Resource Manual for Medical Directors of Transfusion Medicine

Inspiring and facilitating best transfusion practices in Ontario.

TABLE OF CONTENTS

Foreword

Introduction

1.0 Medical Roles and Responsibilities
- 1.1 Indications for Consultation with Transfusion Medicine Medical Staff Qualifications
- Table 1.1: Indications for Immediate Consultation
- Table 1.2: Transfusion Emergency and TM Medical Director or Delegate is not responding

2.0 Quality System Management
- 2.1 Components of Assessment Quality System Essentials

3.0 Informed Consent and Refusal of Consent

4.0 Daily Operations
- 4.1 Patient Identification and Sample Labeling Criteria
- 4.2 Pre-transfusion Examinations
- Table 4.1: Clinical Significance of Antibodies and Provision of Red Blood Cells
- 4.3 Inventory Management

5.0 Appropriate Use of Blood Components for Adults
- 5.1 Transfusion of Red Blood Cells to Adults
- Table 5.1: Transfusion Guidelines for Red Blood Cells
- Table 5.2: Transfusion of Red Blood Cells to Adults
- Table 5.3: Selection ABO Compatible Donor Red Blood Cells
- 5.2 Transfusion of Platelets to Adults
- Table 5.4: Guidelines for Platelet Transfusion in Adults
- Table 5.5: Relative Contraindications to Adult Platelet Transfusion
- 5.3 Transfusion of Frozen Plasma to Adults
- 5.4 Transfusion of Cryosupernatant Plasma to Adults
- 5.5 Transfusion of Cryoprecipitate to Adults
- 5.6 Use of Prothrombin Complex Concentrates (PCCs)

6.0 Special Product Selection
- 6.1 Platelet Selection
- 6.2 Clinical Practice Recommendations for the Use of Non-ABO Specific Platelets
- 6.3 Special Circumstances
- 6.4 Platelet Refractoriness and Indications for HLA matched platelets
- 6.5 Clinical Practice Recommendations for Management of Platelet Refractoriness
- 6.6 CMV Seronegative Red Blood Cells and Platelets
- 6.7 Indications for use of CMV seronegative red blood cells and platelets
- 6.8 Irradiated Blood Components
- Table 6.1: Recommended Indications for the Use of Irradiated Components
- 6.9 Washed Red Blood Cells and Platelets
- 6.10 Indications for Washed Red Blood Cells
- 6.11 Indications for Washed or Plasma Depleted Platelets
- 6.12 Emergency Release of Red Blood Cell Units

7.0 Appropriate Use of Manufactured Blood Products
7.1 Appropriate Use of Plasma Fractionated Products
7.2 Indications for the Use of Albumin
7.3 Indications for the Use of Intravenous Immunoglobulin (IVIG)
Table 7.1: Use of Recombinant* and Plasma Derived Products that Do Not Require a Special Access Program (SAP) Approval
Table 7.2: Use of Products that Require Approval through Health Canada Special Access Program or SAP
7.4 Use of Recombinant Factor VIIa, Erythropoietin

8.0 Appropriate Use of Blood Components in Neonates and Pediatric Patients
8.1 Neonatal Red Blood Cell and Platelet Transfusion
8.2 Neonatal Patient Management
Table 8.1: Threshold and Target Hemoglobin Levels for Neonatal Red Blood Cell Transfusion
Table 8.2: Indications for Neonatal Platelet Transfusion
8.3 Pediatric Blood Component Transfusion
Table 8.3: Pediatric Red Blood Cell Transfusion Guidelines
8.4 Transfusion of Frozen Plasma to Pediatric Patients
8.5 Transfusion of Platelets to Pediatric Patients more than 4 months of age
Table 8.4: Indications for Pediatric Platelet Transfusion (other than neonate)
8.6 Management of Congenital Anemias
8.7 Management of Transfusion in Pediatric Patients with Autoimmune Hemolytic Anemia

9.0 Special Transfusion Situations
9.1 Support of a Patient with a Signed Refusal of Consent for Transfusion
9.2 Management of a Patient Requiring Massive Transfusion
9.3 Switching ABO Group in Massive Transfusion or During Inventory Shortage
Table 9.1: Selection Order of ABO Compatible Donor Red Blood Cells
Table 9.2: Selection Order of ABO Group for Platelets or Plasma
9.4 Switching from RhD Negative to RhD Positive Red Blood Cells in Massive Transfusion
9.5 Massive Transfusion in a Patient with Alloantibodies
9.6 Transfusion Management of Autoimmune Hemolytic Anemia (AIHA)
9.7 Transfusion Support for Patients Following Solid Organ or Allogeneic Bone Marrow or Stem Cell Transplant
9.8 Transfusion Support of Patients with Sickle Cell Syndromes

