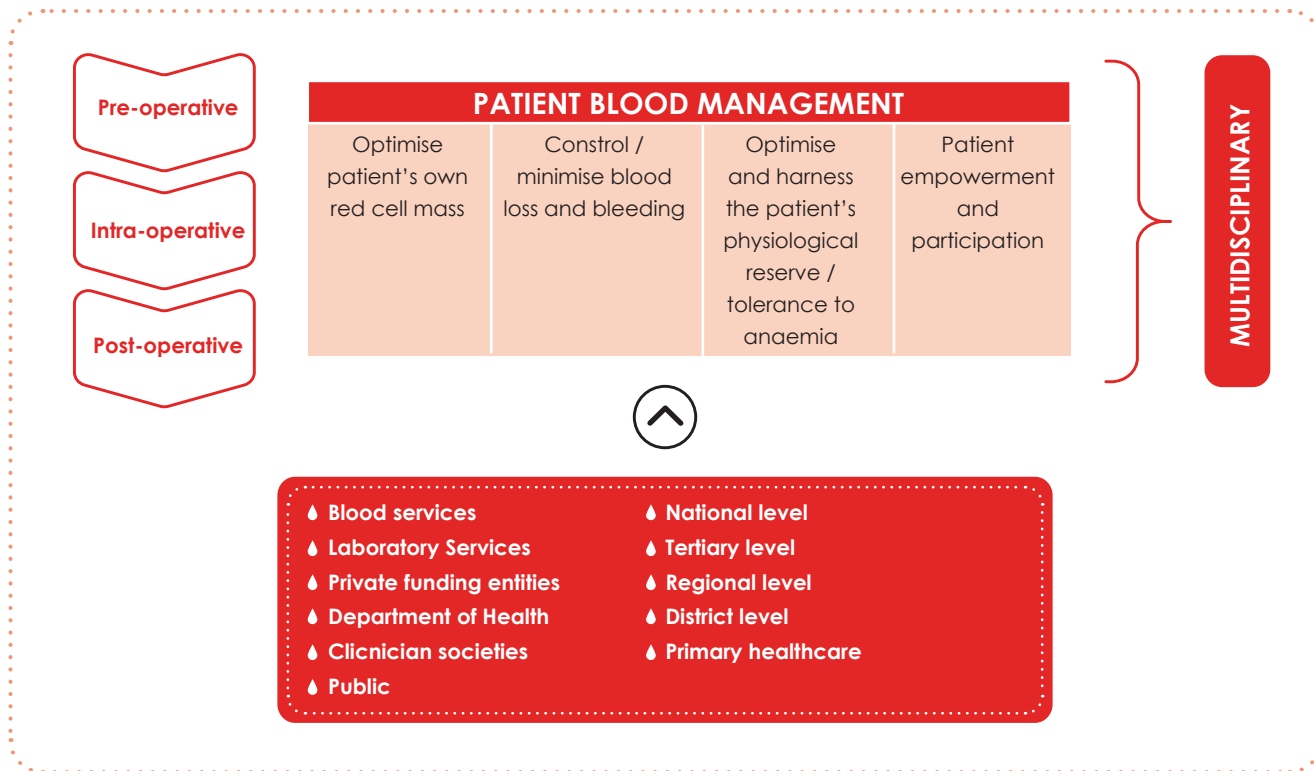
The availability of alternatives (e.g. cell-saver technology) or pharmaceuticals (e.g. tranexamic acid) should always be considered and strived for, even in rural settings.



WHO IS RESPONSIBLE FOR IMPLEMENTING PBM?

PBM principles and programmes are aimed at improving patient outcomes. As such, it remains the responsibility of all role-players in healthcare to contribute to the promotion and implementation of PBM in South Africa.

This is a multidisciplinary, multimodal approach to patient care and involves a variety of role-players, situated at different levels of healthcare:



HOW TO MONITOR A PBM PROGRAMME

Successful PBM programmes look beyond the mere availability of guidelines, to having effective monitoring and feedback systems in place.

The data to be monitored will depend on several factors:

- Which plan/template are you implementing for your PBM programme, e.g. SABM (Society for the Advancement of Patient Blood Management) standards, WHO priorities for action or AABB (Association for the Advancement of Blood & Biotherapies) implementation plan?
- What are the priorities in your specific setting?
- Where are you in your implementation plan – initial stage or advanced stage?
- What resources are available?
- To what extent is data in your setting captured (and available) electronically vs manually?

The quality of the data entered in your monitoring system (whether manual or electronic) will heavily impact on the success of your monitoring efforts. This principle should be communicated to all levels of stakeholders involved in your PBM programme.

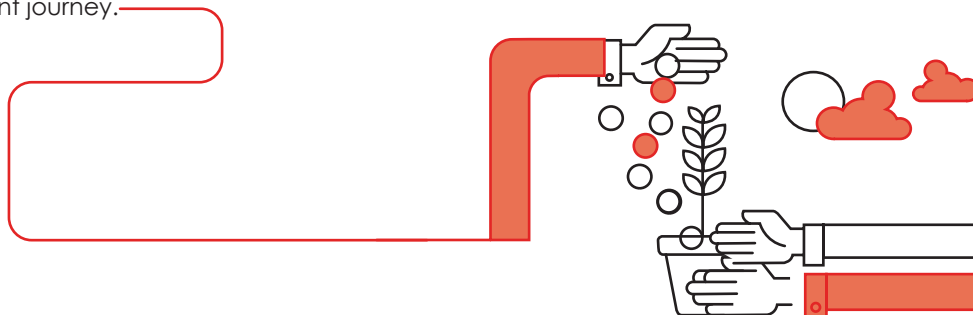
Feedback platforms/discussion groups form a crucial part of a PBM programme. Representatives of your blood-using departments, pharmacies, management, nursing services and supply chain should take part in this forum. Representation from your local blood services will also add value to your discussions, as they form part of the multidisciplinary team involved in PBM.

Benchmarking against best practice should be ongoing and all discussions held and decisions taken should be effectively communicated to all levels of stakeholders in your setting.

PBM IN A RESOURCE-CONSTRAINED SETTING: DO WE WAIT FOR “MORE” OR DO WE START?

Even in a resource-constrained setting, it is possible to start with a simplified PBM programme. The goal is to start small, grow slowly and not leave any stakeholders behind. Even a simplified programme is a start towards improved patient safety and outcomes.

There are ample guiding documents, toolkits and educational materials available to guide you on this important journey.



FURTHER READING

1. World Health Organization. Global Forum for Blood Safety: Patient Blood Management: concept paper. March 2011. Accessed March 13, 2023. https://cdn.who.int/media/docs/default-source/biologicals/blood-products/document-migration/gfbs_01_pbm_concept_paper.pdf?sfvrsn=f189661_3
2. Sixty-third World Health Assembly. Availability, safety and quality of blood products. 21 May 2010. Accessed March 7, 2023. https://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R12-en.pdf
3. Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023. World Health Organization. 19 February 2020. Accessed March 7, 2023. <https://www.who.int/publications/i/item/action-framework-to-advance-uas-bloodprods-978-92-4-000038-4>
4. Society for the Advancement of Patient Blood Management. SABM administrative and clinical standards for Patient Blood Management Programs®. 5th edition. 2019. Accessed March 7, 2023. <https://sabm.org/wp-content/uploads/SABM-Standards-20196.pdf>
5. Patient Blood Management resources. International Foundation for Patient Blood Management. Accessed March 7, 2023. <https://www.ifpbm.org/knowledge>
6. Patient blood management. Association for the Advancement of Blood & Biotherapies. Accessed March 7, 2023. <https://www.aabb.org/news-resources/resources/patient-blood-management>
7. Thomson J, Hofmann A, Barrett CA, et al. Patient blood management: a solution for South Africa. *S Afr Med J*. 2019;109(7):471-476. doi:10.7196/SAMJ.2019.v109i7.13859
8. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1211-1259. doi:10.1016/S0140-6736(17)32154-2
9. Marsicano D, Hauser N, Roodt F, et al. Preoperative anaemia and clinical outcomes in the South African surgical outcomes study. *S Afr Med J*. 2018;108(10):839-846. doi:10.7196/SAMJ.2018.v108i10.13148
10. Tunkyi K, Moodley J. Prevalence of anaemia in pregnancy in a regional health facility in South Africa. *S Afr Med J*. 2015;106(1):101-104. doi:10.7196/SAMJ.2016.v106i1.9860
11. Shander A, Van Aken H, Colomina MJ, et al. Patient blood management in Europe. *Br J Anaesth*. 2012;109(1):55-68. doi:10.1093/bja/aes139
12. Wise R, Bishop D, Gibbs M, et al. South African Society of Anaesthesiologists perioperative patient blood management guidelines 2020. *Southern African Journal of Anaesthesia and Analgesia*. 2020;26(6):S1-68. <https://www.sajaa.co.za/index.php/sajaa/article/view/2496>
13. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. *Transfusion*. 2017;57(6):1347-1358. doi:10.1111/trf.14006
14. Althoff FC, Neb H, Herrmann E, et al. Multimodal Patient Blood Management program based on a three-pillar strategy: a systematic review and meta-analysis. *Ann Surg*. 2019;269(5):794-804. doi:10.1097/SLA.0000000000003095
15. Frietsch T, Shander A, Faraoni D, et al. Patient Blood Management is not about blood transfusion: it is about patients' outcomes. *Blood Transfus*. 2019;17(5):331-333. doi:10.2450/2019.0126-19
16. Rhamy, J. The benefits of Patient Blood Management for the patient and the health care system. Association for the Advancement of Blood & Biotherapies. Accessed March 7, 2023. https://www.aabb.org/docs/default-source/default-document-library/resources/pbm-the-benefits-of-pbm-for-the-patient-and-the-health-care-system.pdf?sfvrsn=3ccf0957_4
17. Meybohm P, Straub N, Füllenbach C, et al. Health economics of Patient Blood Management: a cost-benefit analysis based on a meta-analysis. *Vox Sang*. 2020;115(2):182-188. doi:10.1111/vox.12873
18. Meybohm P, Richards T, Isbister J, et al. Patient blood management bundles to facilitate implementation. *Transfusion Medicine Reviews*. 2017;31(1):62-71. doi:10.1016/j.tmr.2016.05.012
19. Hofmann A, Spahn DR, Holtorf AP, et al. Making patient blood management the new norm(al) as experienced by implementors in diverse countries. *BMC Health Serv Res*. 2021;21(1):634. doi:10.1186/s12913-021-06484-3
20. National Blood Authority Australia. Three pillars of patient blood management. Accessed March 7, 2023. <https://www.blood.gov.au/system/files/documents/pbm-3-pillars.pdf>
21. World Health Organization. Global Forum for Blood Safety: Patient Blood Management: priorities for action. March 2011. Accessed March 13, 2023. https://cdn.who.int/media/docs/default-source/biologicals/blood-products/document-migration/who_gfbs_2011_03_priorities_for_action.pdf?sfvrsn=656b7d95_3
22. Mehra T, Seifert B, Bravo-Reiter S, et al. Implementation of a patient blood management monitoring and feedback program significantly reduces transfusions and costs. *Transfusion*. 2015;55(12):2807-2815. doi:10.1111/trf.13260

Chapter 2:

LEGAL ASPECTS OF BLOOD TRANSFUSION



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

LEGAL ASPECTS OF BLOOD TRANSFUSION

Blood transfusion is a cornerstone of modern medical practice. It is an essential component in the medical management of patients in almost every field of clinical practice.

Medical practitioners who order blood for their patients are faced with the challenge of managing the blood transfusion needs of the patient in an evidence-based approach and balancing the expected clinical benefit with the risks inherent in the transfusion of blood.

Blood should only be ordered when there is an appropriate medical indication for a transfusion and practitioners must be able to justify all requests for blood products. Blood transfusions are currently regulated by the National Health Act (2003) and its associated Regulations. Contravention of provisions of the Act and/or the Regulations may constitute an offence.

In the broad doctor-patient relationship, it is generally accepted that the doctor (and the blood transfusion service) owe a duty of care to the patient. The doctor and the blood service are in a unique position to prevent harm:

- The blood service is required to take reasonable steps to make the blood supply as safe as possible
- The attending doctor, who has a closer relationship with the patient, is responsible for:
 - o assessing the clinical need for a transfusion
 - o informing the patient of the benefits and risks of the treatment prescribed
 - o obtaining informed consent.

RESPONSIBILITIES OF DOCTORS WHO TRANSFUSE BLOOD COMPONENTS

There are several well-documented reasons why the implementation of PBM should receive attention – and even be fast-tracked – in South Africa.

The responsibilities of the practitioner who orders and transfuses blood encompass the following:

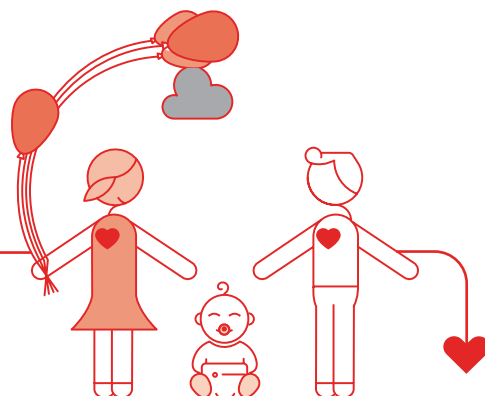
- Transfusing blood only when it is medically indicated
- Warning patients of the potential risks inherent in blood transfusion and informing them of the available alternatives
- Obtaining and documenting informed consent
- Correctly identifying the patient and the number of units of blood to be transfused
- Ensuring that appropriate compatibility tests have been performed
- Ensuring that the blood has been correctly handled prior to and during transfusion
- Ensuring that the blood has not passed its expiry date
- Permitting responsible persons to administer blood to the patient
- Transfusing blood at the proper rate
- Observing and monitoring the patient at the commencement of, and during, the transfusion
- Effectively managing any untoward transfusion reaction
- Retaining blood samples as required
- Reporting untoward reactions or death
- Tracing, counselling and testing recipients of blood transfusions identified through the transfusion-transmissible infection Lookback Programme.

INFORMED CONSENT

As with any medical treatment, patients have a right to decide whether or not they want the treatment. As far as possible, the patient should understand the treatment, agree that the benefits, risks and alternatives to transfusion have been explained, and then consent to the treatment. This is a process which must be acknowledged and documented.

The attending doctor must, in each case, consider alternatives to conventional transfusion therapy (and consider the risks and benefits of those alternative therapies). They are also responsible for discussing alternatives to allogeneic blood transfusion (e.g. autologous or directed donation) with the patient.

Failure to inform the patient of the material risks inherent in blood transfusion and its alternatives could amount to a failure to procure informed consent, resulting in legal liability for the doctor should the patient suffer adverse effects from the transfused blood component.



ASSESSING BENEFITS AND RISKS

While the residual risk of transmitting human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV) infection is remote in the era of individual-donation nucleic-acid testing, doctors must nevertheless assess the benefits and risks in each case and must be able to justify all requests for blood transfusions.

Clinicians must be aware of:

- Other infectious risks, e.g. malaria, cytomegalovirus (CMV) and bacterial contamination (particularly of platelet concentrates)
- Potential non-infectious adverse effects of transfusion, e.g. red cell incompatibility, immune-modulation, transfusion-associated graft versus host disease (TA-GvHD) and transfusion-related acute lung injury (TRALI).

Practitioners are advised to keep up to date with international best practices in the field of transfusion medicine and to adopt a high standard of care at all times, e.g. clinicians need to:

- Be aware of the indications for, and the availability of, leukocyte-depleted blood components and/or gamma-irradiated blood components
- Know the appropriate clinical indications for blood components
- Be aware of the potential risks of transfusion and give consideration to alternative treatment
- Take swift corrective action when problems occur
- Maintain a good doctor-patient relationship
- Initiate private dispute resolution or mediation discussions with aggrieved parties, as doing so is likely to result in a more favourable outcome

The hospital or institution that employs doctors and other healthcare professionals (or permits them to practise in their facilities) also has a responsibility in the selection, education, retention and supervision of its medical staff, including the responsibility of the medical staff to obtain informed consent.

DELICTUAL LIABILITY

Generally, delictual liability arises when some harm or damage is caused to another, either negligently or intentionally, in an unlawful manner.

In general, negligence is deemed to be present if the reasonable person would have foreseen harm to the plaintiff and would have taken steps to avoid such harm, and if the defendant failed to take such steps. In the case of experts and professionals, conduct is measured against the conduct of the reasonable expert or professional.

The basic elements of a claim based on negligence are:

- The defendant owed a duty of care to the plaintiff
- The defendant breached the duty
- The plaintiff's injury was directly or proximately caused by the breach
- The plaintiff suffered damages as a result

It is generally considered that it may be difficult to prove that a blood transfusion service or medical doctor acted negligently in the administering of blood if they adhered to the legislation, regulations and standards for practice applicable at the time of the transfusion.

CRIMINAL LIABILITY

Apart from the statutory offences created by the National Health Act and Regulations, blood transfusions may give rise to criminal liability for the common law crime of culpable homicide and perhaps assault.

If a patient dies as a result of negligence on the part of the practitioner, or of the blood transfusion service, the individuals involved may be charged and convicted of the crime of culpable homicide – the wrongful and negligent causing of the death of another person. In South Africa, a medical practitioner and (on a separate occasion) a blood-transfusion medical-laboratory technician have previously been convicted of culpable homicide after incompatible blood was administered to a patient.

Assault may be deemed to have been committed if a blood transfusion is administered to a patient without the necessary consent. Blood transfusions are an essential component of medical practice. They are frequently life-saving and dramatically improve survival rates and morbidity – particularly in the fields of trauma and surgery – and play a critical role in enabling treatment to be undertaken in medical disciplines, e.g. haematology and oncology. As outlined above, however, practitioners who order blood for their patients must be cognisant of their legal responsibilities with regard to the administration of those blood components.

FURTHER READING

1. South African Government. National Health Act 61 of 2003. Accessed March 7, 2023. <https://www.gov.za/documents/national-health-act>
2. South African Government. Regulations relating to blood and blood products. 2012. Accessed March 7, 2023. https://www.gov.za/sites/default/files/gcis_document/201409/35099rg9699gon179.pdf
3. South African National Blood Service & Western Cape Blood Service. Standards of practice for blood transfusion in South Africa. 2016. Accessed March 7, 2023. <https://satiba.org.za/wp-content/uploads/2021/10/standards-for-blood-transfusion-v7.pdf>
4. International Society of Blood Transfusion. A code of ethics for blood donation and transfusion. 2017. Accessed March 7, 2023. <https://www.isbtweb.org/resource/english.html>
5. Grainger B, Margolese E, Partington E. Legal and ethical considerations in blood transfusion. CMAJ. 1997;156(11):S50-S54.
6. Management of patients who do not accept transfusion. Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. 2014. Accessed March 7, 2023. <https://www.transfusionguidelines.org/transfusion-handbook/12-management-of-patients-who-do-not-accept-transfusion>

Chapter 3:

ORDERING AND ADMINISTRATION OF BLOOD



CLINICAL GUIDELINES FOR

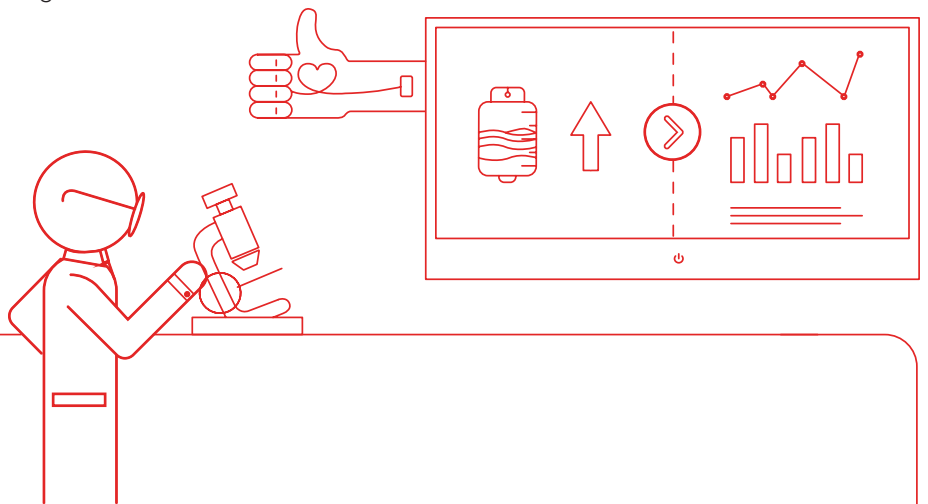
**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

ORDERING AND ADMINISTRATION OF BLOOD

Procedures for the administration of blood may vary in different hospitals, but safety is always the primary concern. As monitoring of the patient during transfusion is often a nursing responsibility, accurate and thorough institutional guidelines or policies should be available for all nurses.

In order to ensure the safety of transfusion, these nursing guidelines should include:

- Preparation of the patient
- Correct identification and verification of the patient and the blood component to be transfused
- Correct aseptic technique
- Careful observation of the patient during transfusion
- Special precautions



PREPARATION OF THE PATIENT

Preparation of the patient for transfusion involves documentation of informed consent. Informed consent for transfusion means a dialogue has occurred between the patient and the doctor. The significant risks, benefits and alternatives to transfusion – including the patient's right to refuse the transfusion – should be explained in terms clearly understandable by the patient.

The length of time that consent is valid may range from a single prescription to an episode of care, or as specified by the treating institution.

As a result of this discussion, the patient should:

- Understand what medical action is recommended
- Be aware of the risks and benefits associated with the transfusion
- Appreciate the risks and possible consequences of not receiving the recommended therapy
- Understand the risks and benefits of alternatives to transfusion
- Have an opportunity to ask questions
- Give consent for the transfusion

The consent must be documented in a consent form or in the patient's hospital record.

In circumstances where it is not possible to obtain informed consent before proceeding with transfusion (e.g. life-threatening emergency, comatose patient or unaccompanied minor patient), it is acceptable to proceed without consent in the patient's best interests, provided such action is documented in the patient's hospital record.

IDENTIFICATION AND VERIFICATION

The safe transfusion of blood products starts with the positive identification of the patient at the time of drawing a blood sample for compatibility testing. Identification is carried out by questioning the conscious patient or a suitable responsible person.