10.0 Disaster and Contingency Plans

11.0 Transfusion Reactions
Table 11.1: Ontario TTISS Transfusion Reaction Chart
Table 11.2: Algorithm for management of transfusion–associated fever
11.1 Urticaria and other allergic reactions
Table 11.3: Management Algorithm for Allergic Reactions
11.2 Dyspnea
Table 11.4: Management Algorithm for Dyspnea
11.3 Transfusion-associated circulatory overload (TACO)
11.4 Hypotension (bradykinin mediated)
Table 11.5: Management Algorithm for Hypotension
11.5 Cytopenias after transfusion
11.6 Transfusion-associated graft-versus-host disease (GvHD)
11.7 Rare causes of transfusion-associated cytopenia
11.8 Hemolysis after transfusion
11.9 Adverse reactions to intravenous immunoglobulin (IVIG)
Table 11.6: Adverse Reactions to IVIG

FOREWORD

The purpose of this Resource Manual for Medical Directors of Transfusion Medicine is to provide support and guidance to physicians responsible for transfusion medicine services in the Province of Ontario. It provides a framework outlining sound transfusion laboratory practice, and seeks to advocate for appropriate current practices in the use of both labile blood components and manufactured products. The manual may also serve to assist Medical Directors of Transfusion Medicine Services in their interactions with hospital administration and medical staff in remediation of shortcomings in Transfusion Medicine resources and practices, and also in the area of promotion of education in Transfusion Medicine.

ACKNOWLEDGEMENTS

ORBCoN gratefully acknowledges:

The Ontario Ministry of Health and Long Term Care for their financial support.

The British Columbia Blood Programs Coordinating Office for granting copyright permission to use their document by the same name as a template for the Ontario version.

Dr. Allison Collins and Dr. Peter Pinkerton who reviewed and edited the document and the contributors and material reviewers of the first edition of the Policy Manual for Medical Directors of Transfusion Medicine.

COMMUNICATIONS

The Ontario Regional Blood Coordinating Network welcomes queries regarding this edition of the Resource Manual for Medical Directors of Transfusion Medicine, and invites suggestions for improvements in future editions. Please refer to www.transfusionontario.org for contact information.

LEGAL DISCLAIMER

INTRODUCTION

This Resource Manual for Medical Directors of Transfusion Medicine has been produced by the Ontario Regional Blood Coordinating Network, acting under the authority of the Ministry of Health and Long Term Care. It is intended to provide a guide towards the operation, consistent throughout the Province, of the Transfusion Medicine Services by Ontario hospitals, within the context of the capacity of individual institutions of variable size and complexity.

The Manual recognizes the need to comply with the standards defined by the Canadian Standards Association (CAN/CSA Z902) and the Canadian Society for Transfusion Medicine (CSTM) and may be used as a guide to determine where there are deficiencies in practice and the measures necessary to remedy these deficiencies. The policies, procedures and processes presented may not address all clinical eventualities and are not intended to replace a physician's clinical judgment nor the need for consultation with an expert in transfusion medicine.

It is recognized that the implementation of the policies, processes and procedures proposed herein may represent a challenge for many institutions which provide Transfusion Medicine services. Thus this document should be regarded initially as a guide to organizing Transfusion Medicine policies and a statement of the policies, processes and procedures to be achieved over time – a kind of "road map" to a destination rather than a statement of the current situation in most hospitals.

1.0 MEDICAL ROLES AND RESPONSIBILITIES

Policy	The Transfusion Medicine Service shall have a Medical Director who is a licensed physician and who will be responsible for the overall conduct of transfusion practice in a hospital or formally recognized group of hospitals.
Qualifications	The Medical Director shall be: • A Physician licensed to practice in Ontario, with established evidence of training and expertise in the practice of Transfusion Medicine • Be required to undertake and document completion of ongoing continuing education in Transfusion Medicine for maintenance of competence
General oversight	The Medical Director shall ensure that the Transfusion Medicine service policies and procedures meet all regulatory and accreditation requirements and are consonant with clinical practice obligations of the hospital(s).
Availability of medical consultation in Transfusion Medicine	The Medical Director or his/her delegate shall be available at all times to provide support and consultation in urgent matters of clinical, technical or administrative importance. Should circumstances dictate that immediate responsibilities are delegated to non-medical personnel, provision shall be made for access to medically qualified transfusion medicine advice.
Personnel	The Medical Director shall: • Supervise the practice of other physicians covering the Transfusion Medicine service in the hospital(s) for which he/she is responsible • Ensure that regular performance review of senior technical staff is completed • Participate in hiring and performance management of senior technical staff
Laboratory Supervision	The Medical Director shall: • Evaluate and determine the appropriate technical examination methods to be used to support the clinical practices of the hospital(s), including reagents, supplies and equipment • Continuously assess and evaluate evolving technologies with potential to provide scientifically improved and/or more cost-effective service • Ensure that policies, processes and procedures are clearly defined in writing, consistently applied and updated in a timely manner when changes are made • Ensure technical and medical staff compliance with defined policies, processes and procedures • Ensure that any external services provide reference laboratory testing on behalf of the blood transfusion service are utilizing validated techniques • Ensure staffing levels to meet the workload requirements to provide for optimal support of patient care • Ensure that laboratory reports are accurate, timely and delivered in clinically helpful terms • Be actively involved in, and sign off on, the regular review of Transfusion Medicine Laboratory Procedure Manual (SOPs) • Ensure that policies and processes for blood sample procurement, patient identification, sample identification and handling and sample processing meet required standards of accuracy and safety • Institute remedial action when examination processes deviate from internal or external quality assurance requirements

Role in clinical transfusion practices and product utilization:	The Medical Director shall: • Approve blood component and product inventory requirements to meet clinical program needs while minimizing component and product wastage • In collaboration with Transfusion Committee members, develop clinical practice guidelines to be referred for approval to the Medical Advisory Committee • Approve policies, processes and procedures for blood component and product ordering and distribution • Ensure that blood products received from other institutions (e.g. as part of a hospital redistribution program) have been stored and shipped according to necessary regulations and requirements • Ensure that protocols and guidelines for prescribing and administering transfusion of blood components and products are up to date and available where these are administered • Ensure that these protocols and guidelines are used to develop training programs for staff administering blood components and products • Provide input into the creation of procedures to ensure the appropriate use of blood components and manufactured products (e.g. IVIG) through prospective and retrospective reviews, consultation and audits • Participate in the activities of hospital transfusion committee(s), including contributing to the composition of appropriate terms of reference • Assist in the establishment of a Hospital Emergency Blood Management Committee (HEMBC) and collaborate with administration on the development of the hospital's contingency plan for the management of blood shortages • Work with clinical, administrative, nursing and other ancillary staff to ensure that transfusion related equipment (e.g. blood salvage and warming devices) and their use meet current regulatory requirements under the Institute for Quality Management in Healthcare (IQMH) and are in compliance with the current versions of the CSA and CSTM. Maintain awareness of regulatory requirements of Health Canada as they relate to the hospital transfusion service • Ensure that all blood product manufacturing processes undertaken by the hospital (including pre-operative autologous donation, intra-operative cell salvage, directed and walking donor programs) are performed according to applicable regulations and requirements • Ensure that all blood products issued for use outside the hospital (e.g. shipment to dispensary facilities, home transfusion programs, or directly to patients for home use) are handled and administered according to applicable regulations and requirements
Consultation and education	The Medical Director shall: • Provide consultation and professional advice to physicians prescribing or administering blood components and products, including, where appropriate, advice on clinical blood component or product usage • Provide continuing education in transfusion medicine standards and practices to physicians, nurses and technologists • Where applicable provide access to education in Transfusion Medicine to medical students and residents • Cooperate with medical, technical and nursing personnel to establish and maintain programs to ensure ongoing quality and competence in transfusion practice • Ensure that medical and non-medical staff members using transfusion related equipment (e.g. blood salvage devices, blood warmers, apheresis devices) are trained and competent to do so, that such training and competence is documented, and that ongoing preventative maintenance protocols for such equipment are in place

Quality Management	The Medical Director shall: • Supervise and participate in the management of quality systems to ensure that examinations performed in the Transfusion Medicine Service provide accurate, reliable and timely results required to support high quality patient care • Ensure implementation of established current Transfusion Medicine Standards as required under IQMH and defined by the CSA and CSTM. • Ensure compliance with all National and Provincial regulatory requirements, including participation in mandated external quality assurance schemes • Review external quality assurance examination results, and initiate and oversee remedial action when these results are unsatisfactory • Ensure mechanisms are in place for the recording of adverse events, of the results of review of quality assurance data (external and internal) and of any consequent remedial actions
External Reporting Relationships	The Medical Director shall ensure: • Compliance with reporting requirements of Health Canada (HC), Public Health Agency of Canada (PHAC), Canadian Blood Services (CBS) and IQMH • Timely participation in lookback and traceback investigations as required by CBS