After taking the appropriate blood samples, these should be clearly labelled at the patient's bedside, with full names, date of birth, hospital number, date of sample withdrawal and ward identification. In the case of an under-aged or unconscious patient, the medical staff may assume the responsibility for identification.

The clinician must complete a requisition form (which may be paper-based or digital), outlining all the above information plus:

- Details of previous medical, obstetric and transfusion history
- Diagnosis
- Reason for transfusion
- Number and type of component required
- Date and time when the blood or blood components should be available

This information will assist the blood bank staff in identifying the recipient and in finding a compatible unit. The blood bank will return all incomplete or illegible requisition forms and improperly labelled samples. The blood service cannot accept any legal responsibility if they are not supplied with sufficient information to identify the patient.

Laboratory tests are carried out on the sample:

- To determine the ABO and Rh status of the patient
- To detect blood group antibodies
- To test for serological compatibility with the requested component

When ordering blood for surgical procedures that only occasionally require intra-operative transfusion (fewer than 30% of cases), a group and screen request is indicated. This involves the typing of a pre-operative specimen from the patient for ABO and Rh groups and a screening test for clinically significant antibodies. Blood is then only cross-matched if clinically significant antibodies are detected or there is unexpected blood loss at surgery.

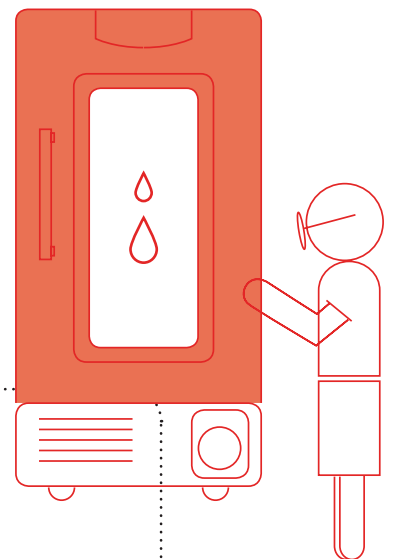
THE BLOOD COMPONENT

Inspect for leaks, especially in port areas, by inverting and applying light pressure to the unit. Observe for missing port covers and abnormalities.

The colour of a red-cell concentrate unit should not be significantly darker than the attached segments. Plasma in the unit should not be murky, purple, brown or red. Platelet units will be a cloudy yellow/straw colour and should not contain grossly visible aggregates. Thawed fresh frozen plasma (FFP) will be clear, varying from yellow to straw coloured. Cryoprecipitate will usually be a cloudy straw colour.

Most acute haemolytic transfusion reactions occur as a result of errors in patient or component identification. When you are ready to start the transfusion, perform the following verification process to help ensure the correct unit will be given to the correct patient:

1. Recheck the physician's order against the component received to verify you have received the correct component type
2. Ideally 2 qualified individuals should verify the patient and component identification at the patient's bedside. This process involves one individual reading the information aloud from one source and the other individual comparing the information to another source (preferably done by a medical practitioner and a registered nurse or by 2 registered nurses)



Although staffing and other requirements do not always make this practicable, special care must be exercised in identification procedures. It should always be assumed that one has the wrong patient or the wrong unit, until all identification has been specifically checked.

The following guidelines should be adhered to:

- All identification is carried out at the patient's bedside
- All information is read aloud by both attendants checking the blood
- The recipient's name and identification number on the unit must be identical to that on the hospital record (folder)
- The identification number on the unit must correlate with the unit identification number on the requisition form and/or label
- The donor's ABO and Rh groups must be recorded on the blood unit (and the transfusion requisition form)
- Compatibility between the donor and the recipient must be verified as having been confirmed
- If possible, the patient's ABO and Rh groups should be confirmed from previous transfusion records in the patient's folder
- The date and time of expiry of the unit must be checked. Expired blood must not be transfused

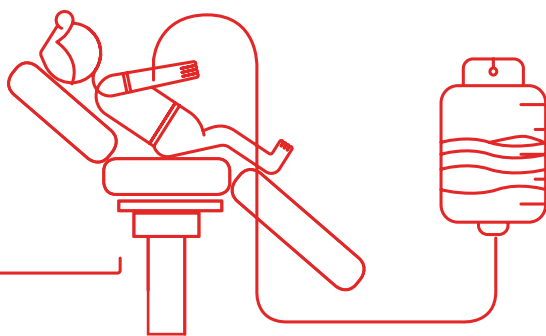
If any abnormalities are noted, the blood component should not be transfused. It should be returned to the hospital's blood bank.

♥ THE PATIENT

Asking for their full name, birth date and other relevant details identifies the patient. The questions should be phrased so that the patient gives a specific answer and not just 'yes' or 'no', e.g. 'What are your full names?' instead of 'Are you Mr J Smith?' The patient information should correlate with that on the blood unit and requisition form.

Extra care must be taken in identifying the unconscious, anaesthetised or unidentified patient by checking identity bands, written records and requisition forms. **Only** if all identification is in order may the transfusion be initiated.

If the patient is to receive autologous (self-donated) or directed units, these should be administered first. If a patient has both autologous and directed units available, autologous units should be given before directed units. If a patient has both directed units and non-directed units available, directed units should be given before non-directed units.



ASEPTIC TECHNIQUE

Blood is usually transfused through a large needle or cannula, the size of which is selected according to the calibre of the patient's veins. Almost any peripheral vein is suitable for transfusion, but the forearm veins are preferable as the patient's movement will not be restricted.

Meticulous skin care and aseptic techniques cannot be over emphasised in transfusion therapy, as blood acts as an ideal culture medium for bacterial growth. The proposed site for venepuncture should be cleaned with the recommended hospital antiseptic, working from clean to dirty areas. Ideally, gloves and a sterile field should always be used to position the cannulae for transfusion, but most especially in immunocompromised or long-term transfusion patients. The site should never be re-palpated after cleansing.

During transfusion, the transfusion site should be visible through a transparent dressing so that any inflammation or infiltration may be seen immediately. The transfusion cannula should be repositioned if inflammation or infiltration is observed.

MONITORING THE PATIENT

A critical part of transfusion therapy is the monitoring of the patient, whether by a nurse or a medical practitioner. The accurate and quick interpretation of adverse effects could prevent a fatal reaction. The unit number, the date of transfusion and the starting and finishing time of each unit transfused should be recorded in the patient's folder. Some services require additional signatures on accompanying forms. All this information should be permanently retained in the patient's folder.

Baseline observations of vital signs should be recorded prior to commencing the transfusion. The patient is then observed closely for the first 30 minutes of the transfusion to detect any untoward reaction, and to ensure that the desired rate of transfusion is maintained.

In cases of major blood loss, ideally the central venous pressure (CVP), pulse, blood pressure (BP), respiratory rate and urinary output should be monitored every 15 minutes throughout the transfusion. In less severe cases, the recipient's vital signs should be checked every half hour after the initial 30-minute observation. Patients at risk for circulatory overload should be observed for 12 – 24 hours after transfusion.

If a transfusion reaction is suspected because the patient complains of symptoms or there are clinically significant changes in vital-sign measurements:

- The transfusion must be stopped immediately
- The drip set must be changed
- The vein must be kept open with a transfusion of normal saline

The following actions must then be undertaken:

- A member of the medical staff must be contacted immediately
- The patient's temperature, pulse, respiratory rate and BP must be recorded
- All clerical and identity checks must be repeated

Further management depends on the type and severity of the reaction.

All empty blood units should be returned to the blood bank, where they must be retained for 48 hours following transfusion, at a temperature of 1 °C – 6 °C.

SPECIAL PRECAUTIONS

Rate of Transfusion

The rate of the transfusion depends on the clinical condition of the patient. A patient in acute shock from massive blood loss will require rapid transfusion, whereas the rate should not exceed 2 ml per minute in a patient with chronic anaemia. A relatively slow rate of 5 ml per minute is recommended for the first 30 minutes and, if there is no sign of untoward reaction, the rate can then be increased.

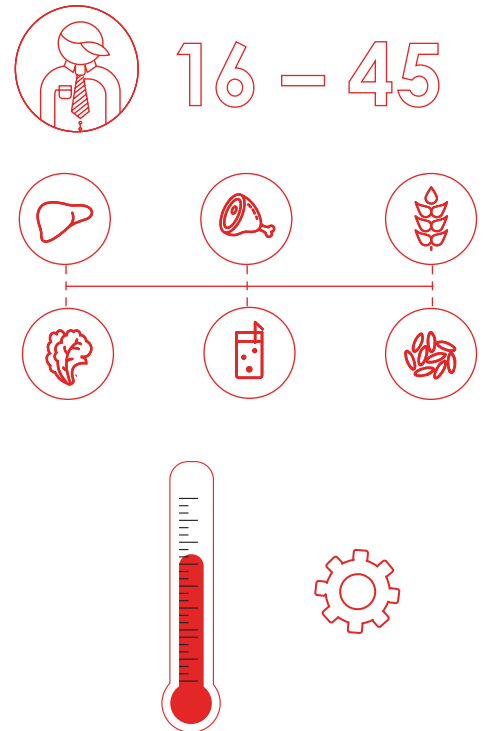
Blood transfusions must be completed within 6 hours of entry of the pack. Blood components that are not used immediately should be stored at the temperature specified by the blood bank. Blood components that are no longer required for a specific patient must be returned to the blood bank, either for correct storage (only if still contained in the original "hamper" packaging with no seals broken) or for disposal.

Filters

Red blood cells (RBCs), whole blood, cryoprecipitate and FFP are administered through a standard blood-recipient set or Y-type giving set. These sets have 170 µm – 240 µm mesh filters to prevent the transfusion of clots or coagulation debris. The filter should be covered with blood to ensure that the full filtering area is used.

A platelet-administration set should preferably be used for platelets, although the standard filter-administration set may also be used in an emergency. The latter results in greater loss of the available platelets due to a larger surface area for adhesion.

The use of microaggregate (40 µm) filters is not recommended.



The administration set should be changed:

- When there is a transfusion reaction, in order to prevent further potentially harmful blood entering the patient's system
- Between red cells and other blood products, and between red cell transfusions of different ABO groups
- Before infusing other fluids, e.g. dextran, Ringers lactate
- Every 12 – 24 hours in patients requiring long-term transfusion

Temperature of the Blood

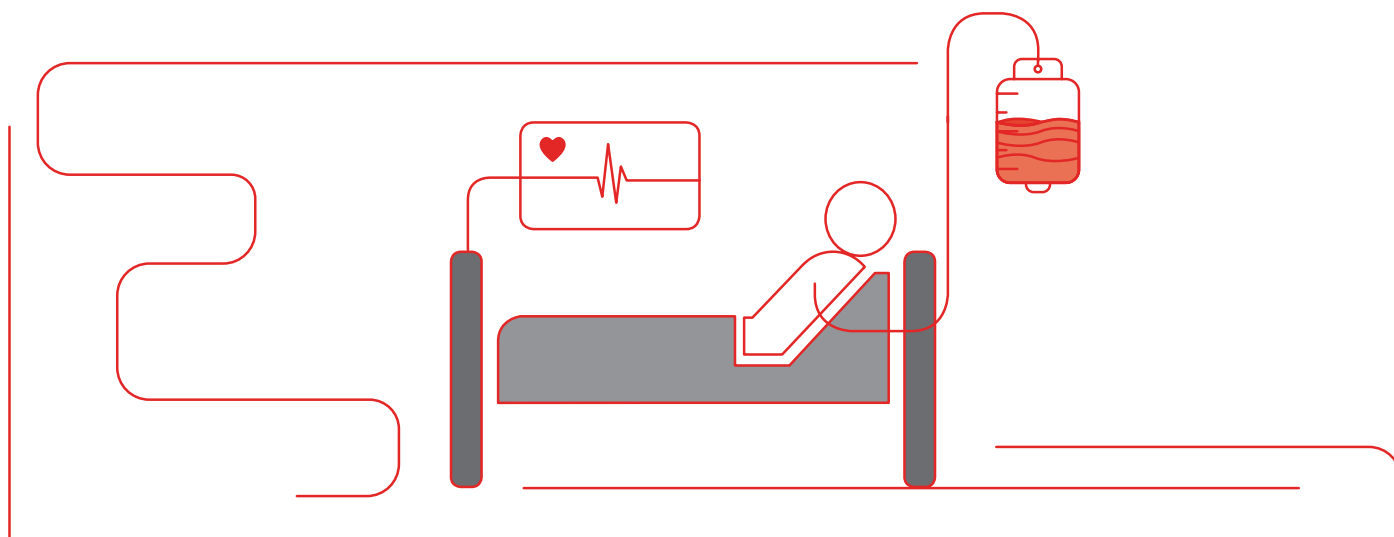
If cold blood is administered at a slow rate, it does not appear to affect the circulatory system. However, in cases where rapid transfusion is necessary, complications such as cardiac arrhythmias can be avoided by warming the blood to not $>37\text{ }^{\circ}\text{C}$. Overheating of the blood can cause extensive haemolysis with renal damage and possible death.

Blood should be warmed with a blood warmer specifically designed for this purpose. This apparatus should be equipped with a visible temperature-monitoring device and should have an audible alarm.

The practice of warming blood in a sink of warm water is ineffectual, as only the outer red cell layers are warmed. It may also present an infectious hazard as the ports may become contaminated. Furthermore, overheating may result in devastating haemolysis of the blood product, with potentially fatal consequences.

Under no circumstances should blood be heated in a microwave oven or similar device. This not only results in extensive haemolysis, but also causes conformational changes and denaturation of proteins.

Blood warming is not routinely indicated and refrigerated blood may be transfused over several hours without harm.



Indications for warming are:

- Massive transfusion of $>50\text{ ml/kg/h}$
- Infants transfused at $>15\text{ ml/kg/h}$
- Neonates receiving exchange transfusion or large-volume transfusion
- Patients with high-titre cold haemagglutinins reactive in vitro at temperatures above $30\text{ }^{\circ}\text{C}$
- Transfusion of blood products through central lines
- Hypothermia

Additives

No medications or other fluid should be added to the blood or blood products before or during a transfusion because:

- Bacterial contamination is a real hazard whenever any unit of blood is entered
- A reaction could occur between the drug and the anticoagulant or nutrient fluid in the blood, e.g. dextrose solutions might cause lysis or aggregation of the red cells in the transfusion set
- Therapeutic levels of a drug may not be achieved if the blood is administered slowly

If it is difficult to infuse medication through an alternative access site, then a Y-piece may be inserted near the junction of the insertion of the intravenous (IV) transfusion cannula.

The only fluids that can be given concurrently through the same IV device as a red cell transfusion are:

- Normal saline
- Calcium-free balanced salt solutions, e.g. Plasmalyte-L, Plasmalyte-B, Balsol, modified Ringer's lactate
- 4% albumin
- Plasma protein fractions
- ABO-compatible plasma



FURTHER READING

1. Blood Transfusion Safety Team. The clinical use of blood : handbook. World Health Organization. 2001. Accessed March 7, 2023. <https://apps.who.int/iris/handle/10665/42396>
2. Safe blood and blood products: manual on the management, maintenance and use of blood cold chain equipment. World Health Organization. 2005. Accessed March 7, 2023. <https://www.who.int/publications/i/item/92-4-154673-5>
3. Pagliaro P, Rebullia P. Transfusion recipient identification. Vox Sang. 2006;91(2):97-101. doi:10.1111/j.1423-0410.2006.00783.x
4. Safe transfusion – right blood, right patient, right time and right place. Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. 2020. Accessed March 7, 2023. <https://www.transfusionguidelines.org/transfusion-handbook/4-safe-transfusion-right-blood-right-patient-right-time-and-right-place>
5. Blood transfusion. Mayo Clinic. 2022. Accessed March 7, 2023. <https://www.mayoclinic.org/tests-procedures/blood-transfusion/about/pac-20385168>
6. Australian and New Zealand Society of Blood Transfusion, Australian College of Nursing. Guidelines for the administration of blood products. 2018. Accessed March 7, 2023. https://anzsbt.org.au/wp-content/uploads/2018/06/ANZSBT_Guidelines_Administration_Blood_Products_3rdEd_Jan_2018.pdf

Chapter 4:

RED CELL COMPONENTS



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

RED CELL COMPONENTS

The transfusion of red cells, when prescribed in the correct clinical setting, has the ability to save lives and markedly improve survival rates and morbidity in patients. Optimal use of RBCs should involve administering enough (minimal amount of) RBCs to maximise clinical outcomes while at the same time avoiding unnecessary transfusions that expose patients to potential – albeit rare – infectious or non-infectious risks as well as increased costs.

There is no consistently accepted haemoglobin (Hb) level below which red cell transfusion should occur for every patient, in every situation. Rather, the decision to transfuse red cells to an anaemic patient should be based primarily on the clinical situation, guided by the Hb level.

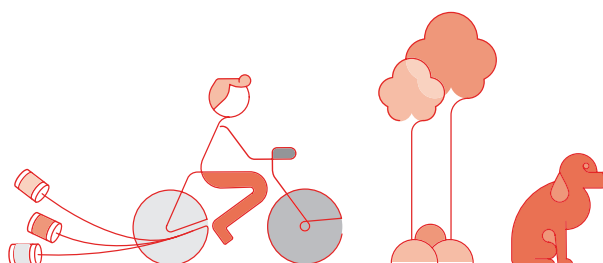
Various clinical factors should be considered, in addition to the Hb level, when deciding whether a red cell transfusion is warranted:

- **Cardiopulmonary reserve:** Effective oxygen delivery depends not only on the patient's Hb level, but also on their cardiovascular condition and ability to compensate for decreased Hb. Patients with normal cardiopulmonary function will likely be able to tolerate lower Hb levels than those with limited cardiopulmonary reserve
- **Acuity:** Patients who develop anaemia slowly develop compensatory mechanisms to allow them to tolerate lower Hb values than patients who become acutely anaemic
- **Presence/risk of ongoing blood loss:** These patients may require a higher Hb target
- **Age:** The normal Hb levels of infants and children vary from those seen in adults, so transfusion triggers and the usual blood component dose will also vary according to age (see below for guidelines on neonatal and paediatric transfusions)

RBCs are not given for volume replacement or for any reason other than correction of acute or chronic anaemia and to restore/improve tissue oxygenation. RBCs should be given only after non-transfusion alternatives have been either assessed and excluded or found to not adequately manage anaemia.

The early application of appropriate PBM principles is required for all patients. Depending on the underlying cause of anaemia, alternative treatments should be considered, e.g. iron (oral/intravenous), vitamin B12, folic acid and erythropoietin stimulating agents. In the surgical setting, cost-effective pharmaceutical preparations that prevent, minimise or control blood loss should be used. Monitoring the patient while treating the underlying conditions contributing to anaemia may be an alternative to transfusion for some patients.

RBC transfusion is usually indicated if Hb <7g/dl and is rarely indicated if Hb >10g/dl. For patients with Hb levels between 6 g/dl and 10 g/dl, other factors should be considered, e.g. age, co-morbidities, risk of ischaemia, and rate and volume of blood loss.



Many studies and guidelines recommend the use of a restrictive transfusion strategy, including in the ICU setting and with post-operative anaemia:

- In hospitalised adult patients who are haemodynamically stable, including critically ill patients, a restrictive RBC transfusion threshold in which the transfusion is not indicated until the Hb level drops to <7g/dl, is recommended.
- For patients undergoing orthopaedic or cardiac surgery and for those with pre-existing cardiovascular disease, a restrictive RBC transfusion threshold of 8 g/dl is recommended. Although the restrictive transfusion threshold of 7 g/dl is likely comparable with 8 g/dl, randomised controlled trial (RCT) evidence is not available for these patients and this more lenient cut-off is therefore recommended.

These recommendations do not apply to patients with:

- Acute coronary syndrome
- Severe thrombocytopenia (patients treated for haematological or oncological conditions who are at risk of bleeding)
- Chronic transfusion-dependent anaemia (there is insufficient evidence)

Of note, patients with thrombocytopenia plus anaemia are more likely to bleed than those with thrombocytopenia alone. The primary aim of red cell transfusions in patients with chronic anaemia is to ameliorate symptoms as opposed to achieving a specific Hb level.

Transfusions are associated with increased morbidity and mortality in high-risk hospitalised patients. Single-unit red cell transfusions should be the standard for non-bleeding hospitalised patients, as this is often adequate to relieve symptoms or raise the Hb to an acceptable level. Additional units should only be prescribed after re-assessment of the patient and their Hb value.

Summary of Recommendations for Red Cell Transfusions

A restrictive RBC transfusion threshold is recommended in hospitalised adult patients who are haemodynamically stable, including in critically ill patients. Transfusion should not be indicated until an Hb level of 7 g/dl is reached.

This recommendation excludes the following conditions, in which transfusion is not indicated until an Hb level of 8 g/dl is reached:

- Orthopaedic surgery
- Cardiac surgery
- Pre-existing cardiac conditions

This recommendation also excludes patients with the following conditions:

- Acute coronary syndrome: Insufficient evidence; a transfusion trigger of 8 g/dl – 10 g/dl may be considered
- Severe thrombocytopenia at risk of bleeding: These patients are more likely to bleed so, although there is insufficient evidence, a transfusion trigger of 8 g/dl may be considered
- Chronic transfusion-dependant anaemias: Aim is to ameliorate symptoms of anaemia, not treat an Hb level

DO NOT



Transfuse blood if other non-transfusion therapies or observation would be just as effective



Transfuse >1 red cell unit at a time when transfusion is required in stable, non-bleeding patients



Transfuse patients based solely on an arbitrary Hb threshold in the absence of symptoms, active coronary disease, heart failure or stroke – or if no benefit was perceived from previous transfusions



Routinely transfuse RBCs in haemodynamically stable ICU patients with an Hb concentration >7 g/dl. A threshold of 8 g/dl may be considered

INDICATIONS FOR RED CELL COMPONENTS

The primary indication for RBC transfusion is the restoration of oxygen-carrying capacity. Red cell concentrates (and in specific situations, whole blood) are used to improve tissue oxygenation when this is impaired by haemorrhage or anaemia.

Acute Blood Loss

Acute blood loss of >30% of blood volume (about 1 200 ml – 1 500 ml blood in an adult) will often result in the need for a red cell transfusion. There must be no delay in ordering blood in situations where blood loss is acute and rapid or where there is a possibility of recurrence or continuation of bleeding.