1.1 Indications for Consultation with Transfusion Medicine medical staff

Policy	The Medical Director, Transfusion Medicine or delegate shall be available at all times for consultation on clinical, technical, administrative or quality issues.
Rationale	The reason for this policy is the requirement for medical input from a physician knowledgeable in transfusion medicine to: • Assess patient needs • Advise in the selection of appropriate blood products in unusual or specialized circumstances • Consult on the management of adverse transfusion reactions • Assist with patient blood management and appropriate blood conservation measures
Responsibility of the Medical Director, Transfusion Medicine	The Medical Director shall be responsible for providing a contact list to Transfusion Medicine Staff and for ensuring the availability of Medical Staff support at all times. The Medical Director shall define the indications for contacting the Medical Director or scheduled delegate, and the procedure to be followed if the Medical Director or delegate is non-responsive (including appropriate documentation).

Table 1.1 Indications for Immediate Consultation

Situation	When
Blood product shortage	• Reasonable possibility that medical or surgical blood products requests will not be met • Amber or red phase blood product shortage declared by Canadian Blood Services • The contingency plan for blood shortages requires it to be implemented • Screening of requests during critical shortages according to policies set by the Hospital Emergency Blood Management Committee, in accordance with the National Plan for the Management of Shortages of Labile Blood Components and the Ontario Contingency Plan for the Management of Blood Shortages
Errors	• Any error with the potential to result in adverse consequences to a recipient such as an incorrect or incompatible blood product has been issued • Clerical or other error has led to release of an incorrect or incompatible unit (even if not actually transfused) • Sampling error detected that may affect one or more patients

Transfusion reactions	• Symptoms suggestive of severe transfusion reaction notified by verbal contact from patient location (MD, RN) or by transfusion reaction report form • Post-transfusion work-up reveals features suggestive of incompatibility such as icteric or hemolysed sample or positive DAT post-transfusion, and further transfusion is medically indicated • Requests received for further blood product transfusion before transfusion reaction investigation is completed • At technologist's discretion
Massive transfusion	• Patient's blood volume is replaced over a short period (>10 units within 24 hours) and there is continuing blood loss • Initiation of Massive Hemorrhage Protocol (MHP) if applicable • Clinically significant antibodies are detected in a sample from a massive transfusion recipient • RhD-negative patient of child-bearing potential is switched from RhD-negative to RhD-positive red blood cells or platelets according to established policy
STAT/urgent/special red blood cell unit requests	• Blood issued "uncrossmatched" is found to be incompatible • Permission is required to issue crossmatched incompatible units, with the exception of patients with autoantibodies where complete investigation has excluded all clinically significant antibodies • Compatible or antigen negative units are not available (e.g. antibody to high incidence antigen; multiple antibodies present; warm reactive auto-antibody) • Request is received for blood for transfusion before an antibody investigation is completed • Release of a large number of O RhD-negative units threatens appropriate inventory levels or cannot be supported by CBS • Clinically significant antibody is found in a neonatal sample and the infant has biochemical evidence of hemolysis • Request for use or dose of blood component or product inappropriate to the institution's Transfusion Medicine guidelines, or where there will be delay in availability for transfusion • Need to transfuse untested or partially tested components or products from CBS
RhD-positive products to RhD-negative patient	• Any RhD-positive product is to be issued for an RhD-negative recipient of child-bearing potential, unless a pre-approved policy or specific instruction is in place • RhD-positive platelets are to be given to an RhD-negative recipient of child-bearing potential and RhIg is required, unless a pre-approved policy or specific instruction is in place