In patients with acute blood loss, volume replacement is often required and, depending on the clinical circumstances, plasma and platelets may also be transfused.

General Surgery

Consider transfusion if:

- The pre-operative Hb level is <8 g/dl and the surgery is associated with major blood loss (>500 ml)
- The intra- or post-operative Hb falls below 7 g/dl. A higher Hb level may be indicated in patients who are at risk for myocardial ischaemia or who are >60 years of age

Pre-operative anaemia must be investigated and corrected in every case, as medical management to raise the Hb level may be more appropriate than transfusion.

In surgical patients, the effect of plasma and blood-volume expansion should be considered when determining the red cell transfusion threshold based on the Hb concentration only, and the limitations of the haematocrit (Hct) level should be taken into account when assessing the need for RBC transfusion in hypovolaemic anaemic patients.

In situations of massive transfusion, the number of RBC units transfused can be used as a surrogate for determining the transfusion requirements of FFP, platelet concentrate and cryoprecipitate. All hospitals should have a protocol in place that addresses massive blood transfusion.

Anaemia in Acute Coronary Syndromes

In patients with acute coronary syndromes (ACS), the latest review of the guidelines cannot recommend for or against a liberal or restrictive RBC transfusion threshold. Further research is needed to determine the threshold.

Transfusion to an Hb level of 8 g/dl – 10 g/dl should be considered acceptable, but the effect of each unit transfused must be evaluated for the risk of heart failure due to fluid overload.

Anaemia

Early investigation and correct management of anaemia is required for all patients. The aetiology of the anaemia should be investigated and, as far as possible, a definitive diagnosis should be made in every case. Medical management will be determined by the cause of the anaemia.

Appropriate alternatives to blood transfusion must be considered. Consider transfusion in normovolaemic patients only if they are severely symptomatic, e.g. shortness of breath at rest, angina, incipient cardiac failure, tachycardia.

Patients with an Hb level <7 g/dl should be considered for a transfusion. In chronic nutritional anaemias, however, an Hb level of >6 g/dl is often well tolerated without associated medical complications and should respond well to treatment of the deficiency without a transfusion being required.

The target (post-transfusion) Hb level will be determined by many factors, including the primary diagnosis. The target Hb will be higher in individuals who require chronic RBC transfusions (e.g. patients with thalassaemia). In general, the target Hb level will be higher in patients with a "medical" anaemia as opposed to patients with a "surgical" anaemia with blood loss. In the latter, the bone marrow is usually normal; whereas in the former, the bone marrow and other organs may be impaired.

The patient's clinical condition should be reassessed after each unit is transfused and the need to continue transfusion therapy should be evaluated. In many cases, transfusion can be stopped when an Hb level is reached where the patient is asymptomatic.

Cardiac Surgery

Current guidelines recommend a restrictive transfusion strategy in which transfusion is not indicated until the Hb level drops below 8 g/dl.

The TRUST (transfusion risk understanding score) index is a validated tool to predict the likelihood of blood transfusion requirements of patients undergoing cardiac surgery, based on pre-operative clinical variables including:

Table 4.1

Patient-related	<ul style="list-style-type: none"> • Weight • Female gender • Age
Laboratory-related	<ul style="list-style-type: none"> • Pre-operative Hb and creatinine
Procedure-related	<ul style="list-style-type: none"> • Non-elective procedure • Previous cardiac surgical procedure • Non-isolated procedure, e.g. coronary artery bypass graft, valve repair

Using this scoring index to stratify patients pre-operatively enables clinicians to anticipate the patient's transfusion needs and prepare the patient and blood bank accordingly.

Obstetric Haemorrhage

During an obstetric haemorrhage, RBCs should be administered to maintain the patient free of signs and symptoms of inadequate tissue oxygen delivery. The Hb should be maintained between 6 g/dl and 10 g/dl during the resuscitation phase.

Special attention must be given to maintaining adequate fibrinogen levels. Fibrinogen replacement in the form of cryoprecipitate may be required.

RED CELL COMPATIBILITY

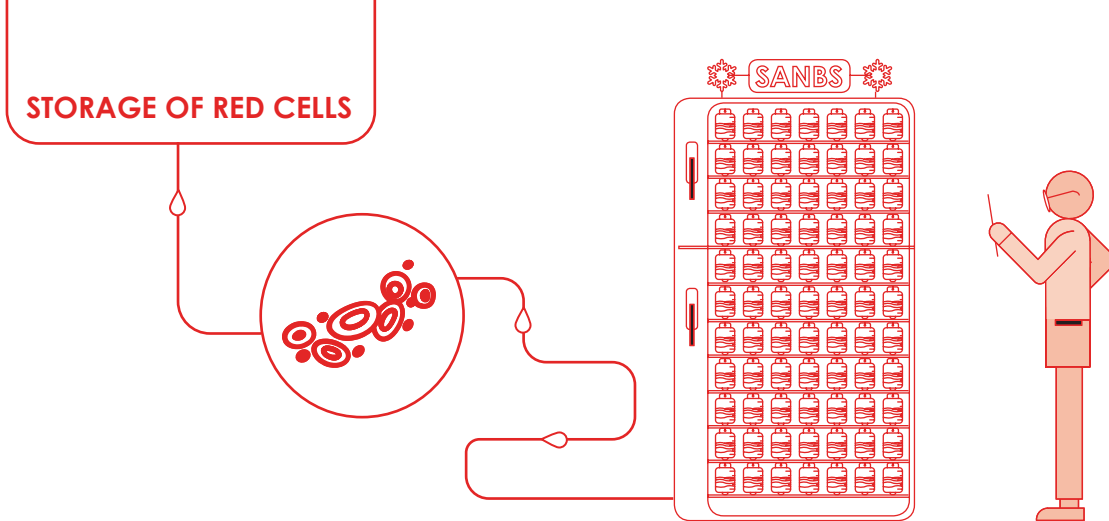
Compatibility tests ("cross-matching") should be performed prior to transfusion of red cells. Red cell transfusions must be ABO compatible.

As far as possible, RBC transfusions should also be Rh-D compatible but in an emergency (e.g. massive blood transfusion or shortage of Rh-D negative blood), Rh-D positive blood may be transfused to Rh-D negative patients provided that the patient does not have pre-formed anti-Rh-D antibodies.

Rh-D positive blood should also be avoided in females of childbearing age who are Rh-D negative.

Antigen negative blood should always be transfused to patients with specific and clinically significant red cell antibodies.





Red cell products are preserved and stored at 1 °C – 6 °C for up to 42 days. While previous guidelines have recommended “fresh” blood (<7 days old) in specific clinical settings, recent recommendations state that patients, including neonates, should receive RBC units selected at any point within their licensed dating period (42 days) rather than limiting patients to transfusion of only fresh (<10 days old) units.

Some guidelines still recommend that the following may warrant the use of RBCs with shorter storage times:

- Intrauterine transfusion
- Large-volume transfusion
- Paediatric transfusions (>25 ml/kg)
- Exchange transfusion
- Cardiac surgery
- Use of irradiated blood products

During the storage of banked blood, changes occur which may be clinically significant. The characteristics of stored blood should be taken into account when transfusing red cell products. Some of the impacting factors are discussed below.

Anticoagulant

Donated blood is collected into a solution containing sodium citrate. Citrate is a stable, minimally toxic anticoagulant with pH-buffering properties. Citrate is metabolised in the Krebs cycle (of respiration) and – after transfusion – is rapidly metabolised by most cells in the body, particularly in the liver, muscle and renal cortex.

However, certain clinical conditions (e.g. liver disease, hypothermia and hypoparathyroidism) may place patients at risk for “citrate toxicity” during rapid transfusion of whole blood or FFP. Newborns without adequate calcium stores, and with immature livers, are also at risk. In these circumstances, citrate has been considered to be the cause of cardiac arrhythmias and decreased cardiac contractility owing to its ability to lower plasma-ionised calcium through chelation.

The flow rate of citrate determines the degree of toxicity. A rate corresponding to 0.04 mmol/kg/min is associated with a significantly increased plasma citrate level and a prolonged QT interval. This situation may especially arise in massive, rapid transfusion of whole blood, but it may – to a much lesser extent – also arise in the transfusion of RBC concentrates.

If possible, ionised calcium levels should be monitored and 10 ml of 10% calcium gluconate administered intravenously (a rule of thumb is 10 ml for every 2 units whole blood given in under 10 minutes).

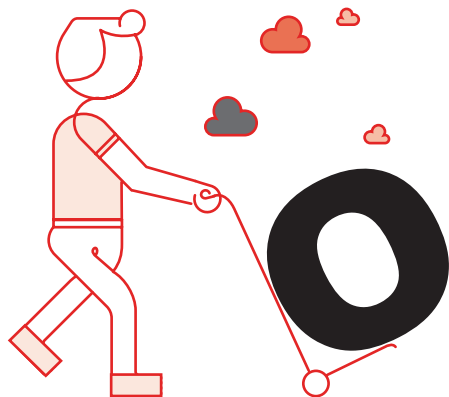
Calcium and any other drug or solution should never be directly added to blood components. If calcium depletion is suspected, most blood gas analysers will give a very rapid measurement of ionised calcium. Any level <0.7 mmol/l should be treated.

Calcium depletion alone is seldom a cause of impaired coagulation as the levels required to reduce coagulation are very low (<0.5 mmol/l).

2,3 Diphosphoglycerate

The function of erythrocyte 2,3 diphosphoglycerate (2,3 DPG) is to facilitate oxygen transport. Its binding with deoxyhaemoglobin, and its interaction with oxyhaemoglobin shifts the oxygen-dissociation curve to the right, decreasing the oxygen affinity of Hb and enhancing oxygen delivery to tissues.

The concentration of 2,3 DPG in blood decreases significantly after approximately 1 week of storage, which results in the oxygen-dissociation being shifted to the left, decreasing oxygen delivery to tissues. After transfusion, however, levels of 2,3 DPG are regenerated in-vivo, with approximately 50% being regenerated within 7 hours, although full restoration of RBC 2,3 DPG can take up to 72 hours.



In clinical situations of hypoxia and lactic-acid production, and with decreasing pH, the oxygen dissociation curve is also shifted to the right, increasing oxygen delivery. Increased oxygen delivery also occurs with an increase in cardiac output.

It is therefore generally considered that low 2,3 DPG levels in stored blood are not usually clinically significant, e.g. fresh blood and aged stored blood have been shown to be equally efficacious in immediately reversing anaemia-induced brain oxygenation deficits in humans. Lower 2,3 DPG red cell concentrations during the first 24 hours of intensive care are also not associated with higher ICU mortality.

Nevertheless, in certain clinical situations, transfusion of blood which has been stored for <5 days may be optimal, including:

- Patients in shock who cannot increase cardiac output to compensate
- Patients receiving large volumes of stored blood, e.g. massive transfusion
- Patients undergoing red cell exchange procedures

Preservative Solutions

RBC concentrates are prepared by removing most of the plasma and the buffy coat layer – which is rich in leucocytes and platelets – from a unit of whole blood. A preservative solution (111 ml volume) is added to the residual red cells. It contains:

- Adenine: Helps maintain adenosine triphosphate (ATP) levels during storage
- Glucose: Provides a substrate for RBC energy pathways
- Saline
- Mannitol: Reduces the haemolysis of the banked red cells during the 42-day storage period

Separating off the buffy layer results in the removal of approximately 70% – 80% of leukocytes present in the original whole blood donation and significantly decreases the occurrence of non-haemolytic febrile transfusion reactions.

The volume of a unit of red cell concentrate is approximately 300 ml – 350 ml (including the additive solution) and the Hct is 0.55 l/l – 0.70 l/l. One unit of RBC concentrate (at a dose of 4 ml/kg) can be expected to increase the Hb level of an average (70 kg) adult by approximately 1 g/dl – 2 g/dl.

Stored red cells experience loss of deformability so on day 42 of storage about 75% of red cells are viable.

Hyperglycaemia has been observed in certain clinical situations (e.g. massive transfusion in orthotopic liver transplantation or following cardiac surgery in infants) and has been attributed to the high glucose concentration in RBC concentrates stored in adenine additive solutions.

Electrolyte Changes

At standard storage temperatures of 1 °C – 6 °C, the sodium-potassium pump is essentially non-functional and intracellular and extracellular levels gradually equilibrate.

Plasma potassium concentration increases nearly eightfold over 28 days of storage although, at expiry, the total potassium load in red cell concentrates is only about 5.5 mmol.

The potassium load is therefore rarely a clinical problem, except in the setting of pre-existing hyperkalaemia. In these situations, fresh (<5 days) or washed red cell concentrates should be used.

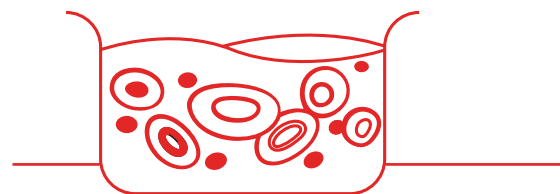
LEUCOCYTE-DEPLETED RED CELLS

See Chapter 7, *Leucocyte Depletion and Irradiation of Blood Components*.

WASHED RED CELLS

Washed red cells are prepared by the removal of plasma and the buffy layer from whole blood donations. The residual red cells are suspended in isotonic saline and centrifuged. The saline from the first saline “wash” is then removed and the red cells are re-suspended in isotonic saline.

Because washed cells are manipulated in an open system, with a possibility of bacterial contamination, they must be transfused within 24 hours of preparation.



Indications for washed red cells

Table 4.2

Indication	Additional information
Patients who have experienced severe, recurrent allergic transfusion reactions not prevented by antihistamines	
Patients with known immunoglobulin A (IgA) deficiency who have formed anti-IgA antibodies	<ul style="list-style-type: none">• Patients with IgA deficiency may experience an anaphylactic reaction if transfused with blood products containing plasma (even minute amounts of IgA protein)
Patients with paroxysmal nocturnal haemoglobinuria (PNH)	<ul style="list-style-type: none">• Traditionally, washed cells have been recommended for RBC transfusions in these patients, but recent evidence suggests that transfusing washed cells in patients with a diagnosis of PNH is not necessary• Washing of red cells is therefore no longer recommended, provided that donor red cells of the same ABO group as the patient are transfused
Neonates with T-activated red cells	<ul style="list-style-type: none">• Immune-mediated haemolysis may occur following transfusion of plasma-containing blood components to patients whose red cell T-crypt antigens have been exposed by bacterial infection• T-activation occurs when bacterial neuraminidase removes N-acetyl neuraminic acid and exposes red cell T-crypt antigens. These antigens are then susceptible to immunoglobulin M (IgM) anti-T which is prevalent in normal plasma, occasionally leading to severe haemolysis. This is particularly associated with necrotising enterocolitis.• However, because there is very little plasma in RBC concentrates, it is probably unnecessary to routinely provide washed red cells to all patients with evidence of T-activation of red cells
Patients where a high potassium concentration in transfused blood may be clinically significant	<ul style="list-style-type: none">• Plasma potassium concentrations increase significantly after 12 hours following a gamma irradiation dose of 25 Gy• Stored red cells which have been gamma irradiated can be washed shortly before transfusion but, in practice, this can best be managed by ensuring that irradiated whole blood is transfused within 24 hours of irradiation (see Chapter 3, Ordering and Administration of Blood)

WARMING BLOOD FOR TRANSFUSION

In general, blood should not be warmed when individual units are being transfused slowly (over a period of 2 – 4 hours per unit). Transfusing ice-cold blood rapidly, however, has been associated with an increased incidence of cardiac arrest. Blood should therefore be warmed to 35 °C – 37 °C when large volumes are being transfused rapidly.

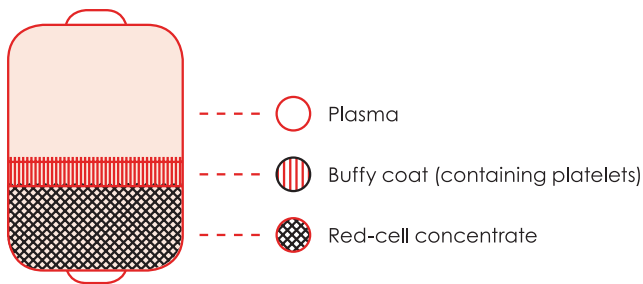
A blood warmer may be indicated for:

- Large-volume rapid transfusions (i.e. >50 ml/kg/hour in adults or >15 ml/kg/hour in children)
- Exchange transfusions
- Plasma exchange for therapeutic apheresis in adults
- Intrauterine transfusions, at the discretion of the specialist
- Patients with clinically significant cold agglutinins
- Trauma situations in which core-rewarming measures are indicated
- The patient-rewarming phase during cardiopulmonary bypass surgical procedures

The best method for warming blood is to use a heat exchanger in which coils of tubing are warmed by electric heating plates. Microwave ovens/hot water/heaters must never be used to warm blood for transfusion – they may damage red cells and cause harm to the patient.

WHOLE BLOOD

Whole blood is a complex tissue from which clinically appropriate components are processed. Many of the components, particularly platelets and clotting factors, deteriorate in whole blood within hours of donation. It is therefore necessary to physically separate the components soon after donation so that they are available for use in the appropriate clinical situation.



The clinical indications for using whole blood are limited, since RBC concentrates are more appropriate in most situations in which oxygen-carrying capacity needs boosting.

Indications for whole blood

- Exchange transfusion in neonates
- Massive haemorrhage

IRRADIATED RED CELLS

See Chapter 6, *Plasma Components and Derivatives*.

BLOOD FOR EXCHANGE TRANSFUSION IN ADULTS

Red cell exchange transfusion may be performed in:

- Patients with malaria who have a high parasite load
- Patients with acute sickle cell crisis

Erythrocytes infected with *Plasmodium falciparum* have been shown to have decreased 2,3 DPG activity. Because of the large volume of red cells transfused over a short period, it is recommended that – for exchange transfusion in adults – red cells that are no older than 5 days be transfused.

The procedure is best managed using apheresis technology.

PAEDIATRIC RED CELL TRANSFUSIONS

Table 4.3

Guiding principles for neonatal and infant transfusions	
Characteristics	Transfusion requirements
Smaller blood volume and higher haematocrit system	<ul style="list-style-type: none">• Smaller-volume transfusions/top-ups• Slow rate of infusion
Reduced metabolic capacity system	<ul style="list-style-type: none">• Fresh components• Correct storage
Immature immune system	<ul style="list-style-type: none">• Leukoreduced products• Single donor products• Maternal ABO/Rh status must be known• Exclude maternal sensitisation to other antigens

INTRAUTERINE TRANSFUSION

Intra-uterine transfusion (IUT) should be done only by specialised units. It is most commonly indicated for correction of foetal anaemia caused by red cell allo-immunisation.

Intra-uterine platelet transfusions are rarely indicated and are essentially used only to correct foetal thrombocytopenia caused by platelet allo-immunisation. However, the use of intravenous immunoglobulin in mothers with allo-immunisation has largely replaced foetal platelet transfusions.

Red cell products for IUT are specially prepared by the blood transfusion service on request by the clinician.

They are usually:

- Group O
- Rh-D negative (preferably also Kell negative)
- Cross-match compatible with maternal plasma/serum
- <5 days old
- Leucocyte depleted
- Irradiated

NEONATAL TRANSFUSION

Exchange Transfusion

Exchange transfusion may be used to manage severe anaemia at birth and to treat severe hyperbilirubinaemia, usually caused by haemolytic disease of the foetus and newborn (HDFN). The aim in exchange transfusion is to remove Rh-D positive red cells, reduce bilirubin levels and remove maternally derived anti-D.

The bilirubin level at which an exchange transfusion is indicated varies according to the weight and gestational age of the baby and the *South African Neonatal Academic Hospitals' Consensus Guidelines* should be followed.

The early administration of intravenous immunoglobulin (dose: 1 g/kg) to Coombs-positive infants with neonatal jaundice significantly reduces the level of exchange transfusions for hyperbilirubinaemia.

The red cell component used for exchange transfusion varies nationally and internationally. Some centres use unmodified whole blood while others plasma-reduce whole blood to an Hct of 0.5 l/l – 0.6 l/l.

Some centres, particularly in the USA, reconstitute RBC concentrates with FFP, but this increases donor exposure and is not recommended unless whole blood is unavailable.

The unit should be:

- Group O (or ABO compatible with maternal and neonatal plasma)
- Rh-D negative
- Cross-match compatible with maternal and neonatal plasma
- <5 days old
- Irradiated (must be transfused within 24 hours of irradiation)
- Leucocyte depleted

An exchange of double the infant's circulating blood volume is recommended: 180 ml/kg – 200 ml/kg for pre-term infants and 160 ml/kg – 180 ml/kg for term infants. For bigger infants, where the calculated volume needed exceeds the amount in 1 unit of whole blood, only 1 unit should initially be ordered. Serum bilirubin results post-exchange transfusion will determine whether further blood is required.

Blood should not be transfused directly from cold storage. It should be warmed during the procedure with care taken to avoid overheating.

In normal-term infants, the routine use of calcium gluconate is unnecessary, but monitoring of ionised calcium is advisable in ill preterm neonates as the citrate toxicity may result in hypocalcaemia.

Small-Volume Red Cell Transfusion

Estimated blood volume (EBV) is 100 ml/kg – 120 ml/kg in extremely preterm infants and is 80 ml/kg – 85 ml/kg in term infants. In neonates, the transfusion volume is calculated using the following equation:



Hb content of RBCs can vary. In general, each 10 ml/kg – 15 ml/kg transfused is expected to increase the infant's Hb level by approximately 1 g/dl – 2 g/dl.

The usual volume of RBCs administered to neonates is 10 ml/kg – 20 ml/kg per transfusion. Some suggest a volume of 15 ml/kg for infants ≤1 500 g or <32 weeks' gestational age (GA), because an association has been reported between a greater total volume of infused blood and transfusion-related necrotising enterocolitis in infants with very low birth weight.

Blood bank pre-transfusion testing during the first 4 months of life differs from adult testing. If there are no clinically significant red cell antibodies in the infant or maternal plasma and the direct antiglobulin test is negative, a full cross-match is not necessary – although the ABO and Rh-D group should be re confirmed prior to each subsequent transfusion.