Other blood product requests requiring consultation with the Medical Director, Transfusion Medicine	• Urgent request for use or dose of any blood component or product outside the institution's Transfusion Medicine guidelines • A new request is received for irradiated and/or CMV sero-negative product does not meet established indications • A new request is received for: » Washed or plasma-depleted cellular component » HLA matched platelets » IVIG not meeting MOHLTC guidelines unless a pre-approved policy assigns this responsibility to other physicians at the facility » Coagulation factor products for new single factor patient » Rarely requested products (e.g. recombinant factor VIIa, C1 esterase inhibitor) » Exchange or intra-uterine transfusions • Platelets are requested for a patient with a diagnosis of ITP, TTP/HUS, heparin induced thrombocytopenia or undiagnosed thrombocytopenia • Urgent request for platelets for transfusion and no platelets are immediately available • Infusion of any component or product beyond its expiration time • Allogeneic unit is sought when autologous unit(s) is (are) available • Urgent request (e.g. from OR) for red blood cells for a patient with alloantibodies • Request for red blood cells in presence of high thermal amplitude cold agglutinin • Request for red blood cells for a patient with a sickle cell syndrome (see section 9.8) • Request for prothrombin complex concentrates for other indications than emergency warfarin reversal • Requests for therapeutic apheresis
Issues of product quality	• There is any doubt about component or product quality and clinical circumstances require urgent transfusion • Identification of a component or product of questionable quality leading to quarantine should be reported on the next working day
"Code Orange" (Disaster Plan Notification)	• On receipt of a "code orange" notification, whether external (e.g. major transportation crash) or internal (e.g. extended computer downtime or power failure)
Miscellaneous issues	• Patient with refusal to consent to transfusion: » Blood components or products are subsequently requested for or transfused to a patient who refused transfusion based on religious or other beliefs • Unusual situations not covered above: » Immediate notification at the discretion of medical laboratory technologist

Table 1.2: Transfusion Emergency and TM Medical Director or delegate is not responding

If	Then
Transfusion is urgently required	• Contact patient's physician immediately to confirm patient's clinical needs outweigh potential hazards of transfusion • Prepare and release requested products • Continue to try to contact Transfusion Medicine Director or delegate • Document the episode

The patient is at risk of hemolytic transfusion reaction or other identifiable severe hazard of transfusion	• Information emerges (e.g. technical error) putting a patient at risk of hemolytic transfusion reaction or other identifiable severe hazard of transfusion: » Contact patient location immediately to request transfusion be stopped » Notify the patient's physician as soon as possible » Continue to try to contact Transfusion Medicine Director or delegate

REFERENCES

9. Aubuchon, JP. 1999.
46. Domen, RE. 1997.
61. Goodnough LT, 1999.
68. ORBCoN, Informed Consent Card, 2014.
108. Popovsky, MA. 1996.

2.0 QUALITY SYSTEM MANAGEMENT

Policy	• The Transfusion Medicine Service has established policies, processes and procedures to ensure full compliance with accepted regulatory and accreditation requirements, and good laboratory practices • The Medical Director has overall responsibility for the quality of work performed in the Transfusion Medicine laboratory and for all transfusion activities
Responsibilities of the Medical Director, Transfusion Medicine	• Maintain awareness of the current applicable standards and requirements: CAN/CSA, CSTM and IQMH and oversee compliance with these standards • Ensure implementation of the quality management system • Monitor the effectiveness of the quality management system through, but not necessarily confined to: » Participation in or if necessary chairing the Transfusion Committee » Providing consultation on proposed audits and other internal quality assessments to the Transfusion Committee and overseeing such audits » Establishing internal indicators to assess the quality of practice within the Transfusion Medicine Service » Ensuring errors, incidents and accidents involving the hospital's blood transfusion service are reported to the appropriate error management programs • Participate in reviewing the performance of the Transfusion Medicine Service, collaborate in the development of corrective action when deficiencies are recognized, and promote quality improvement measures
Responsibilities of Transfusion Medicine Service Staff	• Perform technical procedures and quality examinations according to established policies, processes and procedures • Inform and consult with the Medical Director, Transfusion Medicine (or delegate) on any instances of non-compliance, adverse event or failed performance on quality control samples and any other issues of quality system concern • Be familiar with and follow the policies defined in section 1.1 regarding notification of the Medical Director (or delegate) of matters of potential clinical concern
Transfusion Medicine Quality Assessments	• The following have been established to carry out quality oversight: » Transfusion Committee (or other Committee charged with oversight of the Transfusion Service), reporting to the Medical Advisory Committee » Audit and utilization management processes » System to investigate and document adverse events and errors including the Transfusion Transmitted Injury Surveillance System (TTISS)