Table 4.4

Suggested transfusion thresholds for infants <4 months of age	
Anaemia in the first 24 hours	Hb <12 g/dl
Neonate receiving mechanical ventilation	Hb <12 g/dl
Respiratory distress/ congenital heart disease	Hb <12 g/dl
Acute blood loss	>10% blood volume lost
Oxygen dependent (not ventilated)	Hb <8 g/dl – 11 g/dl
Symptoms of anaemia*, stable patient	Hb <8g/dl

*apnoea, bradycardia, tachycardia, decreased vigour, poor weight gain

The age of the unit does not matter for small-volume top up transfusions, but large-volume transfusions (exchange transfusion or acute blood loss) should be <5 days old in order to avoid hyperkalaemia and reduced 2,3 DPG levels with impaired oxygen release.

Leucocyte-depleted products are also recommended for infants (see Chapter 7, *Leucocyte Depletion and Irradiation of Blood Components*).

Neonatal units should arrange with their blood banks that those neonates with extended transfusion needs are placed on a “limited donor exposure” programme, where the transfusion requirements of an infant are met by reserving units bled from a single donor for that specific infant. This minimises the infectious risk and red cell antigen exposure.

RED CELL TRANSFUSION IN OLDER CHILDREN (>1 YEAR)

Older children tolerate low Hb levels relatively well, unless there is accompanying respiratory or cardiac compromise. An Hb threshold of 7 g/dl is suggested, unless there is underlying severe cardiopulmonary disease. The recommended threshold would then be 10 g/dl – 12 g/dl.

As in adults, there is a tendency to more restrictive strategies since recent studies have shown no significant increase in morbidity as a result.

The recommended top-up transfusion dose for children is 10 ml/kg – 20 ml/kg via a standard blood administration set or syringe with equivalent filtration. An initial dose of 15 ml/kg is ideal, but as much as 20 ml/kg may be transfused in a haemodynamically stable patient if further transfusions are required.

A 40 kg child receiving 1 standard red cell concentrate (\pm 300 ml) is receiving <10 ml/kg and therefore older children may require >1 unit, even with a restrictive strategy. Another approach is to use the following formula:

$$\text{Hb(target)} - \text{Hb(actual)} \times \text{weight} \times \text{transfusion factor (4 for RBC concentrates and 6 for whole blood)}$$

In normovolaemic patients, furosemide (1 mg/kg) may be prescribed to prevent volume overload.

All infant and paediatric small-volume RBC concentrates are leucocyte depleted but, in older children where adult RBC concentrates are used, a specific request must be made for a leucocyte-depleted product. The guidelines for which patients require leucocyte-depleted products are given in Chapter 7, *Leucocyte Depletion and Irradiation of Blood Components*, but they bear repeating:

- Patients who have previously experienced febrile non-haemolytic febrile reactions
- Patients receiving multiple or lifelong transfusions
- Patients likely to receive organ or haemopoietic stem-cell transplants
- Patients at high risk for CMV infection
- Critically ill patients and those who undergo cardiac surgery

If anaemia is accompanied by thrombocytopenia at a level requiring a platelet transfusion, fluid overload may result if platelets are rapidly transfused first.

The blood bank can usually issue group-specific RBC concentrates within 20 minutes of receiving the cross-match request – or immediately if the patient’s blood group has previously been documented. In the event of a dire emergency, uncross-matched Group O blood can be given from the emergency fridge.

Since Rh-D negative blood is usually in short supply, this should generally be reserved for females. Males can usually quite safely be given Group O Rh-D positive blood in emergency situations.

SPECIFIC COMPONENTS FOR NEONATES AND INFANTS

Given the volumes required, the use of an adult RBC concentrate, FFP or platelet concentrate for infants and small children would result in significant wastage. The blood services therefore prepare special products for paediatric use as follows:

Table 4.5

Product	Quantity for paediatric use
RBC concentrates	25 ml – 150 ml
FFP	100 ml – 160 ml
Platelets	50 ml – 60 ml, usually obtained from a single apheresis platelet unit which is split into 5 or 6 units

FURTHER READING

1. Horn AR, Kirsten GF, Kroon SM, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. *S Afr Med J*. 2008;96(9):819. doi:10.7196/SAMJ.1256
2. Villeneuve A, Arsenault V, Lacroix J, Tucci M. Neonatal red blood cell transfusion. *Vox Sang*. 2021;116(4):366-378. doi:10.1111/vox.13036
3. Carson JL, Guyatt G, Heddle NM, et al. Clinical practice guidelines from the AABB: red blood cell transfusion thresholds and storage. *JAMA*. 2016;316(19):2025-2035. doi:10.1001/jama.2016.9185
4. Australian and New Zealand Society of Blood Transfusion, Australian College of Nursing. Guidelines for the administration of blood products. 2018. Accessed March 7, 2023. https://anzsbt.org.au/wp-content/uploads/2018/06/ANZSBT_Guidelines_Administration_Blood_Products_3rdEd_Jan_2018.pdf
5. Carson JL, Triulzi DJ, Ness PM. Indications for and adverse effects of red-cell transfusion. *N Engl J Med*. 2017;377(13):1261-1272. doi:10.1056/NEJMr1612789
6. European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS). Guide to the preparation, use and quality assurance of blood components. 20th Edition. European Directorate for the Quality of Medicines & HealthCare. Accessed March 7, 2023. <https://www.quotidianosanita.it/allegati/allegato8291904.pdf>
7. Wise R, Bishop D, Gibbs M, et al. South African Society of Anaesthesiologists perioperative patient blood management guidelines 2020. *Southern African Journal of Anaesthesia and Analgesia*. 2020;26(6):S1-68. <https://www.sajaa.co.za/index.php/sajaa/article/view/2496>



Chapter 5:

PLATELET PRODUCT TRANSFUSION



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

PLATELET PRODUCT TRANSFUSION

Platelets are responsible for the cessation of bleeding by the formation of platelet plugs at sites of vascular injury. Platelet transfusions can be indicated to prevent or stop active bleeding as a result of reduced platelet numbers or abnormalities of platelet function.

Platelet concentrates, like other blood components, carry risks and are costly to produce, and should therefore be used judiciously.

PLATELET PRODUCTS

There are 2 types of platelet concentrates available.

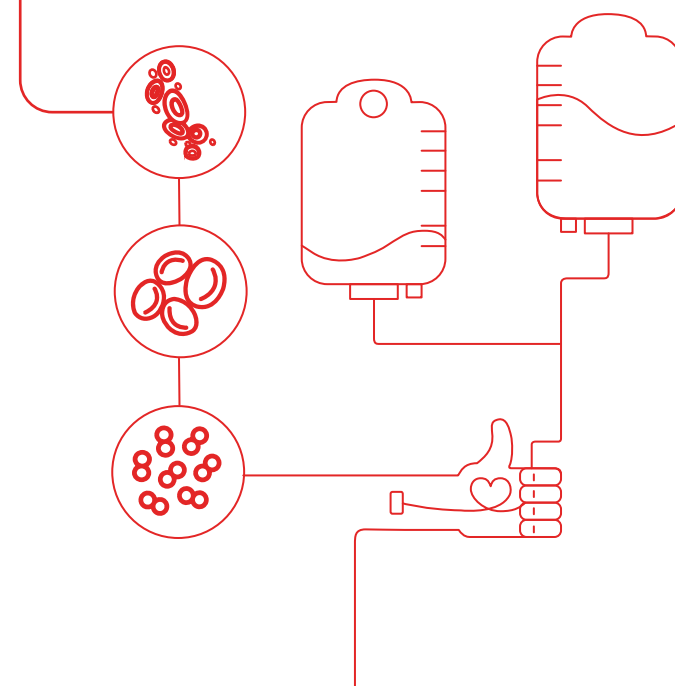
Table 5.1

Platelet product	Description
Random donor platelet (RDP) products	<ul style="list-style-type: none"> Derived from buffy coat layers of whole blood donations, separated within 8 hours of donation The buffy coats from 4 – 6 different donations are pooled and re-suspended in either plasma or platelet additive solution (PAS) Following a gentle spin, the platelets separate from the other cells to yield a concentrated platelet suspension
Single donor apheresis platelet (SDAP) products	<ul style="list-style-type: none"> Collected from a single donor by an apheresis technique. The donation takes 90 minutes on average and involves centrifugation of the donor's blood in the apheresis machine, the removal of platelets and a variable amount of plasma, and the return of the remaining blood components to the donor Blood banks do not keep large stocks of SDAP products to avoid wastage These products are suspended completely either in the donor's plasma or in a combination of plasma (30% – 40%) and platelet additive solution (60% – 70%) SDAP products are automatically leucocyte depleted in the apheresis machine The donor's pre-donation platelet count and total blood volume will determine the number of platelets that can be collected in a single donation. Donations with high platelet yields can be split into 2 or 3 products

RDP and SDAP products have been shown to be therapeutically equivalent in terms of post-transfusion increments and haemostatic efficacy. The major differences between these products are the donor-exposure risk and cost.

The use of RDP concentrates exposes the patient to a higher number of donors, with associated risks of transfusion-transmitted infection and alloimmunisation. This is why patients with chronic platelet-transfusion needs (e.g. with haematological malignancies or undergoing stem-cell transplants) should receive SDAP products.

SDAP products are more costly to produce due to the high cost of the apheresis donation kits.



Studies show that using leucocyte-reduced (filtered) RDP products is equivalent to using SDAP products in terms of platelet alloimmunisation, so they should be considered in settings where SDAP products are scarce.

Leucocyte-Depletion of Random Donor Platelet Products

The benefits of leucocyte-depletion of RDP products include a reduction in:

- Alloimmunisation (antibody formation to human leucocyte antigens and human platelet antigens) rates
- Transfusion-transmissible CMV infection
- Febrile non-haemolytic transfusion reactions (FNHTR)

There is an additional cost for this service that must be weighed up in resource-constrained settings.

Irradiation of Platelet Products

Platelets may be irradiated with no loss of function (see Chapter 7, *Leucocyte Depletion and Irradiation of Blood Components*, for indications).

Dose and Efficacy

RDP and SDAP products both contain a minimum of 2.4×10^{11} /l platelets and their volumes range between 200 ml and 300 ml. Comparative studies using higher platelet doses show a higher risk of patient adverse events, with no clinical benefit.

Infant SDAP products are produced by dividing Group O negative SDAP units into 4 doses. Each infant product has a volume of 40 ml – 60 ml and a platelet yield of $0.5 - 0.9 \times 10^{11}$ /l.

Compatibility

A and B red cell antigens are expressed on platelets. ABO-compatible platelet products are the components of choice, although clinical demand and stock availability may not allow for this.

Some studies have indicated poorer platelet increments with ABO non-identical platelet products, but this has not been shown to be clinically significant in terms of haemostatic efficacy. In the event that ABO-incompatible products must be used, products with low antibody titres will be selected by the blood bank.

Since platelet concentrates may contain a small number of red cells, Rh-D negative platelets should be given to premenopausal Rh-D negative women. If this is not possible, administration of anti-D immunoglobulin should be considered once the platelet count is corrected.

Product Storage

Platelet products are stored at room temperature (20 °C – 24 °C) in the blood bank for up to 5 days, under gentle agitation on a platelet shaker or “agitator”.

The shelf life of platelet products is extended to 7 days in certain countries that use pathogen-reduction treatment and/or pre-issue bacterial screening protocols.

PLATELET PRODUCT ADMINISTRATION

Platelet products should be transfused through a platelet administration set over a period of 15 – 30 minutes within 6 hours of issue from the blood bank. They should not be transfused through giving sets that have been used for red cell concentrates or whole blood.

Platelet products should be kept at room temperature, not refrigerated, and transfused to the patient as soon as possible.

Monitoring the Response to Platelet Transfusions

If platelets are given therapeutically for active bleeding, the patient's clinical response is the best indication of efficacy. Response to prophylactic platelet transfusions is best assessed by measuring the increase in the platelet count following the transfusion.

One platelet product (which is equivalent to 1 therapeutic dose) should increase the patient's platelet count by 35 – 45 x 10⁹/l within 10 – 60 minutes post transfusion. Failure of the platelet corrected-count increment (CCI) to reach a level of at least 5 x 10⁹/l within 1 hour after transfusion should raise suspicion of refractoriness.

Although the platelet dose is not recorded on platelet products in South Africa and can range from 2.4 – 5 x 10¹¹ per platelet unit, it can be calculated if the actual platelet-product dose is known:

$$\text{CCI} = \frac{\text{Post transfusion platelet increment (x } 10^9/\text{l) x body surface area (m}^2\text{)}}{\text{Platelet dose (x } 10^{11}/\text{l)}}$$

The following CCIs are regarded as unsatisfactory:

- 10 minutes to 1 hour after transfusion: <7.5 x 10⁹/l
- 1 – 17 hours after transfusion: <10% recovery of platelet count
- 18 – 24 hours after transfusion: <5 x 10⁹/l

Platelet Transfusion Refractoriness

Platelet transfusion refractoriness (PTR) is defined as the repeated failure to obtain satisfactory responses to platelet transfusions and can be attributed to immune or non-immune mechanisms.

Immune causes will result in both 1-hour and 24-hour CCI values being poor, whereas non-immune causes will show a normal 1-hour CCI but a poor 24-hour CCI. The aetiology of PTR is often multifactorial.

Non-immune causes account for about 80% of PTR episodes. These include:

- Fever
- Infection or sepsis
- Drugs, e.g. antibiotics
- Splenomegaly
- Graft-versus-host disease
- Ongoing bleeding
- Veno-occlusive disease
- Disseminated intravascular coagulation (DIC)

The major immune cause is the formation of antibodies against human leucocyte antigen (HLA). A less frequent cause is human platelet specific antigens (HPA) exposure through multiple platelet transfusions.

If PTR is confirmed in a patient, and non-immune causes have been excluded, HLA tissue typing of the patient is advised for the selection of HLA-matched SDAP products. In South Africa, this is performed in conjunction with the South African Bone Marrow Registry (SABMR), which supplies the blood services with a list of HLA-compatible donors to contact.

Even with HLA-matched products, 20%–30% of these patients may have ongoing poor responses to the platelet transfusions, which could be related to unrecognised non-immune causes of platelet refractoriness, drugs or autoantibodies. It is also important to note that patients can lose antibodies over time (1 week to several months), so repeat assessment of antibody status is useful to avoid unnecessary use of HLA-matched SDAP products.

Platelet Product Risks

The risk of bacterial contamination is greater with platelet products because they are stored at room temperature. Bacterial screening is performed on a defined number of platelet products as per the quality-control specifications to monitor this.

The use of pathogen-reduction treatment of platelet products reduces the risk of bacterial contamination and other transfusion-transmissible infections, and this technology is being considered for use by the South African blood services. Adverse transfusion reactions can occur with platelet transfusions, like with any other blood component. The most common types are FNHTR and allergic reactions, the incidence of both being about 3%. Allergic transfusion reactions are reduced by using platelet additive solution in platelet products – because the proportion of plasma is far less, the patient exposure to plasma proteins is reduced.

Alloimmunisation is also a risk of repeated platelet product transfusions. This risk for patients with chronic platelet transfusion needs is reduced through the use of SDAP (leucocyte depleted) or filtered RDP products.

INDICATIONS FOR PLATELET TRANSFUSIONS

Platelet transfusions are indicated for the prevention (prophylactic transfusions) and treatment (therapeutic transfusions) of bleeding in patients with thrombocytopenia or platelet function defects. The cause of the thrombocytopenia should be established before a decision is made to transfuse.

Unless there is life-threatening bleeding or the patient requires an urgent procedure where alternative therapies to recover their platelet count are ineffective, platelet transfusions are contraindicated (or relatively contraindicated) in patients with:

- Thrombotic microangiopathies, e.g. thrombotic thrombocytopenia purpura (TTP)
- Immune thrombocytopenias, e.g. immune thrombocytopenia (ITP), heparin-induced thrombocytopenia (HIT), post-transfusion purpura (PTP)

The following recommendations for adult transfusions are based on guidelines produced by the BSH (British Society for Haematology) in 2017 and by the AABB (formerly the American Association of Blood Banks) in 2015.

Therapeutic Platelet Transfusions

Table 5.2

Patient status	Transfusion guidance
Severe bleeding (WHO grade 2 or above)	Maintain the platelet count $>50 \times 10^9/l$
Multiple trauma, traumatic brain injury or spontaneous intracerebral haemorrhage	Maintain platelet count $>100 \times 10^9/l$
Bleeding that is not severe or life-threatening (WHO grade 2 or above)	Consider platelet transfusion if the platelet count is $<30 \times 10^9/l$

Patients with Bone Marrow Failure or Critical Illness (in the absence of planned procedures)

Table 5.3

Patient status	Transfusion guidelines
Active, severe bleeding and thrombocytopenia	Therapeutic platelet transfusions are unequivocally indicated
Platelet count of $<10 \times 10^9/l$	Prophylactic platelet transfusions are indicated to reduce the risk of spontaneous bleeding: <ul style="list-style-type: none"> • 1 unit of platelets is advised for prophylactic purposes (greater doses are not more effective) • Consider increasing this threshold to $10 - 20 \times 10^9/l$ for patients with additional risk factors for bleeding, e.g. sepsis, antibiotic treatment, abnormalities of haemostasis such as DIC • Consider not giving prophylactic transfusions to well patients with no evidence of bleeding who have had an autologous stem-cell transplant
Chronic stable thrombocytopenia due to sustained failure of platelet production, e.g. myelodysplasia, aplastic anaemia	<ul style="list-style-type: none"> • May not bleed abnormally despite consistently low platelet counts • Prophylactic platelet transfusions are best avoided owing to the risk of alloimmunisation, but can be considered for patients on intensive treatment if the platelet count is $\leq 10 \times 10^9/l$ • Generally, platelets should only be given therapeutically to treat overt bleeding episodes

Prophylaxis for Surgery and Invasive Procedures

The following are guidelines only since there is a lack of evidence to direct therapeutic decisions in this setting.

Table 5.4

Surgical or invasive procedure	Threshold platelet value
Major non-neuraxial surgery	$>50 \times 10^9/l$
Lumbar puncture	$>40 \times 10^9/l$ (BSH) $>50 \times 10^9/l$ (AABB)
Venous central-line placements	$>20 \times 10^9/l$
Neurosurgery or ophthalmic surgery	$>100 \times 10^9/l$
Percutaneous liver biopsy	$>50 - 80 \times 10^9/l$
Insertion or removal of epidural catheter	$>80 \times 10^9/l$
<ul style="list-style-type: none"> • Bone marrow aspirate or trephine biopsy • Cataract surgery • Peripherally inserted central catheters • Traction removal of tunnelled central-venous catheters 	Routine platelet transfusions not required

Immune Thrombocytopenias

Prophylactic platelet transfusions are not indicated for ITPs unless the patient is undergoing an urgent procedure and their platelet count cannot be corrected by other treatment options. Platelet transfusions should be reserved for life-threatening haemorrhage, together with other therapies, e.g. intravenous immunoglobulin and corticosteroids.

In post-transfusion purpura, intravenous immunoglobulin is the treatment of choice.

Tranexamic Acid Use

Tranexamic acid (TXA) has been recommended by the BSH as an alternative or addition to platelet transfusions in the following circumstances:

- For early administration to trauma patients who are bleeding or at risk of bleeding
- For surgical patients who are expected to have >500 ml blood loss, unless contraindications exist
- In patients with chronic thrombocytopenia caused by bone marrow failure

NEONATAL AND PAEDIATRIC PLATELET TRANSFUSIONS

Dosage

The platelet dosage that is recommended is 10 ml/kg – 20 ml/kg, using a platelet administration set over a period of 30 – 60 minutes. Infant platelet concentrates are produced from Group O negative SDAP products.

Indications for Transfusion

Owing to great variability in the literature regarding platelet value transfusion thresholds for babies and children, it is advised to seek paediatric consultant advice from your institution. Restrictive ordering practices are encouraged.

Platelet transfusions for ITP should be avoided unless there is life-threatening haemorrhage, as per adult guidelines.

Guidelines for Neonatal Platelet Transfusion

Thrombocytopenia is a relatively common haemostatic complication in the neonatal ICU setting and is associated with an increased risk of severe intra- and peri-ventricular haemorrhage. Transfusion thresholds are difficult to establish as studies do not demonstrate severity of thrombocytopenia to be a major predictor of bleeding.

It is advised to consider prophylactic transfusions in all neonates at $<30 \times 10^9/l$, but to consider $<50 \times 10^9/l$ if there is an increased bleeding risk:

- $<1\ 000$ g or <1 week old
- Clinically unstable
- Previous major bleeding
- Current minor bleeding
- Coagulopathy
- Planned surgery or exchange transfusions

Neonatal Alloimmune Thrombocytopenia

Neonatal alloimmune thrombocytopenia (NAIT) results most commonly from maternally derived anti-human platelet antigen 1a or 5b antibodies. If the diagnosis is suspected, maternal antibody testing can be arranged via the South African National Blood Service (SANBS) Tissue Immunology Laboratory in Johannesburg (011 761 9227/8). Blood samples from both the mother and baby are needed.

If antibodies are detected in the maternal sample, the baby's blood will be genotyped to establish if there is a correlation. HLA/HPA matched blood can be arranged via the SANBS Tissue Immunology Laboratory or with assistance from SABMR.

The use of maternal SDAP platelets is also an option, along with steroid administration for the baby.

Guidelines for Paediatric Platelet Transfusion

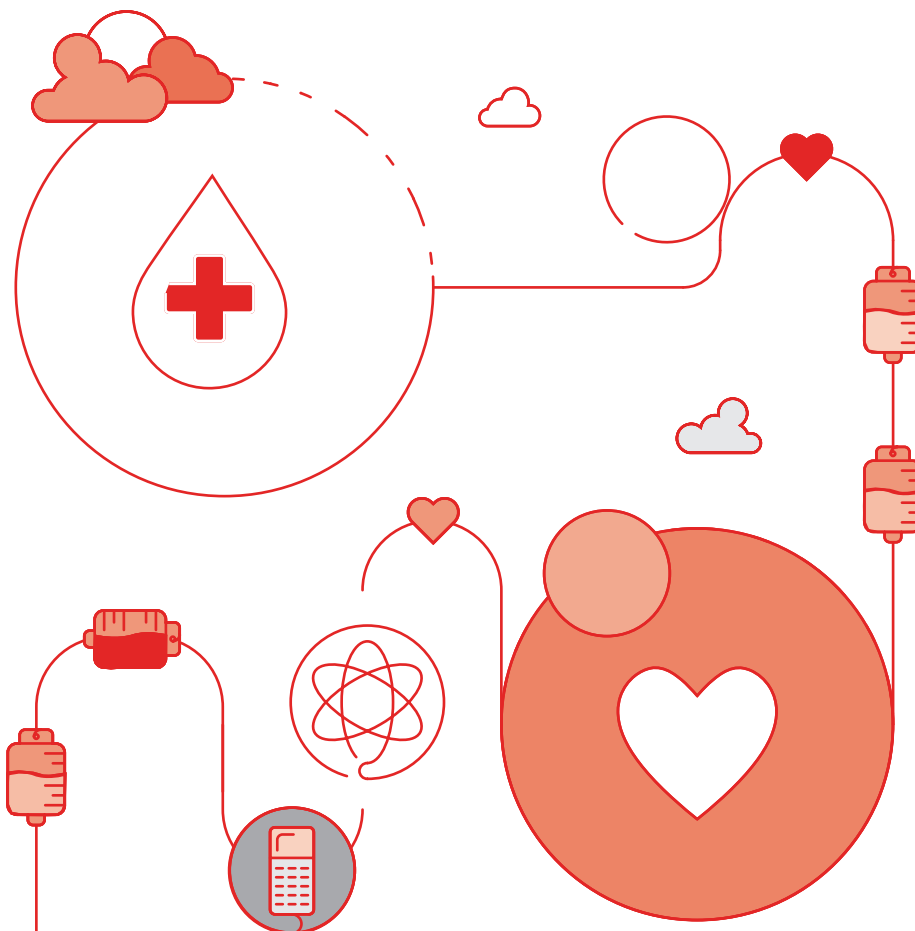
Hypoproliferative thrombocytopenia as a result of chemotherapy or irradiation is a common reason for platelet transfusions in children. These children are at a higher risk of bleeding than adults are, due to the intensity of the chemotherapy and the functional differences in interactions between the vascular endothelium and platelets.

Therapeutic platelet transfusions are recommended for any child with active bleeding and thrombocytopenia.

There is little data to guide prophylactic platelet transfusions in children and extrapolation of the adult guidelines is often resorted to.

FURTHER READING

1. Estcourt LJ, Birchall J, Allard S, et al. Guidelines for the use of platelet transfusions. *Br J Haematol.* 2017;176(3):365-394. doi:10.1111/bjh.14423
2. Kaufman RM, Djulbegovic B, Gernsheimer T, et al. Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med.* 2015;162(3):205-213. doi:10.7326/M14-1589
3. Patel RM, Josephson C. Neonatal and pediatric platelet transfusions: current concepts and controversies. *Curr Opin Hematol.* 2019;26(6):466-472. doi:10.1097/MOH.0000000000000542
4. Slichter SJ. Evidence-based platelet transfusion guidelines. *Hematology Am Soc Hematol Educ Program.* 2007:172-178. doi:10.1182/asheducation-2007.1.172
5. Solves Alcaina P. Platelet transfusion: and update on challenges and outcomes. *J Blood Med.* 2020;11:19-26. doi:10.2147/JBM.S234374



Chapter 6:

PLASMA COMPONENTS AND DERIVATIVES



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

PLASMA COMPONENTS AND DERIVATIVES

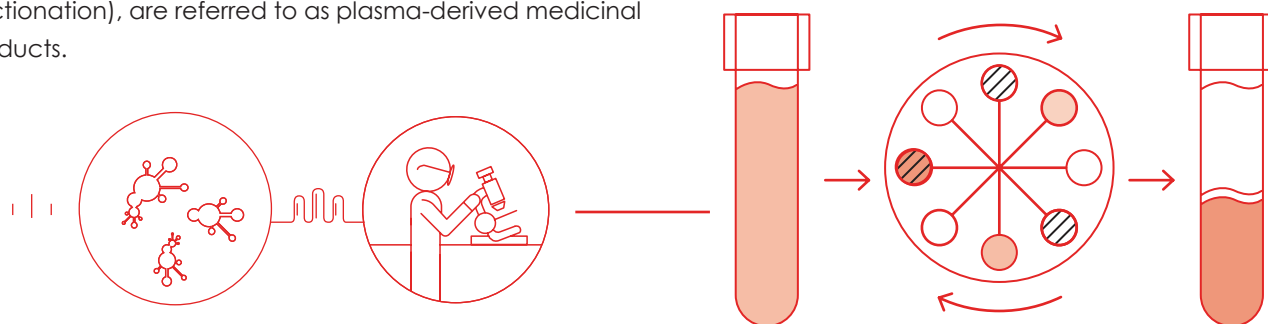
OVERVIEW

Plasma products are diverse and comprise both plasma components and plasma derivatives. Plasma components are those products produced by purely physical separation methods, e.g. centrifugation. These products include FFP and cryoprecipitate.

Products like albumin, which are derived from large plasma pools of >12 donations and subject to more complex physical and chemical processes (e.g. alcohol-based fractionation), are referred to as plasma-derived medicinal products.

Below is an outline of the various plasma products, their accepted usage guidelines and their dosage schedules.

The information on plasma derivatives is provided for guidance and easy reference only. Detailed prescribing information is provided in the respective products' approved package insert and other prescriber guidelines, e.g. South African Medicines Formulary.



GENERAL PRECAUTIONS FOR THE USE OF PLASMA PRODUCTS

All plasma products are potentially antigenic and therefore may elicit allergic and/or anaphylactic reactions.

With each transfusion, the recipient should be observed with regular assessment of vital signs at least every 15 minutes for the first half hour of each unit (severe transfusion reactions are most likely to occur during the first 30 minutes of a unit being transfused); thereafter half-hourly or according to hospital policy.

The management of transfusion reactions is described in Chapter 8, *Haemovigilance, Risks and Adverse Reactions Associated with Blood Transfusion*.

In one study, it was demonstrated that all coagulation factors showed significant reduction of activities over 5 days of storage, with the most decrease being in factor VIII, followed by von Willebrand factor antigen (vWF Ag). Prothrombin time (PT), activated partial thromboplastin time (APTT) and vWF Ag levels were all significantly influenced by time and temperature interaction.

The impact of twice-thawed-and-refrozen FFP on the levels of vitamin K-dependent factors (factors II, VII, IX and X) and fibrinogen remained stable and adequate for transfusion.

The first choice is to administer FFP of the same ABO blood group as the patient. If not available, a different ABO group can be given provided the anti-A and anti-B titres are low. Blood group O FFP should preferably be given only to group O patients.

Paediatric Considerations

Group O should especially be avoided in non-group O neonates since this may result in haemolysis from passive infusion of anti-A and -B.

PLASMA COMPONENTS

Fresh Frozen Plasma

Plasma for FFP is separated from anticoagulated whole blood (donated unit) within 18 hours of donation (see figure below). Separation is by centrifugation of whole blood in a closed sterile system and then rapidly freezing the plasma to below -18 °C. The resultant FFP contains all the coagulation factors at normal physiological levels.

The transfusion services in South Africa have introduced a donor plasma-retest quarantine programme (also for cryoprecipitate and cryo-poor plasma) to minimise the risk of a window-period infection. In areas where this programme is not in place, only plasma from regular donors is used for FFP production.

No pathogen transmissions have been reported since the introduction of the programme. However, patients likely to receive large or repeated doses may benefit from pathogen-inactivated plasma.

FFP contents

FFP is hyperosmolar due to the solutes listed in Table 6.2 below. In elderly and very young patients, care should be taken not to precipitate pulmonary oedema if cardiopulmonary function is compromised and tissue oedema is present.

Hypernatraemia and hypokalaemia may occur if large volumes are transfused.

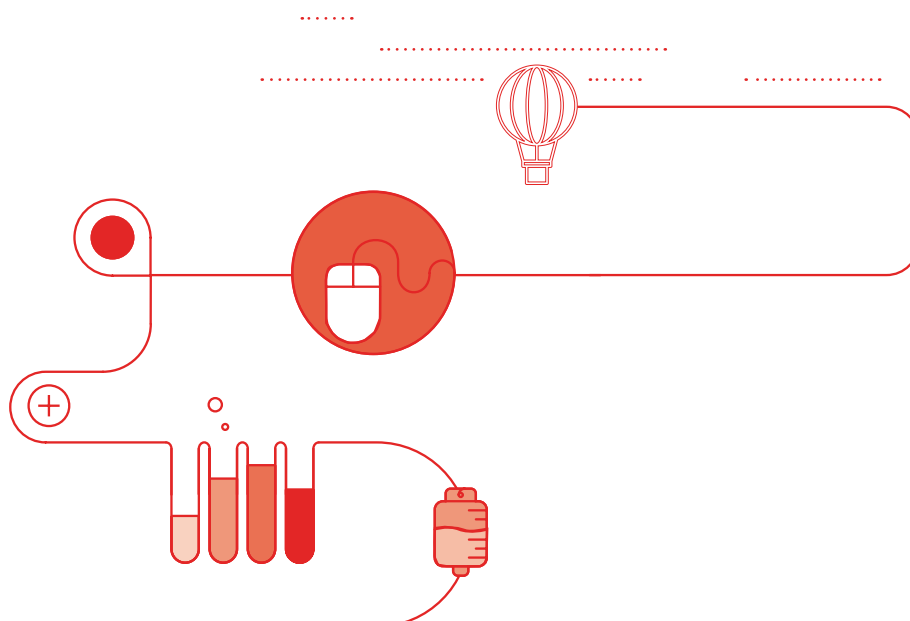
How to administer FFP

FFP must be administered through a blood-giving set, after thawing at 30 °C – 37 °C. The unit should be transfused as rapidly as possible (15 – 20 minutes per unit), with a recommended maximum delay after thawing of up to 4 hours, as labile coagulation factors deteriorate within a few hours of thawing or reconstitution.

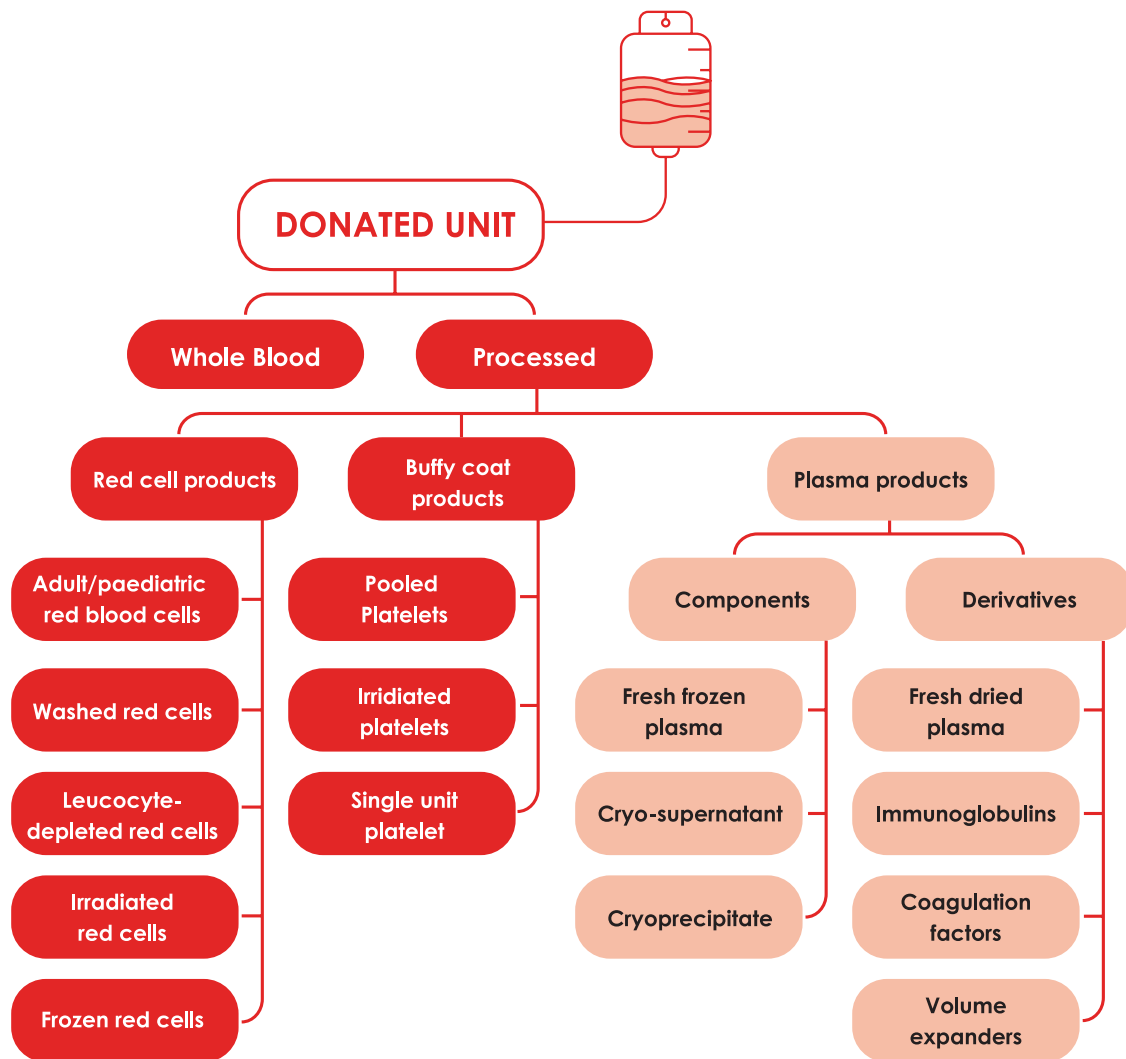
Volume and dosage guidelines

The volume of an adult unit of FFP is 240 ml – 300 ml and its important constituents are listed in Tables 6.1 and 6.2.

The initial dose recommendation is 10 ml/kg – 15 ml/kg. Further therapy is dependent on clinical response and laboratory monitoring.



Donated unit processing



The coagulation factors and solutes in FFP are shown in Tables 6.1 and 6.2 below.

Table 6.1

Donated unit processing: Coagulation factors and other proteins	
Factor	Average levels
Fibrinogen	500 mg per unit of FFP
Factor II	1.03 IU/ml
Factor V	0.64 IU/ml
Factor VII	1.21 IU/ml
Factor VIII	0.85 IU/ml
Factor IX	0.95 IU/ml
Factor X	1.25 IU/ml
Factor XI	0.79 IU/ml
Antithrombin III	104 IU/ml
Plasma pseudo-cholinesterase	3 000 IU/ml – 10 000 IU/ml

Table 6.2

Donated unit processing: Solutes	
Solutes	Average Levels
Glucose	24.8 mmol/l
Potassium	3.2 mm/l
Sodium	165 mmol/l
Chloride	79 mmol/l
Osmolarity	322 mmol/l
pH	7.9

Indications in adults

The evidence-based clinical indications for FFP in adults are:

- Replacement of inherited single factor deficiencies where a specific factor concentrate is not available
- Multiple coagulation factor deficiencies (DIC, massive blood transfusion, liver disease) with active bleeding and abnormal coagulation screening tests
- TTP (preferably use cryo-poor plasma)
- Reversal of warfarin overdose if a prothrombin complex concentrate is not available
- Vitamin K deficiency associated with active bleeding, e.g. haemorrhagic disease of the newborn (HDN)
- Suxamethonium (scoline) apnoea

Use of FFP is not justifiable and therefore not recommended in the following scenarios:

- Hypovolaemia
- First resuscitation fluid in haemorrhagic shock
- Plasma exchange (except in TTP)

In June 2010, AABB (formerly the American Association of Blood Banks) published a meta-analysis and evidence-based guidelines for plasma transfusion. The guidelines suggest that plasma transfusion be used in 2 patient groups – those requiring massive transfusion and those with intracranial haemorrhage related to warfarin therapy.

Plasma transfusion at high plasma:red cell ratios (1:1) in massive transfusion was associated with a reduction in the risk of death and multi-organ failure, although the quality of the evidence was low. There was insufficient data to recommend for or against transfusion of plasma in patients undergoing surgery in the absence of massive transfusion or in the absence of intracranial haemorrhage.

Many institutions are using plasma that has been thawed and stored in a liquid state at 1 °C – 6 °C for 5 days post thawing. Ideally, a diagnosis of coagulopathy should be rapidly established before FFP is given – preferably using point-of-care tests, e.g. thromboelastography (TEG) or rotational thromboelastography (ROTEM). Such tests can provide results within 15 minutes.

Indications in paediatric patients

Indications for FFP in paediatric patients include:

- Neonates with a significant risk of bleeding: international normalized ratio (INR) or APTT >1.5
- Haemorrhagic disease of the newborn (while waiting for response to vitamin K)
- Congenital coagulation deficiencies where a specific factor concentrate is not available or the deficient factor has not been identified

FFP is not recommended:

- To treat sepsis
- As a volume replacement fluid
- To treat erythrocytosis/polycythaemia
- For routine prophylactic use to treat pulmonary venous hypertension (PVH) in pre-term infants

ABO group-specific plasma (or preferably AB plasma if available) is recommended. Group O FFP should not be given to neonates who are not group O unless the anti-A and anti-B titres have been screened for and are low. A dose of 10 ml/kg – 20 ml/kg is recommended, to be administered via a standard blood-administration set (170 µm – 200 µm filter) or via a syringe with equivalent filtration.

As FFP is hyperosmolar, fluid overload is a risk in normovolaemic patients and close monitoring is advisable.

Cryoprecipitate

This is the cold-insoluble fraction of FFP and is obtained by thawing FFP at 0 °C – 4 °C. It can be stored at or below -18 °C for up to 1 year. It is available in volumes of up to 15 ml. Cryoprecipitate contains:

- Factor VIII/von Willebrand factor (vWF) – approximately 100 IU per unit
- Fibrinogen (150 mg – 200 mg per unit)
- Fibronectin
- Factor XIII

Table 6.3

Indications and dosing	
Adults	<ul style="list-style-type: none"> • Cryoprecipitate is indicated primarily for treating congenital or acquired hypofibrinogenaemia (defined as fibrinogen below the lower limit of the reference range for the laboratory) or dysfibrinogenaemia • The dose is 1 unit cryoprecipitate/10 kg body weight or 8 – 12 units per adult dose • It is given through a standard blood-administration set • It may also be used for treating hereditary factor XIII deficiency • It has been recommended for both obstetric haemorrhage and massive transfusion where there is a demonstrable fibrinogen deficit (<1.5 g/l)
Paediatrics	<ul style="list-style-type: none"> • Indicated for acquired (DIC most commonly) or congenital hypofibrinogenaemia • The threshold for transfusion is <1.5 g/l depending on clinical circumstances, e.g. active bleeding, invasive procedure • Recommended dose is 5 ml/kg infused rapidly • It is dispensed as individual units each containing 10 ml – 15 ml cryoprecipitate and approximately 200 mg fibrinogen

Cryosupernatant (cryo-poor FFP)

This is the component available following extraction of cryoprecipitate from FFP. It is stored in limited quantities.

Cryosupernatant is indicated for use in therapeutic plasma exchange in the management of TTP.

PLASMA-DERIVED MEDICINAL PRODUCTS

In terms of the legislation of medicines in South Africa (Regulation 609, 2003), plasma-derived products manufactured from a pool of >12 donations are classified as medicines.

All registered medicines are supplied with a Patient Information Leaflet (PIL), approved by the South African Health Products Regulatory Authority. This leaflet contains detailed information regarding the safe and effective use of the medicine.

Solvent-Detergent Treated FFP

Bioplasma FDP, 28/30.3/405 (S4), National Bioproducts Institute NPC

Produced from pooled fresh human plasma, Bioplasma FDP undergoes a pathogen-inactivation procedure using a solvent-detergent treatment process which inactivates lipoprotein-coated viruses including HIV, HBV and HCV. After reconstitution with water for injection, each 100 ml contains 4 g – 6 g plasma proteins and a minimum of 0.4 IU/ml of each coagulation factor (II, V, VIII, IX and XI).

Bioplasma FDP can be used when plasma and/or coagulation factors are required.

This product is available as either a 50 ml or 200 ml pack, with water for injection and reconstitution (set included). It is stored at room temperature (at or below 25 °C) and contains no antimicrobial agents or preservatives.

Coagulation Factor Concentrates

Haemosolvate® Factor VIII (S4), National Bioproducts Institute NPC

- Haemosolvate® Factor VIII 300 IU, human factor VIII concentrate, 31/30.3/392
- Haemosolvate® Factor VIII 500 IU, human factor VIII concentrate, Y/30.3/292

This is a factor VIII concentrate prepared from pooled fresh human plasma. Each vial is reconstituted with 10 ml water for injection, for direct intravenous injection and is clinically indicated for the treatment and prophylaxis of coagulation defects caused by haemophilia A and von Willebrand disease (vWD).

It undergoes a viral inactivation step using a solvent-detergent process which inactivates lipid-enveloped viruses, e.g. HIV, HBV and HCV. See Table 6.4 for further details and also refer to the PIL.

Haemosolvex® Factor IX (S4), National Bioproducts Institute NPC

- Haemosolvex® Factor IX, human factor IX complex, W/30.3/191

This is a prothrombin complex concentrate containing prothrombin (factor II), proconvertin (factor VII), Stuart-Prower factor (factor X) and Christmas factor (factor IX). It is reconstituted with 10 ml water for injection, for direct intravenous injection. It is indicated for the treatment of coagulation defects caused by haemophilia B and the treatment of warfarin-induced bleeding.

It undergoes a viral inactivation step using a solvent-detergent process which inactivates lipid-enveloped viruses, e.g. HIV, HBV and HCV. Refer to Table 6.4 and the PIL for further details.