2.1 COMPONENTS OF ASSESSMENT QUALITY SYSTEM ESSENTIALS

Transfusion Committee	Members include key stakeholders and representatives from the major users in the institution including the Director of Transfusion Medicine. The committee must function under the authority of the Medical Advisory Committee. Guidance in the establishment and conduct of hospital Transfusion Committees can be found in the "Transfusion Committee Handbook" at www.transfusionontario.org. The committee meets regularly to: • Assist in defining blood transfusion policies appropriate to the hospital's clinical programs • Contribute to the development of criteria for the evaluation of ordering practices, usage (including wastage of blood components and products), administration policies and the ability of the Transfusion Medicine Service to meet the clinical needs of the hospital • Ensure that regular evaluations of transfusion practices are undertaken and to review the results of such evaluations • Evaluate reports of adverse transfusion events and all transfusion errors, as well as relevant external (Provincial, Federal or international) reports on adverse transfusion events • Recommend corrective measures as required • Ensure that patients are made aware of any alternatives to allogeneic blood transfusion that are available to them, and that such alternatives are in place wherever feasible with appropriate recommendations on their use • Facilitate the dissemination of information and promote education relevant to transfusion medicine • Review any changes in blood components or products available through CBS (new products or changes to existing products or components)
Audit and Utilization Management	• The audit process is used to monitor and improve blood transfusion practices. Audit or utilization review may be retrospective or prospective • Criteria that trigger audits are based on current practice guidelines. The process is used to provide educational feedback to physicians using blood components or products in a manner inconsistent with guidelines • Audit can be used to monitor and improve component and product wastage and inventory management • Audits are initiated through the local or regional Transfusion Committee and results are analyzed and reported by this group • Audit and utilization management reports are sent to appropriate administrative personnel within the hospital corporation and/or regional laboratory program where appropriate • Where the clinical use of blood component or product may be outside of the hospital's guidelines or deviate from evidence based 'best practices', audit and utilization management data are shared with the appropriate clinical department head • Prospective utilization reviews may be indicated if there is the potential for inappropriate transfusion decisions due to inexperience, particularly with expensive or rarely prescribed items • Transfusion practices and patient care may be improved and costs diminished by assessing transfusion requests against guidelines before products/components are given, and advising clinicians of non-conformance to guidelines

Adverse Events and Error Management	• The Transfusion Medicine Service has policies, procedures and processes to define, detect and document adverse transfusion events and errors, both within the Service and externally throughout the hospital. The process includes the documentation of "near misses" where an error or adverse event did not actually occur because it was detected in time to be corrected • Adverse event and error reporting data are reviewed regularly including root cause analysis • A summary of non-serious events and near misses and a comprehensive report of events resulting in potential or actual serious harm are reviewed by the Transfusion Committee and communicated to hospital management • The results of adverse event and error reporting are to be used to create quality improvements within the Transfusion Medicine Service or elsewhere in the hospital • If available and appropriate, the Transfusion Medicine Service shall participate in any national or provincial error or injury surveillance programs (e.g. TTISS)
Policies regarding management of transfusion in HPC and solid organ transplant recipients	• In collaboration with the regional referral centre for solid organ and tissue transplant, each facility should establish policies and procedures for the management of pre and post transplant patients **Note:** The management of transplant patients varies throughout the province. Consultation with referral centres is advised.

REFERENCES

8. Aubuchon JP, 2004.
13. Berte LM, 2000.
22. Callum JL, 2001.
30. CSTM, 2017.
31. CAN/CSA-Z902-15.
69. IQMH, 2018.
75. Kaplan HS, 2002.
90. Murphy MF, 2011.
100. ORBCoN, Transfusion Committee Handbook, 2016.
121. Saxena S, 2006.