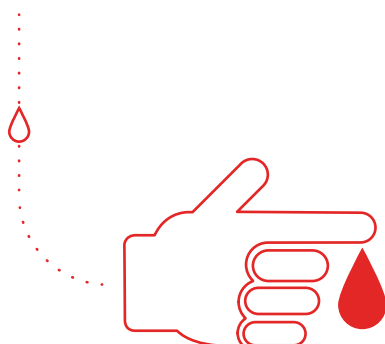


Table 6.4

Coagulation factor concentrates			
Product	Content	Units	Volume
Haemosolvate® Factor VIII 300 IU (NBI)	Factor VIII/vWF	300 IU factor VIII >300 IU vWF	10 ml per vial, after reconstitution with water for injection
Haemosolvate® Factor VIII 500 IU (NBI) 2 pack sizes: 500 IU and 2x 500 IU	Factor VIII/vWF	500 IU factor VIII >500 IU vWF	As above
Haemosolvex® Factor IX	Factor IX, factor II, factor VII, factor X	500 IU factor IX	As above

Dosage schedules and treatment guidelines

For details, refer to your local haemophilia centre and South African treatment guidelines. It is important that all haemophiliacs or any patient with an inherited bleeding disorder be registered with the South African Haemophilia Foundation and be referred to the nearest haemophilia centre for management.

Haemophilia A	<p>Factor VIII has an average half-life of 12 hours. Treatment should therefore be given every 8 – 12 hours according to the clinical indication. Treatment intervals for Haemosolvate vary depending on the severity of the bleed and, in the case of surgical prophylaxis, the extent of the surgery to be performed. After major surgery factor VIII infusions may be required for up to 10 days post-operatively</p> <p>The dosage (in units of factor VIII) can be estimated as follows:</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> $\text{Required dose (IU factor VIII)} = \text{body mass (kg)} \times 0.5 \times \text{desired factor VIII increase (\% of normal)}$ </div> <p>Transfusion of factor concentrates should be commenced as soon as possible when required, but they should be administered as a slow intravenous injection. Patients should be observed for any adverse reactions, particularly those of an allergic nature</p> <p>Haemophilia A patients may develop antibodies to factor VIII (inhibitors) and may therefore not respond to therapy. For patients with low titer inhibitors (<5 Bethesda units), a higher dose of factor concentrate is recommended. For patients with high titer inhibitors (>5 Bethesda units), a bypassing agent – e.g. factor eight inhibitor bypass activity (FEIBA) or recombinant factor VIIa (rVIIa) – should be used.</p>
Von Willebrand Disease	<p>Haemosolvate® Factor VIII is the treatment of choice when DDAVP (a vasopressin analogue) is not indicated or ineffective. This concentrate contains the high-molecular-weight multimeric molecule, vWF</p> <p>Dosing recommendations vary, so the best methods of monitoring the response are clinical assessment and measurement of factor VIII levels. Initial dosage recommendation is 50 IU factor VIII concentrate per kg body weight. Laboratory monitoring should be every 24 hours with regular interim clinical observation.</p>
Haemophilia B	<p>The clinical picture of haemophilia B (congenital factor IX deficiency) is identical to that of haemophilia A. The levels required are similar to those for factor VIII, although slightly lower levels of factor IX are usually adequate for normal haemostasis. Factor IX has a longer half-life (16 – 30 hours) and therefore once-daily dosage is often sufficient.</p> <p>The dosage (in units of factor IX) can be estimated as follows, bearing in mind that dosing recommendations are a guideline only and dosing is to be oriented towards clinical efficacy:</p> <div style="border: 1px solid black; padding: 5px; text-align: center;"> $\text{Required dose (IU)} = \text{body weight (kg)} \times \text{desired FIX increase (\%)} \times 1.2$ </div> <p>If therapy with high doses for >3 – 4 days is required, the patient should be carefully monitored for development of thrombosis, which has been reported with some prothrombin complex concentrates.</p>

Plasma Expanders (Albumin)

- Albusol® 4%, human plasma albumin 4%, T/30.3/738 (S4), National Bioproducts Institute NPC
- Albusol® 20%, human plasma albumin 20%, T/30.3/739 (S4), National Bioproducts Institute NPC

Both the above are prepared from pooled human plasma. Each donation has been individually tested by serologic and nucleic acid amplification technology for HIV, HBV and HCV and is non-reactive for these tests.

Albumin solutions are prepared by cold ethanol fractionation which further reduces the risk of viral transmission. The albumin solutions are sterilised by filtration and, finally, pasteurised by heat for 10 hours at 60 °C, a process validated to inactivate HIV, HBV and HCV.

Albusol® 4% is a sterile solution containing 4% *m/v* human plasma albumin, available in a 200 ml pack size (8 g/200 ml). It is stabilised with 0.16 mmol sodium caprylate per gram protein and 3% *m/v* dextrose. The solution is at pH 7 and each litre contains <130 mmol sodium, <2 mmol potassium and <4 mmol citrate.

Albusol® 20% is a sterile solution containing 20% *m/v* human plasma albumin, available in 50 ml (10 g/50 ml) and 100 ml (20 g/100 ml) pack sizes. It is stabilised with 16 mmol/l sodium acetyltryptophanate and 16 mmol/l sodium caprylate. The solution is at pH 7 and contains <100 mmol/l sodium, <10 mmol/l potassium and <20 mmol/l citrate.

Clinical indications

Blood volume expansion: Fluid resuscitation in acute clinical conditions associated with hypovolaemia (e.g. trauma) remains controversial. It is not the intention of this guideline to provide a comprehensive review of the subject, but the following is a short summary of current opinions and practice principles:

- Management of hypovolemia involves assessment and treatment of the underlying cause, identification of electrolyte and acid-base disturbances, and assessment and treatment of the volume deficit – all of which influence the choice of fluid and the rate at which it should be administered
- The initial resuscitation fluid of choice for volume expansion is a crystalloid solution – probably a balanced salt solution, although an ideal solution does not exist. Hypo-osmolar solutions may pose a risk to patients with head injuries
- If further therapy is required after 2 l – 3 l of crystalloids have been infused, it is appropriate to continue with a colloid solution. Which colloid to use depends to some extent on the duration of effect required and on cost
- An ideal colloid should have a molecular weight of \pm 70 kDa (MW albumin 69 kDa; gelatin 30 kDa; HES 60 kDa – 70 kDa; dextrans 40 kDa – 70 kDa)
- Since there is no clinical trial data to support a clear-cut therapeutic advantage for either crystalloids or colloids, the final choice of fluids for resuscitation is ultimately influenced by individual clinician experience and cost considerations

Replacement fluid following paracentesis: Albumin is beneficial in preventing acute complications of hypoproteinaemia caused by loss of plasma proteins and renal impairment.

Therapeutic plasma exchange: Albumin is the replacement fluid of choice for most procedures. The exception is TTP, where FFP or cryosupernatant are indicated.

Burns: Often used after the first 24 hours in severe burns, but there is a lack of randomised clinical trials.

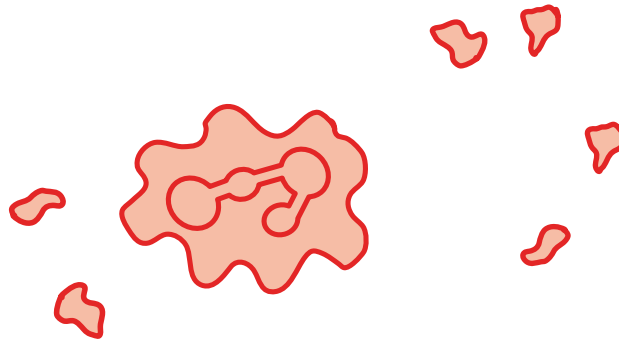
Nephrotic syndrome: May have a short-term, limited role in combination with diuretics for the control of oedema, where diuretics alone have failed.

Dosing guidelines

Refer to package inserts for dosing guidelines.

Clinical contraindications

Albumin solutions appear to have no useful role in malnutrition, cirrhosis and chronic nephrotic syndrome. The above protein solutions should not be given to any patient with a known sensitivity or allergy to human proteins.



Immunoglobulins

Immunoglobulin is the antibody-containing fraction of human plasma obtained by fractionation of pooled plasma units. Each unit has been individually tested and found non-reactive for HIV, HBV and HCV using both serological and nucleic acid amplification technology.

Polygam

- Polygam® 1 g, polyvalent human normal immunoglobulin, Z/30.2/367 (S4), National Bioproducts Institute NPC
- Polygam® 3 g, polyvalent human normal immunoglobulin, Z/30.2/368 (S4), National Bioproducts Institute NPC
- Polygam® 6 g, polyvalent human normal immunoglobulin, Z/30.2/369 (S4), National Bioproducts Institute NPC
- Polygam® 12 g, polyvalent human normal immunoglobulin, 29/30.2/511 (S4), National Bioproducts Institute NPC

This is a polyvalent human normal immunoglobulin for intravenous use, containing mainly immunoglobulin G (IgG), with a broad spectrum of antibodies against infectious agents. It is prepared by cold ethanol fractionation and pH 4.0 pepsin treatment to further reduce the risk of viral transmission. The pH 4.0 pepsin process has been validated and shown to be effective against enveloped viruses, e.g. HIV, HBV and HCV.

Polygam® is available as a lyophilised powder and is reconstituted to a 50 ml volume (1 g/50 ml, 2% solution); a 100 ml volume (3 g/100 ml, 3% solution); a 200 ml volume (6 g/200 ml, 3% solution); and a 400 ml volume (12 g/400 ml, 3% solution). Each pack consists of a clear glass bottle containing lyophilized powder, bag(s) of 0.9% m/v sodium chloride solution and a reconstitution set.

Clinical indications

- Replacement therapy in primary antibody deficiency syndromes
- Myeloma or chronic lymphocytic leukaemia with severe hypogammaglobulinaemia and recurrent infections
- Children with congenital Acquired Immunodeficiency Syndrome (AIDS) and recurrent infections
- For immunomodulation in:
 - Primary ITP in children and adults
 - Kawasaki Disease
 - Guillain-Barré Syndrome
- Allogeneic bone marrow transplantation
- Parvovirus B19-positive pure red cell aplasia

Clinical contraindications

Polygam® should be given with caution to patients with antibodies to IgA or with selective IgA deficiency, as the small amount of IgA present in Polygam® may cause sensitisation. This could lead to a severe allergic reaction and anaphylaxis or subsequent reactions to other IgA-containing products.

Table 6.5

Replacement therapy in immunodeficiency: Guidelines for intravenous dosage regimens for Polygam®		
Indication	Dose	Frequency of infusions
Primary immunodeficiency	Starting dose: 0.4 g/kg – 0.8 g/kg Thereafter: 0.2 g/kg – 0.8 g/kg	Every 2 – 4 weeks to obtain IgG trough levels of at least 4 g/l – 6 g/l
Secondary immunodeficiency	0.2 g/kg – 0.4 g/kg	Every 3 – 4 weeks to obtain IgG trough levels of at least 4 g/l – 6 g/l
Children with AIDS	0.2 g/kg – 0.4 g/kg	Every 3 – 4 weeks
Immunomodulation		
Primary ITP	0.8 g/kg – 1 g/kg or 0.4 g/kg/day	On day 1 May be repeated once within 3 days or For 2 – 5 days May be repeated if relapse occurs
Kawasaki Disease	2 g/kg or 1.6 g/kg – 2 g/kg	As a single dose in conjunction with aspirin or In divided doses for 2 – 5 days in conjunction with aspirin
Guillain-Barré Syndrome	0.4 g/kg/day	For 3 – 7 days
Allogeneic bone marrow transplantation		
Treatment of infections and prophylaxis of graft versus host disease (GvHD)	Starting dose: 0.5 g/kg	Every week, starting 7 days before transplantation and up to 3 months after transplantation
Persistent lack of antibody production	0.5 g/kg	Every month, until antibody levels return to normal



Immunoglobulins for intramuscular injection

Immunoglobulins for intramuscular injection are produced from the same donor pool as the immunoglobulins described above and are screened in identical fashion.

There are various preparations available, most of which are hyperimmune globulins with high titres for specific antibodies for passive immune prophylaxis.

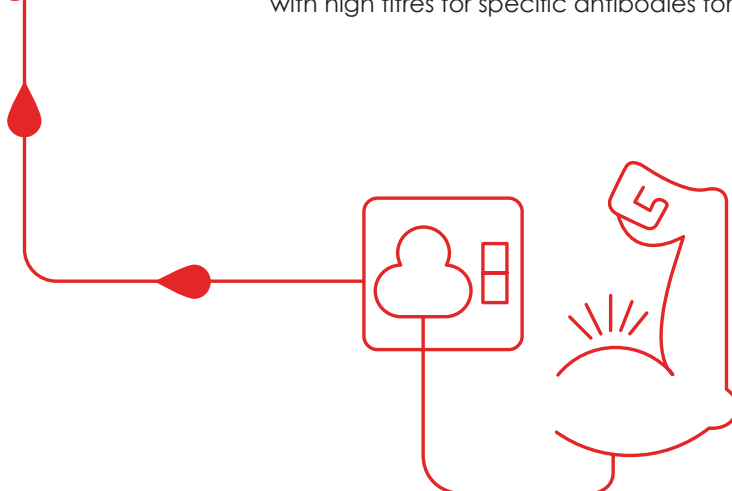


Table 6.6

Further details for intramuscular immunoglobulin preparations			
Product	Composition	Indication	Dose
Hebigam® IM Human hepatitis B immunoglobulin solution for intramuscular (IM) injection T/30.2/746 (S4)	100 IU/ml 2 ml ampoule	Immunoprophylaxis of hepatitis B: <ul style="list-style-type: none"> • Needle-stick injury • Mucosal exposure • Sexual exposure 	>10 years: 500 IU 5 – 9 years: 300 IU <5 years: 200 IU Treat preferably within 48 hours, and not >7 days after exposure Repeat after 28 days unless recipient has been shown to be immune or has received hepatitis B vaccine
Intragam® 2 ml/5 ml Human normal immunoglobulin for IM injection T/30.2/740 (S4) T/30.2/741 (S4)	16% gammaglobulin 2 ml and 5 ml ampoules	Newborn babies born to hepatitis B surface antigen (HBsAg)-positive mothers, especially those who are also hepatitis B e-antigen (HBeAg)-positive Hepatitis A prophylaxis: <ul style="list-style-type: none"> • Pre-exposure prophylaxis (continued exposure): <ul style="list-style-type: none"> ○ Travellers to endemic areas ○ Visit <3 months ○ Visit >3 months • Post-exposure prophylaxis: <ul style="list-style-type: none"> ○ Within 1 week of household contact • Congenital immunoglobulin deficiencies • Transient hypogammaglobulinaemia 	200 IU Treat preferably at birth, or within 48 hours after birth First dose of Hepatitis B vaccine must be administered at the same time • 0.02 ml/kg • 0.06 ml/kg every 4-6 months • 0.02 ml/kg – 0.04 ml/kg • 0.2 ml/kg – 0.5 ml/kg, repeat every 4 – 8 weeks, or • 0.2 ml/kg – 0.5 ml/kg, repeat when necessary
Rabigam® IM Human rabies immunoglobulin solution for IM injection T/30.2/748 (S4)	150 IU/ml 2 ml ampoule	Indicated for all persons known or suspected to have been exposed to the rabies virus. Used in conjunction with the rabies vaccine (active immunisation) <ul style="list-style-type: none"> • Rabies immunoglobulin must be given for any mucous membrane exposure to saliva, e.g. licks and all single and multiple bites or scratches inflicted by a suspected rabid animal – especially if associated with any signs of bleeding – irrespective of the interval between exposure and initiation of treatment, up to the 7th day after the first dose of vaccine was given 	• 20 IU/kg (children and adults) • Administered at the same time as the vaccine, but at a different anatomical site • Infiltrate the dose of Rabigam® IM into the depth of and around the wound if anatomically possible • Administer any remainder of the dose by intramuscular injection at a site separate from that used for the vaccine • Ensure that the wound has been adequately infiltrated with immunoglobulin locally before suturing, if suturing is necessary

Table 6.6 continued

Further details for intramuscular immunoglobulin preparations			
Product	Composition	Indication	Dose
Rhesugam IM	500 IU (100 µg) per 2 ml ampoule	Antenatal prophylaxis	500 IU (100 µg) is given at 28 and/or 34 weeks gestation
Human anti-D (Rho) immunoglobulin solution for IM injection T/30.2/750 (S4)		Prophylaxis following potentially sensitising events, including abortions	250 IU (50 µg) is recommended for events up to 20 weeks. For events occurring after 20 weeks, a dose of 500 IU (100 µg) is recommended
		Postnatal prophylaxis	500 IU (100 µg) is recommended
		Transfusion of Rho incompatible blood	The dose is calculated to clear the estimated quantity of red cells given: 125 IU (25 µg) for each ml of red cells
Tetagam IM 250 IU Human tetanus immunoglobulin solution for IM injection T/30.2/743 (S4)	125 IU/ml 2 ml ampoule	Transfusion of Rho positive platelets in Rho negative women of childbearing age	250 IU (50 µg) for each adult dose unit of platelets. If >2 adult platelet doses are given, administer 500 IU (100 µg)
		Prophylaxis: High risk injuries to non-immune and immune patients	250 IU (500 IU if 24 hours have passed since injury or if there is a risk of heavy contamination)
		Treatment: Clinical tetanus	3 000 IU – 6 000 IU as a single dose by infiltration into the wound site as well as IM

FURTHER READING

1. Martinowitz U, Livnat T, Zivelin A, et al. Concomitant infusion of low doses of rFVIIa and FEIBA in haemophilia patients with inhibitors. *Haemophilia*. 2009;15(4):904-910. doi:10.1111/j.1365-2516.2009.02028.x
2. Noordin SS, Karim FA, Mohammad WMZBW, et al. Coagulation factor activities changes over 5 days in thawed fresh frozen plasma stored at different initial storage temperatures. *Indian J Hematol Blood Transfus*. 2018;34(3):510-516. doi:10.1007/s12288-017-0879-8
3. Phillip J, Sarkar RS, Pathak A. The effect of repeated freezing and thawing on levels of vitamin K-dependent coagulation factors and fibrinogen in fresh frozen plasma. *Asian J Transfus Sci*. 2013;7(1):11-15. doi:10.4103/0973-6247.106715
4. Moore HB, Moore EE, Chapman MP, et al. Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial. *Lancet*. 2018;392(10144):283-291. doi:10.1016/S0140-6736(18)31553-8
5. South African Government. Government Gazette Regulation 609. Guidelines with respect to the Medicines and Related Substances Act (101 of 1965) as amended, 2003. Accessed March 7, 2023. https://www.sahpra.org.za/wp-content/uploads/2020/02/Government_Gazette_Medicines_and_Devices_Act_Jun_2017-1.pdf
6. O'Shaughnessy DF, Atterbury C, Bolton-Maggs P, et al. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol*. 2004;126(1):11-28. doi:10.1111/j.1365-2141.2004.04972.x
7. Roback JD, Caldwell S, Carson J, et al. Evidence-based practice guidelines for plasma transfusion. *Transfusion*. 2010;50(6):1227-1239. doi:10.1111/j.1537-2995.2010.02632.x
8. Murad MH, Stubbs JR, Gandi J et al The effect of plasma transfusion on morbidity and mortality: a systematic review and meta-analysis. *Transfusion*. 2010;50:1370-1383. Doi:10.1111/j.1537-2995.2010.02630.x
9. Yazer MH, Cortese-Hassett A, Triulzi DJ. Coagulation factor levels in plasma frozen within 24 hours of phlebotomy over 5 days of storage at 1 to 6 degrees C. *Transfusion*. 2008;48(12):2525-2530. doi:10.1111/j.1537-2995.2008.01913.x
10. Barron ME, Wilkes MM, Navickis RJ. A systematic review of the comparative safety of colloids. *Arch Surg*. 2004;139(5):552-563. doi:10.1001/archsurg.139.5.552
11. James MA. Volume expanders: crystalloids vs plasma colloids vs synthetic colloids. *ISBT Science Series*. 2006;1:52-58
12. Ahmed S, Harrity C, Johnson S, et al. The efficacy of fibrinogen concentrate compared with cryoprecipitate in major obstetric haemorrhage—an observational study. *Transfus Med*. 2012;22(5):344-349. doi:10.1111/j.1365-3148.2012.01178.x
13. South African National Blood Services. Navigation to a safe blood transfusion – nurses guide. 2020. Accessed March 7, 2023. <https://sanbs.org.za/wp-content/uploads/2020/01/Navigation-to-a-safe-blood-transfusion-nurses-guidelines-Feb-2020-revision-2-002.pdf>
14. Sørensen B, Bevan D. A critical evaluation of cryoprecipitate for replacement of fibrinogen. *Br J Haematol*. 2010;149(6):834-843. doi:10.1111/j.1365-2141.2010.08208.x
15. Mahlangu JN, Gilham A. Guideline for treatment of haemophilia in South Africa. *S Afr Med J*. 2008;98(2):126-140. doi:10.7196/SAMJ.336

Chapter 7:

LEUCOCYTE DEPLETION AND IRRADIATION OF BLOOD COMPONENTS



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

LEUCOCYTE DEPLETION AND IRRADIATION OF BLOOD COMPONENTS

In certain circumstances, blood products may require further processing in the interests of patient safety. Residual leucocytes and lymphocytes in blood products are associated with complications, which may be mitigated by either leucocyte depletion and/or irradiation of blood products prior to transfusion.

Transfusion-related immunomodulation (TRIM) refers to the well-documented laboratory evidence of immune alterations following allogeneic blood transfusions, e.g. clonal deletion or anergy, induction of suppressor cells, production of anti-idiotypic antibodies, suppression of natural killer (NK) cell activity.