3.0 INFORMED CONSENT AND REFUSAL OF CONSENT

Policy	• Procedures for the administration blood components and products shall include a mechanism for obtaining informed consent • Elements of informed consent include discussion of: » A description of the blood component(s) and /or product(s) which may be transfused » The risks of such transfusion » The expected benefits of such transfusion » Possible alternatives to transfusion and the risks and benefits of such alternatives » The patient must be given the opportunity to ask questions and have concerns addressed » The clinical indication for transfusion shall be recorded in the patient's medical record • In the case of planned elective transfusion, this discussion should take place well in advance of the planned procedure or course of treatment to allow for the application of possible alternatives • Evidence of acceptance or refusal of informed consent for the transfusion of blood components or products shall be recorded in the patient's medical record, whether written or electronic
Reason	• Informed consent is a process undertaken jointly by a patient (or substitute decision maker where required) and a physician to make a therapeutic decision in a manner that preserves the patient's primary decision-making role in determining a course of treatment • Obtaining consent for medical treatment in general is a principle of common law (Ontario Consent to Treatment Act, 1996) • Consent specifically for transfusion of blood components and products, while not expressly required by law in Ontario, is a requirement of the standards published by the CSA, CSTM and IQMH
Patient population	• All patients for whom transfusion is indicated or may be indicated • In circumstances where consent cannot be obtained (e.g.under anaesthesia or trauma)
Responsibilities of Medical Director, Transfusion Medicine	Provide information, promote education for and consult with all health professionals involved in the transfusion process about: • The risks and benefits of transfusion of blood components and products • The appropriate use of blood components and products • Alternatives to transfusion
Responsibilities of Treating physician	• Obtain consent for or refusal of transfusion and document in the patient's medical record • Complete the facility specific form for consent or refusal if applicable
Responsibilities of Treating nurse	• Confirm that consent has been recorded in the patient's medical record before requesting product from the Transfusion Medicine Service • Inform or send a record of refusal (if applicable) of transfusion to the Transfusion Medicine Service for entry in its record system
Responsibilities of Transfusion Medicine Staff	• Record refusal of consent to transfusion in Transfusion Medicine Service patient information file on receipt of notification of refusal • Check patient history in Transfusion Medicine Service information file on receipt of request for component or product • Notify Medical Director, Transfusion Medicine when blood component or product is requested for a patient for whom a record of refusal of consent is on record

Refusal of consent	• The discussion and refusal of consent shall be recorded in the patient's medical record • The Transfusion Medicine Service should have a notation of the refusal of consent in its patient information file, as a secondary check to prevent release of blood component or product that is ordered erroneously

REFERENCES

1. AABB, 2006.
17. Bodnaruk ZM, 2004.
25. Callum JL, 2016.
29. CSTM, Informed Consent-Position paper.
43. Davis RE, 2011.
52. Farrell AM, 2010.
63. Krever, H, 1997.
64. BC PBCO, 1999.
69. IQMH, 2018.
80. Lima A, 2015.

4.0 DAILY OPERATIONS

Policy	The Transfusion Medicine Service has established policies, processes and procedures for the: • Control of collection and examination of samples that ensure accurate and reliable examination results • Maintenance of inventory that is appropriate to the clinical service needs and the needs of satellite sites where inventory sharing and redistribution is in place • Issue of components and products that are safe and appropriate to support patient care
Reason	• The Transfusion Medicine Service provides services and blood components and products that are critical to patient care but carry inherent risk to recipients. The risk is reduced through the establishment and implementation of, and adherence to, controlled processes
Responsibilities of the Medical Director, Transfusion Medicine	• Overall responsibility for the daily laboratory operations of the Transfusion Medicine Service, including selection of instrumentation, and establishment of policies, processes and procedures for the collection and examination of samples • The Medical Director, Transfusion Medicine shall be aware of and ensure implementation of published standards for sample collection and examination • Detailed requirements are listed in the subsections that follow
Responsibilities of Transfusion Medicine Staff	• Follow technical procedures as written Transfusion Medicine Operating Procedures • Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated in procedures or by circumstances • Train as required to maintain competency

REFERENCES

31. CAN/CSA-Z902-15.

4.1 PATIENT IDENTIFICATION AND SAMPLE LABELING CRITERIA

Policy	• The Transfusion Medicine Service Shall develop and implement policies, processes and procedures for patient identification, and sample collection and identification, using first and family name plus at least one other unique identifier (e.g. hospital medical record number) • An alternative process must be developed to provide for interim identification of patients when name and other unique identifiers are unavailable
Reason	• Most serious and potentially fatal transfusion reactions are due to the administration of the wrong unit of blood to the wrong patient, so the transfusion service must take steps to ensure correct identification of patient samples, sub-samples and intended recipients • The Transfusion Medicine Service has a major role in educating nurses and other health care professionals collecting or administering blood, in correct recipient identification and should be involved in the development of appropriate patient identification systems