There are also clinical effects that may be the result of TRIM, such as:

- Enhanced survival of renal allografts
- Increased risk of post-operative bacterial infections and recurrence of resected cancers
- Increased short-term mortality from all causes in transfused versus non-transfused patients
- Activation of pre-existing CMV or HIV infection in transfused versus non-transfused patients

TRIM is probably mediated by:

- Allogeneic mononuclear cells that remain viable for at least 2 weeks in stored RBC concentrates
- Pro-inflammatory soluble mediators released from white cells, which accumulate in the supernatant of red cell concentrates during storage
- Soluble class I HLA molecules in allogeneic plasma

LEUCOCYTE DEPLETION OF BLOOD PRODUCTS

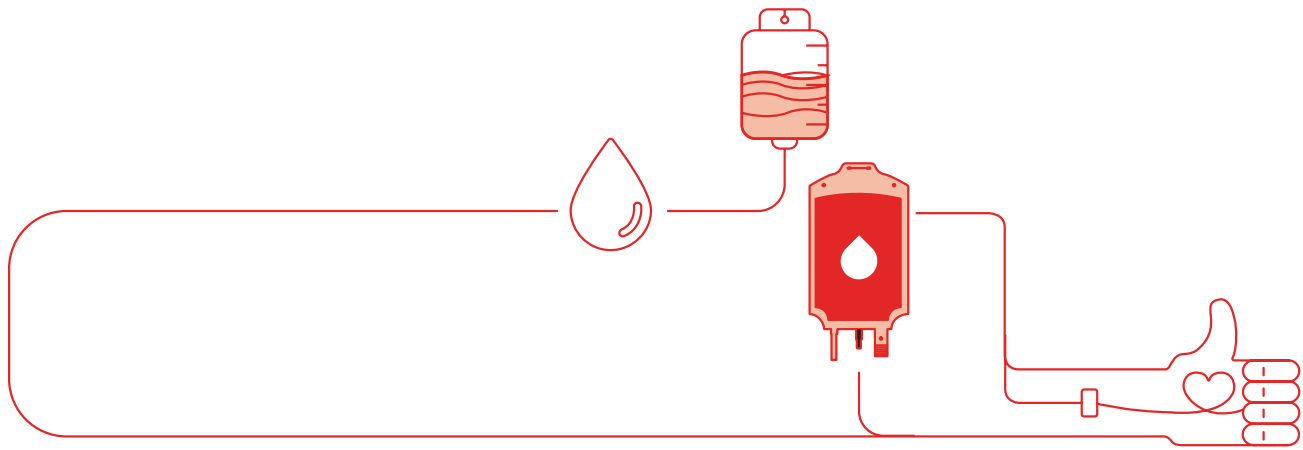
Leucocytes appear to be the prime mediators of the pro-inflammatory and TRIM effects. Filters capable of removing them by several orders of magnitude are readily available and effectively reduce the number of white cells in a red cell concentrate product to $<1 \times 10^6$.

A less efficient, but also less costly, process for removing white cells from blood components is to remove the buffy coat layer from red cell concentrates and to prepare random donor platelet concentrates from the buffy coats. The resulting red cell and platelet concentrates contain leucocytes intermediate in number between filtered components and those where the buffy coat is retained.

A number of well-resourced countries (e.g. the United Kingdom), have adopted a policy of universal pre-storage leucocyte depletion using the filters described above, while others have recommended a policy of selective leucocyte depletion of blood components.

The costs associated with universal leucocyte depletion are significant, amounting to approximately 24% of the total annual turnover of the blood services. Given the competing health priorities in South Africa as a middle-income developing country, there needs to be convincing evidence that universal leucocyte depletion of blood products is clinically beneficial and cost-effective.





Having reviewed the literature, we conclude the following:

- There is good evidence to support the avoidance of FNHTRs by using leucocyte-depleted components
- Administering leucocyte-depleted platelet concentrates reduces the incidence of refractoriness to platelet transfusions
- Administering leucocyte-depleted components significantly reduces the risk of transfusion-transmitted CMV infection in susceptible recipients (e.g. neonates)
- The evidence for reduction of the incidence of post-operative bacterial infection and recurrent cancer following resection is not consistent
- Evidence to support an increase in short-term mortality using non-leucocyte-reduced components is inconsistent; however, subgroup analyses do suggest a benefit for cardiac surgery and critically ill patients
- An association with reactivation of viral infections (HIV and CMV) and survival has not been demonstrated
- Sensitisation to transplant antigens can be lessened by administering leucocyte-depleted products where HLA-alloimmunisation is important
- Using leucocyte-depleted products may reduce potential prions in blood components, but there is as yet no evidence that this will avoid transmission of variant Creutzfeldt Jakob disease (vCJD) by transfusion

The blood services in South Africa have therefore adopted the following policy with respect to leucocyte depletion of blood components:

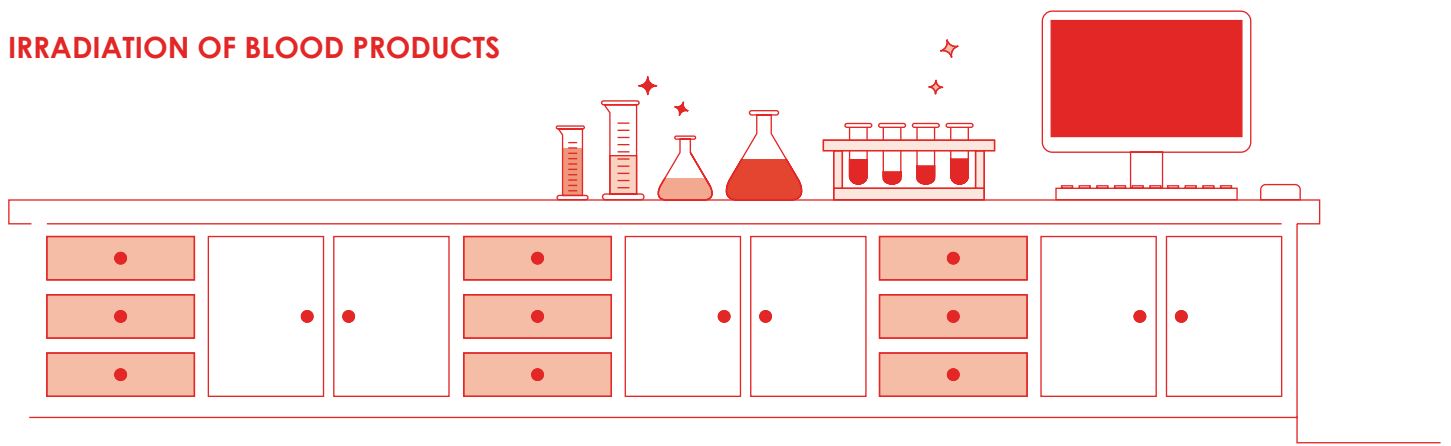
- All standard red cell concentrates are buffy coat depleted
- Random donor platelet concentrates are prepared from buffy coats
- Single donor platelet concentrates collected by apheresis must incorporate a leucocyte-depletion process (standard practice with current apheresis technology)
- The following patients should receive leucocyte-depleted components:
 - o Patients on chronic transfusion regimens
 - o Those at risk for CMV infection
 - o Infants <1 year old
 - o Critically ill, cardiac surgery and trauma patients (particularly those requiring massive transfusion)
- Pre-storage (<48 hours after donation) leucocyte depletion in blood-processing laboratories is recommended.

If this is unobtainable, the freshest components available may be filtered in the blood bank for immediate use (24-hour expiry). Bedside leucocyte-depletion filters are not recommended unless neither of the former 2 options is available.

It is emphasised that the above are guidelines in a subject where there is some controversy.

If individual clinicians wish to use leucocyte-depleted products outside the guidelines, they should order them and the blood banks will issue if they have stock. By continually monitoring the usage and gearing up accordingly, the services should be in a position to meet such demands.

IRRADIATION OF BLOOD PRODUCTS



TA-GvHD is an extremely rare but often fatal complication which may follow the transfusion of lymphocyte-containing blood components. Under certain conditions (e.g. immunosuppression or when donor and patient share HLA haplotype) the infused lymphocytes engraft and proliferate in the recipient. Cellular interaction between donor T lymphocytes and recipient cells leads to cellular damage (particularly in the skin, thymus, gastro-intestinal tract, liver and spleen) very similar to GvHD seen after allogeneic stem-cell transplantation.

An additional specific feature of TA-GvHD is severe bone marrow hypoplasia.

Where patients require irradiated cellular blood components, components must be requested and clearly prescribed as irradiated. Specific requirements, including the need for irradiated blood components, must be part of the bedside check prior to administration of all blood components. Checks must be documented.

X-ray or gamma irradiation by validated systems are currently the only recommended method for prevention of TA-GvHD. There is insufficient evidence to recommend only leucocyte-depleted components use to prevent TA-GVHD in susceptible patients.

TA-GvHD has been reported following transfusion of whole blood, red cell concentrates, platelets and granulocytes. It has not been reported following transfusion of cryoprecipitate, FFP or fractionated products.

The minimum dose achieved in the irradiation volume is 25 Gy, with no part receiving >50 Gy.

Red cell concentrates can be irradiated up to 14 days after collection and stored for a further 14 days without significant loss of viability, but irradiating red cells leads to an accelerated leakage of potassium and an increase in extracellular levels of potassium.

Hyperkalaemia may be a potential complication in rapid, large-volume transfusions, e.g. intrauterine transfusion or neonatal exchange transfusion. In these at-risk transfusion settings, it is recommended that irradiated red cells are transfused within 24 hours of irradiation. If the unit is <5 days old, this complication is unlikely.

If fresh blood is not available, washing of the red cells will prevent hyperkalaemia in the recipient. If washed red cells are irradiated, they should be transfused as soon as possible.

Platelets can be irradiated at any stage during storage and can thereafter be stored up to their normal shelf life after collection.

All granulocytes for transfusion should be irradiated before issue. They should be transfused with minimum delay. For allogeneic sources, it is not necessary to irradiate FFP, cryoprecipitate or fractionated plasma.

All transfusions of cellular components and fresh plasma from first- or second-degree relatives should be irradiated, even if the patient is immunocompetent. All HLA-selected components should be irradiated even if the patient is immunocompetent.

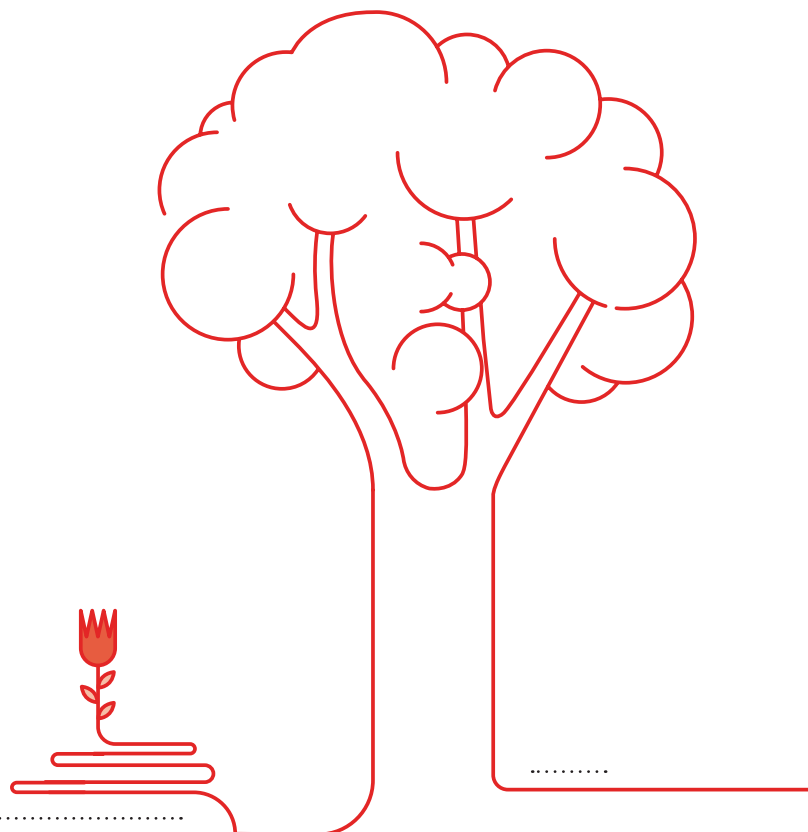
CLINICAL INDICATIONS FOR IRRADIATED BLOOD COMPONENTS

Table 7.1

Clinical indication	Notes
Blood components donated by blood relatives	
Paediatric use	<ul style="list-style-type: none"> IUT with red cells and/or platelets Red cells and/or platelets in a previous IUT recipient, until 6 months after expected delivery date Exchange transfusion (ET) Recommended for all ETs, provided this does not unduly delay the ET T-lymphocyte immunodeficiency syndromes (confirmed or suspected)
Allogeneic stem-cell transplant	<ul style="list-style-type: none"> All recipients of allogeneic haemopoietic stem-cell transplantation (HSCT), from time of initiation of conditioning regimen. This should continue until all the following criteria are met: <ul style="list-style-type: none"> >6 months has elapsed since the transplant date The patient is free of active, chronic GvHD The patient is off all immunosuppression Lymphocytes are $>1 \times 10^9/l$ Post-allogeneic transplant, if chronic GvHD is present or continued, immunosuppressive treatment is required. Irradiated blood components should be given indefinitely Treatment with irradiated blood components should continue indefinitely if this is required based on transplant conditioning, underlying disease or previous treatment, e.g. previous diagnosis of Hodgkin's lymphoma (HL) or previous purine analogue treatment Allogeneic cellular blood components transfused to bone marrow and peripheral blood stem-cell donors of all ages within 7 days prior to or during the harvest should also be irradiated
Autologous stem cell transplant	<ul style="list-style-type: none"> Patients (adult and paediatric) undergoing bone marrow or peripheral blood stem-cell collections for future autologous re-infusion should receive irradiated cellular blood components for 7 days prior to and during the bone marrow/stem-cell harvest to prevent the collection of viable allogeneic T lymphocytes, which can potentially withstand cryopreservation All patients undergoing autologous stem-cell transplant (ASCT), irrespective of underlying diagnosis or indication for this treatment, should receive irradiated cellular blood components from initiation of conditioning chemo/radiotherapy until 3 months post-transplant (6 months if total body irradiation was used in conditioning) – unless conditioning, disease or previous treatment determine indefinite duration, e.g. previous diagnosis of HL or previous purine analogue treatment
Other patient groups which should receive irradiated blood components	<ul style="list-style-type: none"> HL patients Indefinitely for all patients treated with purine analogues, e.g. fludarabine, cladribine, bendamustine and pentostatin Patients with chronic lymphocytic leukaemia (CLL) or other haematological diagnosis treated with alemtuzumab Patients with aplastic anaemia, undergoing treatment with antithymocyte globulin (ATG) or alemtuzumab Patients receiving ATG or other T-lymphocyte-depleting serotherapy for rare types of immune dysfunction conditions Patients (adult and paediatric) undergoing peripheral blood lymphocyte collections for future CAR-T cell re-infusion: for 7 days prior to and during the harvest, to prevent the collection of viable allogeneic T lymphocytes; then continued until 3 months following CAR-T cell infusion – unless conditioning, disease or previous treatment determine indefinite duration, e.g. previous diagnosis of HL or previous purine analogue treatment
Patient groups for which irradiated blood components are not routinely recommended	<ul style="list-style-type: none"> Patients with aplastic anaemia, transfusion of irradiated cellular components – except for HLA-selected platelets, transfusion of granulocytes, donations from first- or second-degree relatives, or planned relevant treatment, e.g. ATG, alemtuzumab and sacrococcygeal teratoma (SCT) Adult patients or children treated for acute leukaemia or non-Hodgkin's lymphoma (NHL), including CLL (unless treated with alemtuzumab) – except for HLA-selected platelets, transfusion of granulocytes, donations from first- or second degree relatives, or due to current or previous treatment

FURTHER READING

1. Blajchman MA, Vamvakas EC. Transfusion related immunomodulation. In Murphy MF, Pamphilon DH, eds. *Practical Transfusion Medicine*. 3rd ed. Wiley-Blackwell; 2009
2. Bird A, Crookes R. Leucocyte depletion of blood components -- guidelines of the Blood Transfusion Services of South Africa. *S Afr Med J*. 2006;96(5):395-396
3. Blumberg N. Deleterious clinical effects of transfusion immunomodulation: proven beyond a reasonable doubt. *Transfusion*. 2005;45(2 Suppl):33S-39S; discussion 39S-40S. doi:10.1111/j.1537-2995.2005.00529.x
4. Vamvakas EC. Deleterious clinical effects of transfusion immunomodulation: proven beyond a reasonable doubt. *Transfusion*. 2006;46(3):492-494. doi:10.1111/j.1537-2995.2006.00748.x
5. Foukaneli T, Kerr P, Bolton-Maggs PHB, et al. Guidelines on the use of irradiated blood components. *Br J Haematol*. 2020;191(5):704-724. doi:10.1111/bjh.17015
6. X-ray irradiation of blood components. Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. 2020. Accessed March 7, 2023. <https://www.transfusionguidelines.org/document-library/documents/x-ray-irradiation-of-blood-components>



Chapter 8:

HAEMOVIGILANCE, RISKS AND ADVERSE REACTIONS ASSOCIATED WITH BLOOD TRANSFUSION



CLINICAL GUIDELINES FOR

**THE USE OF BLOOD AND
BLOOD PRODUCTS IN
SOUTH AFRICA**

HAEMOVIGILANCE, RISKS AND ADVERSE REACTIONS ASSOCIATED WITH BLOOD TRANSFUSION

HAEMOVIGILANCE

Haemovigilance involves the recording, reporting, analysis and evaluation of suspected adverse donation and transfusion events. Corresponding measures are then derived to improve the quality and safety of transfusions, thereby promoting patient safety. The system is based on the reporting of all incidents and reactions occurring during the transfusion process, from donor selection to the administration of blood products to the patient.

The evaluation of haemovigilance provides a picture of the current transfusion-related risks, can pinpoint the cause of preventable transfusion incidents, and can reveal areas where corrective measures are necessary and possible.

Accurate and valuable haemovigilance monitoring is dependent on reliable reporting. This responsibility lies with the donor, the blood transfusion services (as producers of labile blood products) and the prescribing clinicians. The treating doctor is responsible for identifying and then reporting a transfusion reaction that occurs in their institution to a reporting body.

The analysis and evaluation of this data provide an up-to-date overall picture of transfusion safety and the nature and magnitude of the risks expected during the transfusion of labile blood products. In order to obtain a comprehensive overview of transfusion-related incidents, the involvement of all institutions that administer blood components is essential. This requires direct communication between all involved stakeholders, as haemovigilance thrives on the interdisciplinary cooperation of all professionals involved in the handling of blood products.

The implementation and maintenance of a high-quality haemovigilance system poses a major challenge that should not be underestimated. It requires great commitment from responsible stakeholders, as well as considerable resources and time.



Reporting of Transfusion-Related Adverse Events

SANBS and Western Cape Blood Service (WCBS) have in place systems whereby healthcare professionals can report TRAEs occurring as a result of transfusion of blood and blood products. This is done by submitting a transfusion reaction form to the blood bank via fax or email, or by making a telephonic report.

Management of Reported Transfusion-Related Adverse Events

1. Reporting forms are either dispensed by SANBS or WCBS with the issued products or they are kept in hospital wards and the local blood bank. A form must be completed by the attending healthcare worker should a TRAE occur or be suspected.
2. The healthcare worker must then send the form and 2 post-transfusion ethylenediamine tetraacetic acid (EDTA) blood samples from the patient to the blood bank to reach the Haemovigilance Officers and the appropriate laboratory – Red Cell Serology (RCS) laboratory in SANBS or Immunohaematology laboratory at WCBS – for further investigation.
3. Once received, the clinical information will be analysed by the blood bank staff or Haemovigilance Officer to establish the suspected reaction type.
4. Serological testing is performed on the samples by the blood bank, RCS or Immunohaematology laboratories.
5. Complicated or severe transfusion reactions are referred to the Independent Haemovigilance Committee for impartial review.
6. A transfusion reaction is classified according to definitions provided by the International Haemovigilance

Network (IHN), and a report or letter is sent to the treating doctor of the patient (private sector) or the clinical manager of the hospital (public sector).

7. The results of all TRAEs for SANBS and WCBS are summarised in the annual Haemovigilance Report. No patient identification details are provided in this report.
8. The latest Haemovigilance Report is available on both the SANBS and WCBS websites: www.sanbs.org.za and www.wcbs.org.za.

RISKS ASSOCIATED WITH BLOOD TRANSFUSION

Mortality Associated with Transfusion

As per Section 68 of the National Health Act 61 of 2003, in the event that a patient demises while receiving or following a transfusion, the following steps must take place:

1. The blood bank must be notified of the case as a 'Mortality following a transfusion'.
2. Post-transfusion samples must be taken immediately and sent to the blood bank.
3. A post-mortem must be conducted to establish the cause of death.
4. The treating doctor's report and post-mortem results must be sent to the blood bank or directly to the Haemovigilance office.
5. Once the blood transfusion service has completed the investigation, a report will be sent to the treating doctor and/or hospital manager, and the Deputy Director-General of the National Department of Health.
6. The case will be classified according to the outcome of the investigations and post-mortem results.

Lookback Programme

The objective of the Lookback Programme is to trace all patients who are identified as potential window-period recipients of blood from donors who, on subsequent donations, test positive for transfusion-transmissible infections (TTIs) for which SANBS and WCBS test.

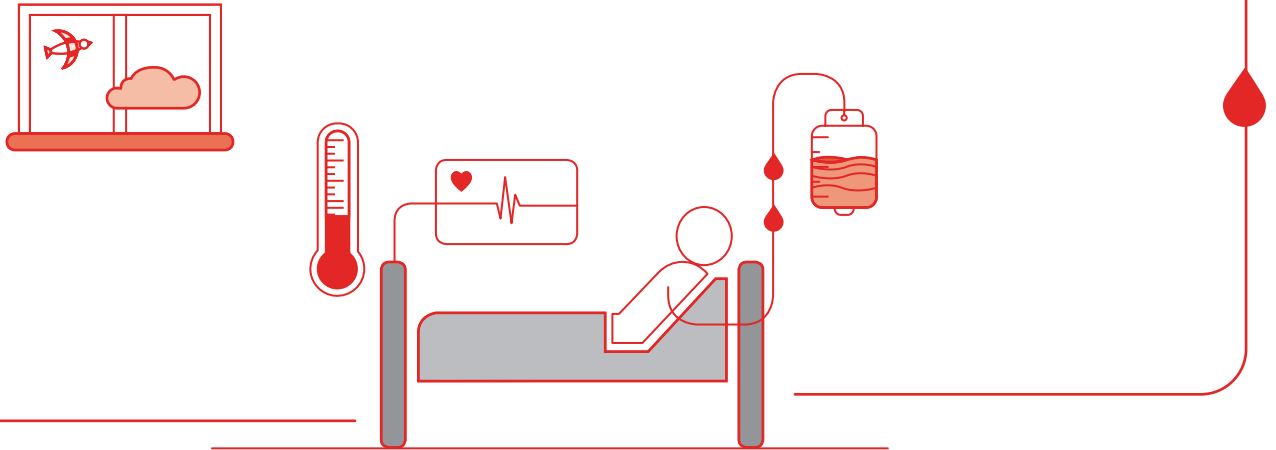
The Lookback Programme also investigates cases where the recipient of a blood transfusion alleges that they were infected with a TTI through blood transfusion.

Types of lookback process

Donor-triggered lookback process	Recipient-triggered lookback process
<i>Initiated when a repeat donor tests positive for a viral marker for which SANBS/WCBS tests</i>	<i>Initiated when a recipient of a transfusion tests positive for a pathogen that the attending doctor suspects was transmitted via a blood product</i>
<ol style="list-style-type: none"> 1. The Lookback Office (LBO) initiates a lookback investigation. 2. Recipients of the donor's last negative donation are identified. 3. Hospital Medical Manager/attending doctor is notified. 4. Medical Manager/Attending doctor traces each recipient. 5. Recipient is counselled and tested for viral marker. 6. Test results are forwarded to the LBO. 7. If the test results are negative, the case is closed. 8. If the test results are positive, further tests are done to determine if this infection is transfusion transmitted. Phylogenetic testing is used to determine if there is correlation between the viruses from the donor and recipient (HIV, HBV and HCV). 9. If there is no genetic linkage, the case is closed. 10. If there is a genetic linkage, the case is elevated to the Senior Manager who deals with lookbacks and to the Medical Director. 	<ol style="list-style-type: none"> 1. The attending doctor reports to SANBS or WCBS if they suspect a TTI. 2. The attending doctor completes the relevant form and forwards it to the LBO. 3. Upon receipt of the form, the LBO initiates a lookback investigation. 4. The implicated donors are each recalled for testing. 5. Donor is counselled and retested for the appropriate pathogens. 6. If the test results are negative, the case is closed. 7. If a donor tests positive, phylogenetic analysis is conducted where applicable and available. 8. If the phylogenetic tests indicate no genetic linkage, the case is closed. 9. If there is a genetic match, the case is elevated to the Senior Manager who deals with lookbacks and to the Medical Director.

TRANSFUSION REACTIONS

A transfusion reaction is defined as any potentially adverse sign or symptom which occurs after the start of any transfusion of blood or blood products. It stands to reason that, in order to notice any adverse effect, the patient's condition prior to, during and after the transfusion must be monitored.



It is good medical practice to err on the side of caution when a reaction is suspected, and to take swift action. The steps are simple and apply in all instances:

1. Stop the transfusion immediately.
2. Maintain venous access with crystalloids in a new drip set, in case fluid, medication or further transfusion therapy is required.
3. Manage the acute symptoms and stabilise the patient.
4. Contact the transfusion service for advice, if needed.
5. Complete the reporting form for the blood services and submit with post-transfusion blood samples from the patient.

Monitoring

The basic monitoring of the patient prior to the start of the transfusion and during the infusion includes:

- Pulse
- BP
- Temperature
- Respiration rate
- General visual observation
- Verbal enquiry as to the patient's well-being

Any abnormal symptoms at the start of transfusion should be noted, e.g. dyspnoea, chills, oliguria. Changes in intensity of these symptoms may indicate the potential for a transfusion reaction and should be assessed clinically. These patients are, however, usually closely monitored for changes in their primary condition and transfusion reactions are readily detected.

Extra care must be taken to monitor and react to changes in vital signs in the unconscious patient. Excessive oozing from the operative site or venous access points and unexplained hypotension may indicate that a haemolytic transfusion reaction is occurring.

Signs and Symptoms Highly Suggestive of a Transfusion Reaction

- Chills/rigors
- Tachycardia/bradycardia
- Hypertension/hypotension
- Chest/flank pain
- Haemoglobinuria
- Agitation
- Fever/sweating
- Dyspnoea/bronchospasm
- Urticaria/pruritus
- Nausea/vomiting
- Oliguria/anuria
- Jaundice

Investigation

The transfusion service has a specific set of instructions for investigating reactions and it is the legal responsibility of the clinician to assist with this undertaking. The clinician should send clearly labelled appropriate samples, including the following as a minimum requirement:

- Clotted blood sample
- EDTA tube
- Post-transfusion urine sample, depending on the nature of the reaction
- Suspected unit/s, empty blood bags and drip set, returned to the nearest blood bank. If there is concern about possible bacterial contamination of the implicated unit:
 - ensure that the blood bank is informed so that cultures and gram stains are performed
 - obtain blood for blood culture from the patient
- Completed reaction report form, specifying:
 - patient details
 - reason for transfusion
 - pre- and post-transfusion signs and symptoms

Transfusion Reaction Classification

The list of potential reactions is lengthy and there are many different criteria for classification. Reactions include those attributable to:

- Incompatibility
- Transmissible disease
- Bacterial contamination
- Storage lesions due to the age of the transfused blood products

However, for most practical purposes, the following table lists and describes the most frequently observed or serious TRAEs:

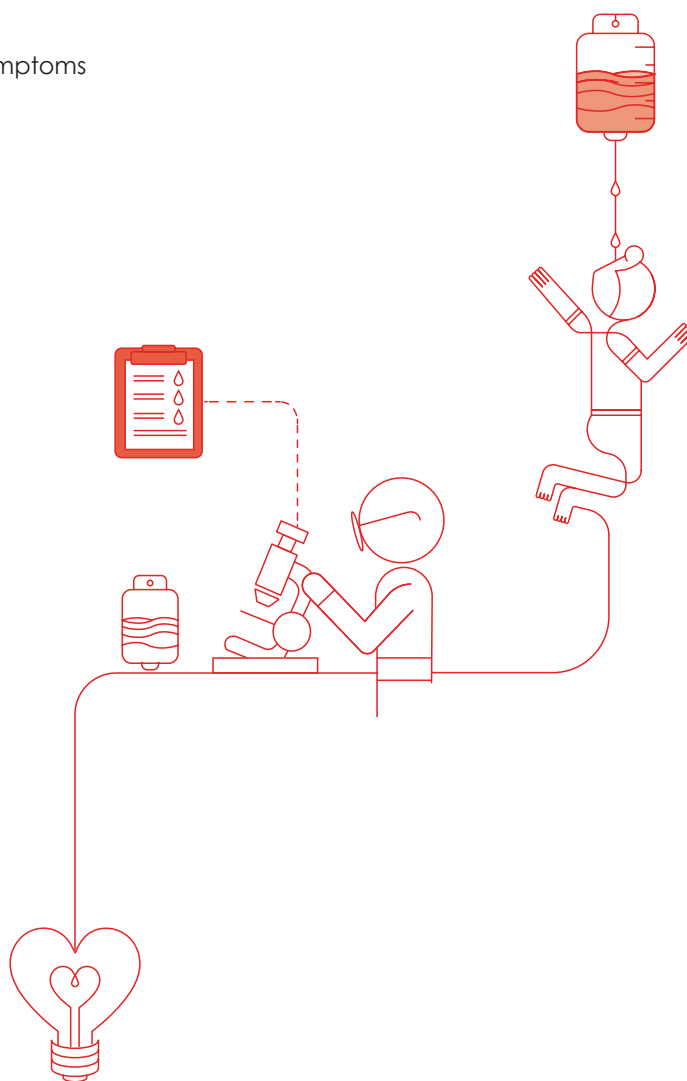


Table 8.1

Acute haemolytic reactions (Intravascular haemolysis)	Signs/symptoms	Management
<ul style="list-style-type: none"> Caused by exposure of patient to incompatible donor red cells (usually ABO mismatched blood) Apparently similar reactions can result from incorrectly heeded/stored red cell products <p>NOTE: In the case of an acute haemolytic reaction, the transfusion service's medical officer on-call will be informed and will communicate with the patient's doctor.</p>	<ul style="list-style-type: none"> Usually abrupt in onset and within 15-20 minutes after initiation of any red cell containing blood product Fever, chills, nausea, vomiting, pain – flank, back, chest, dyspnoea, hypotension, tachycardia, unexpected degree of anaemia, renal failure, DIC Abnormal bleeding and hypotension may be the only signs in the unconscious patient <p>Further signs</p> <ul style="list-style-type: none"> Haemoglobinuria/anaemia Haemoglobinuria 	<ul style="list-style-type: none"> Stop the transfusion, change the transfusion set and filter. Maintain venous access with crystalloid/colloid solutions. Notify the blood bank for to perform a clerical check i.e. patient/donor ID numbers, and send unit/tubing to blood bank with the urine specimen, blood samples and reaction report. Monitor vital signs, including in some instances the pulmonary arterial pressure or CVP. Measure urinary output, observe for abnormal bleeding, especially if the patient is in post-operative stage. Maintain intravascular volume and urinary output with crystalloid/colloid solutions. Prevent/treat renal failure with furosemide iv 120 mg (and mannitol 1 gram). Vasopressors (e.g. dopamine) may be required. Monitor patient closely. Consult renal department with a view to starting haemodialysis to reduce plasma haemoglobin and prevent acute renal failure. Consult haematology department for further assessment of coagulation profile if required.
Febrile non-haemolytic transfusion reactions	Signs/symptoms	Management
<ul style="list-style-type: none"> Usually caused by recipient leucocyte or platelet antibodies to transfused donor cells Cytokine collection in stored products has also been implicated 	<ul style="list-style-type: none"> Onset usually within 1 – 2 hours after start of transfusion Headache, myalgia, malaise, fever, chills, tachycardia and hypertension Commonly found in multiparous or multi-transfused patients 	<ul style="list-style-type: none"> Stop the transfusion. Maintain venous access with crystalloid/colloid solution Notify blood bank and send urine, post-transfusion samples and pack to blood bank. Must be differentiated from early acute haemolytic transfusion reaction Administer antipyretics Further management: If repeated on further transfusion, then transfuse with leucocyte-depleted blood
Allergic	Signs/symptoms	Management
<ul style="list-style-type: none"> Caused by allergens to plasma proteins 	<ul style="list-style-type: none"> Usually mild NO fever Itching, hives, urticaria, erythema Limited to skin only 	<ul style="list-style-type: none"> Stop the transfusion. Keep intravenous access open Notify blood bank and send post-transfusion samples, urine and packs Administer antihistamines Commence transfusion with a new unit once blood bank has ascertained that this is not a haemolytic transfusion reaction
Bacterial contamination	Signs/symptoms	Management
<ul style="list-style-type: none"> Caused by any contaminated blood product (most frequently associated with platelet concentrates) 	<ul style="list-style-type: none"> Usually rapid onset, about 1 hour post-transfusion. Chills, fever, abdominal cramps, vomiting or diarrhoea, renal failure, flushed and dry skin, hypotension, shock 	<ul style="list-style-type: none"> Stop the transfusion. Change filter and tubing. Maintain venous access with crystalloid or colloid solution Notify blood bank and send blood samples with unit and tubing/filter to the blood bank for gram stain and culture Take an immediate blood culture from the patient for potential comparison with the bacterial isolated from the blood product Monitor vital signs and administer broad-spectrum antibiotics, vasopressors, steroids, fluids and electrolytes

Table 8.1 continued

<p>Anaphylactic reactions</p> <ul style="list-style-type: none"> Severe, usually due to antibodies to IgA immunoglobulin Less frequently severe reactions to other plasma proteins 	<p>Signs/symptoms</p> <ul style="list-style-type: none"> Sudden onset Symptoms include dyspnoea, hypotension/shock, facial and/or glottal oedema plus explosive GI symptoms May lead to cardiac arrest/death 	<p>Management</p> <ul style="list-style-type: none"> Stop the transfusion. Maintain venous access and maintain IV volume and BP with crystalloid or colloid solutions Give adrenaline, dopamine, steroids and oxygen Monitor vital signs Prevention: Patient may be IgA-deficient and require assessment of immunoglobulin profile. Further therapy must be with washed red cells that are plasma-free
<p>Transfusion-related acute lung injury (TRALI)</p> <ul style="list-style-type: none"> Severe, usually caused by leucoagglutinins in the plasma of the donor Generally under-recognised and under-reported 	<p>Signs/symptoms</p> <ul style="list-style-type: none"> Dyspnoea, hypotension, fever, bilateral pulmonary oedema usually occurring within 4 hours of transfusion 	<p>Management</p> <ul style="list-style-type: none"> Management should be initiated as soon as possible Consists of fluid support to maintain blood pressure and cardiac output Ventilation support may be required Diuretics should not be used as they may have a deleterious effect
<p>Delayed transfusion reaction (Extravascular haemolytic reaction)</p> <ul style="list-style-type: none"> Caused by exposure to incompatible red cells in the presence of an atypical IgG antibody, e.g. anti-Kell or anti-Duffy Severity variable 	<p>Signs/symptoms</p> <ul style="list-style-type: none"> May appear within hours in a severe reaction (often anti-Kell) Characterised by a drop in haemoglobin and jaundice In some cases there may be additional complications, e.g. renal failure and DIC Most cases are mild and go unnoticed or are only noticed some 2 – 10 days after the transfusion, with mild jaundice and anaemia 	<p>Management</p> <ul style="list-style-type: none"> Severe reactions should be managed with supportive measures appropriate to the patient's condition In cases with renal failure, measures such as haemodialysis should be implemented, and most cases resolve completely If there is a bleeding diathesis, then appropriate transfusion therapy should be given. In most cases the reaction is mild and no particular interventions are required
<p>Transfusion-associated graft vs host disease (TA-GVHD)</p> <ul style="list-style-type: none"> This extremely rare condition results from the transfusion of donor lymphocytes that share an HLA haplotype with the recipient Characteristically, the donor lymphocytes are homozygous for a particular HLA haplotype whereas the recipient is a heterozygote The condition is more likely to occur in situations where blood relatives of the patient are the donors It can be prevented by irradiation of the blood at 25 – 30 Gy Leucocyte depletion is not considered to be adequate to prevent TA-GVHD 	<p>Signs/symptoms</p> <ul style="list-style-type: none"> The reaction is often florid and occurs 10 – 14 days after transfusion Patient presents with severe jaundice, a maculopopular rash, pancytopenia and diarrhoea 	<p>Management</p> <ul style="list-style-type: none"> This condition carries an extremely high mortality rate Therapy is directed at eliminating the clone of engrafted lymphocytes by chemotherapy. This should be done by a specialist oncology unit

Table 8.1

Post-transfusion purpura	Signs/symptoms	Management
<ul style="list-style-type: none"> This rare condition results from recipient alloantibodies directed against donor platelet antigens The antibodies are usually directed against HPAla or HP A5a Since most individuals have these antigens, antibodies are rare In most cases the recipient is female 	<ul style="list-style-type: none"> Characterised by a marked thrombocytopenia occurring about 9 – 10 days after transfusion In this reaction, recipient's own platelets appear also to be destroyed (by unknown mechanisms) 	<ul style="list-style-type: none"> This potentially lethal reaction is ideally treated with intravenous immunoglobulin (2 g/kg over 2 – 5 days) Platelet support (if possible HP A-compatible) may be necessary, but this often requires high doses in the presence of appropriate immunosuppressive therapy (e.g. steroids) In some cases, plasma exchange may be successful

FURTHER READING

1. SANBS/WCBS. Haemovigilance reports. Accessed March 7, 2023. <https://sanbs.org.za/clinical-services/ or https://www.wcbs.org.za/wp-content/uploads/2021/11/2020-south-african-haemovigilance-report.pdf>
2. Serious Hazards of Transfusion.SHOT Report 2019. Accessed March 7, 2023. <https://www.shotuk.org/shot-reports/report-summary-and-supplement-2019/>
3. Blood safety and availability. World Health Organization. 26 May 2022. Accessed March 7, 2023. <https://www.who.int/news-room/fact-sheets/detail/blood-safety-and-availability>
4. Global status report on blood safety and availability. World Health Organization. 2021. Accessed March 7, 2023. <https://www.who.int/publications/item/9789240051683>
5. Basu D. Diseases of public health importance in South Africa. Southern African Journal of Public Health. 2018;2(3):48. doi:10.7196/SHS.2018.v2i3.72
6. South African National Blood Service. <http://www.sanbs.org.za>
7. Western Cape Blood Service. <http://www.wcbs.org.za>
8. Sauer DA, McDonald CE, Boshkov L. Errors in transfusion medicine. Laboratory Medicine. 2001;32(4):205-207. <https://doi.org/10.1309/WHVV-VUC9-J1VT-W4NL>

ABBREVIATION LIST *P1 of 3*

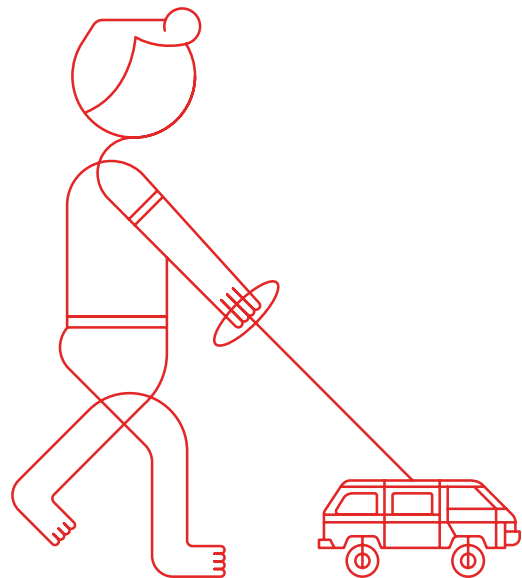
2,3 DPG	2,3 diphosphoglycerate
AABB	Association for the Advancement of Blood & Biotherapies
AABB	Formerly the American Association of Blood Banks
ACS	acute coronary syndromes
AIDS	Acquired Immunodeficiency Syndrome
APTT	activated partial thromboplastin time
ASCT	autologous stem cell transplant
ATG	antithymocyte globulin
ATP	adenosine triphosphate
BP	blood pressure
BSH	British Society for Haematology
CCI	corrected-count increment
CLL	chronic lymphocytic leukaemia
CMV	cytomegalovirus
CVP	central venous pressure
DIC	disseminated intravascular coagulation
EBV	estimated blood volume
EDTA	post-transfusion ethylenediamine tetraacetic acid
ET	exchange transfusion
FEIBA	factor eight inhibitor bypass activity
FFP	fresh frozen plasma
FNHTR	febrile non-haemolytic transfusion reactions
GA	gestational age
GI	gastro-intestinal
GvHD	graft versus host disease
Hb	haemoglobin
HBeAg	hepatitis B e-antigen
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
Hct	haematocrit
HCV	hepatitis C virus
HDFN	haemolytic disease of the foetus and newborn
HDN	haemorrhagic disease of the newborn
HIT	heparin-induced thrombocytopenia
HIV	human immunodeficiency virus



ABBREVIATION LIST

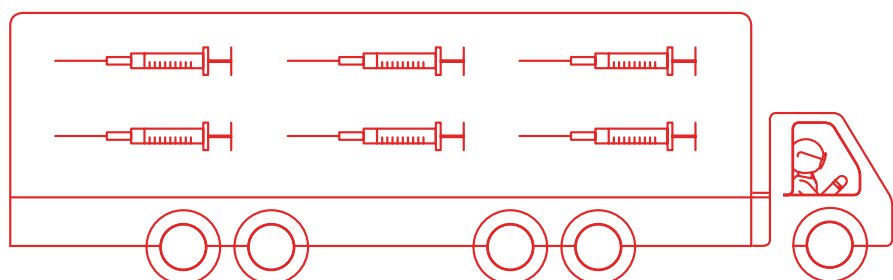
P2 of 3

HL	Hodgkin's lymphoma
HLA	human leucocyte antigen
HPA	human platelet specific antigens
HSCT	haemopoietic stem-cell transplantation
ICU	intensive care unit
IgA	immunoglobulin A
IgG	immunoglobulin G
IgM	immunoglobulin M
IHN	International Haemovigilance Network
IM	intramuscular
INR	international normalized ratio
ITP	immune thrombocytopenia
IUT	intra-uterine transfusion
IV	intravenous
IVI	intravenous injection
LBO	Lookback Office
NAIT	neonatal alloimmune thrombocytopenia
NHL	non-Hodgkin's lymphoma
NK	natural killer
PAS	platelet additive solution
PBM	Patient Blood Management
PIL	Patient Information Leaflet
PNH	paroxysmal nocturnal haemoglobinuria
PT	prothrombin time
PTP	post-transfusion purpura
PTR	platelet transfusion refractoriness
PVH	pulmonary venous hypertension
RBC	red blood cell
RCS	Red Cell Serology
RCT	randomised controlled trial
RDP	random donor platelet
ROTEM	rotational thromboelastography
rVIIa	recombinant factor VIIa
SABM	Society for the Advancement of Patient Blood Management
SABMR	South African Bone Marrow Registry



ABBREVIATION LIST P3 of 3

SANBS	South African National Blood Service
SCT	sacrococcygeal teratoma
SDAP	single donor apheresis platelet
TACO	transfusion-associated circulatory overload
TA-GvHD	transfusion-associated graft versus host disease
TEG	thromboelastography
TRAEs	transfusion-related adverse events
TRALI	transfusion-related acute lung injury
TRIM	transfusion-related immunomodulation
TRUST	transfusion risk understanding score
TTI	transfusion-transmissible infection
TTP	thrombotic thrombocytopenia purpura
TXA	tranexamic acid
vCJD	variant Creutzfeldt Jakob disease
vWD	von Willebrand disease
vWF	von Willebrand factor
vWF Ag	von Willebrand factor antigen
WCBS	Western Cape Blood Service
WHO	World Health Organization



Notes

18 horizontal red rounded rectangular lines for taking notes.

Notes

18 horizontal red rounded rectangular lines for taking notes.

CLINICAL GUIDELINES FOR
THE USE OF BLOOD AND BLOOD PRODUCTS IN SOUTH AFRICA



SANBS Head Office

1 Constantia Boulevard, Constantia Kloof,
Johannesburg
www.sanbs.org.za



WCBS Head Office

3 Oude Molen Road, Ndabeni, 7405
Postal address :
P.O. Box 79, Howard Place, 7450