Patient identification at sample collection	Sample collection policies, processes and procedures for patients must include but are not limited to the following: • Samples should not be collected from patients lacking patient identification at least meeting the criteria above (see section 4.1 under policy) • Phlebotomists should only collect blood from in-patients displaying defined identification, e.g. hospital armband or other institutionally approved device • A specific policy should be developed to ensure accurate identification of out-patients and patients in the pre-admission process who are not displaying such defined identification • Instructions must include: » Measures required when the patient is not able to use an armband or other means of identification as normally defined » Measures to identify patients requiring urgent transfusion in the absence of identifying information, and to reconcile temporary identification with name and unique identifier information
Patient identification at transfusion	• Procedures defining the measures to be taken to identify patients to whom transfusion is to be administered shall be developed, which match the patient's unique or interim identifiers to the information provided on the label on the blood component or product • Transfusions shall not be administered to patients who lack some positive (including interim) identification • Procedures defining the measures required to cover emergency transfusions for unidentified patients and patients "not yet identified" shall be developed
Patient identification and sample labeling criteria	• Sample labeling policies and procedures must include, but are not limited to the following: • The phlebotomist must label the blood sample tubes with the first and family name of the patient, plus the unique identifier(s), and the collection date **BEFORE** leaving the patient • The phlebotomist must be identifiable on the sample label or the associated requisition and this information must be retrievable for one year (CSA Z902-15 20.6.3.5) • Policies, procedures and processes must include the steps to be followed by laboratory staff when the information on the blood sample tube(s) does not match that on the request form (i.e. sample rejection criteria)

REFERENCES

66. Hamrock DJ, 2006.
80. Lima A, 2015.
106. Pierce LR, Jain N. 2003.

4.2 PRE-TRANSFUSION EXAMINATIONS

The following examinations must be performed before transfusion:	
Serologic examinations	ABO and RhD type • To provide ABO- group-compatible red blood cells, there shall be at least two determinations of the recipient's blood group on record: one from a current sample and the second from the recipient's previous records; testing of a separate sample collection; or retesting of the same sample where positive patient identification technology was used at the time of sample collection. **Note:** *Positive patient identification technology refers to a computerized system that uses a barcode, radio- frequency identification (RFID), or another electronically readable element on a patient's identification band to confirm identity.* • The indirect antiglobulin test (IAT) for weak expression of the RhD antigen is recommended in the following circumstances: » All patients where anti-D reagent(s) give <2+ reactions on immediate spin phase of tube testing and weak anti-D testing has not previously been performed. (Note: if D typing is automated, standardized cut off grading and interpretation for weak D testing should be established according to validation of Rh typing prior to implementation of automated platform) » Where RhD typing discrepancies are found between current and previous results, where previous results were RhD negative and one or both current anti-D test results are <2+ on immediate spin phase of testing » For RhD negative newborn infants to determine the need for RhIG for an RhD negative mother » For RhD negative fathers upon request to determine the need for RhIG in a RhD negative mother • Tests for weak RhD antigen are NOT recommended in the following circumstances: » Patients whose sample reactions are negative with both anti-D reagents » Weak anti-D testing has already been performed » If the DAT is positive on the test sample » If the patient has received transfusion within the previous 3 months with red blood cells of a different Rh type » Routine examination for other Rh antigens is not recommended » Policies should be established for Rh phenotyping and the provision of Rh phenotypically matched red blood cells when the diagnosis indicates chronic transfusion is likely e.g. myelodysplastic syndrome, sickle cell disease » If an RhD typing problem is detected and urgent transfusion is required, RhD negative components should be used if available, pending resolution Note: A policy for the administration of Rh Immune Globulin should be established for obstetrical patients who type as weak D. Rh genotyping is available through the National Reference Laboratory at CBS and could be considered for confirmation of weak D typing to determine the need for Rh prophylaxis in pregnant women.

	In addition to the determination of the ABO and RhD type: • The patient's historical record should be reviewed • Antibody screen of patient's serum/plasma for unexpected red blood cell antibodies should be completed before red blood cells are transfused in non-emergency settings » Examination method for antibody screening must be sensitive enough to detect clinically significant antibody above a commonly accepted threshold level. » Acceptable methods include solid phase, gel or indirect antiglobulin test » Negative controls or check cells must be included to validate negative saline indirect antiglobulin tube test results • There should be a guideline for the standardized interpretation and grading of hemagglutination reactions (see references)
Routine crossmatch examinations	• Blood samples for crossmatch examination should be collected and examined no more than 96 hours before the intended transfusion » This interval may be extended in patients with a history of no transfusion or pregnancy within 3 months » Procedures should be in place to ensure that "group and screen" results are completed and available before elective surgery commences where the chance of blood transfusion support being required is >5% • The hospital shall have a policy defining how long in advance of an intended surgical procedure pre-admission samples may be collected, and examined provided **ALL** of the following conditions are met: » Antibody screen is negative and » Patient has not been transfused within the last 3 months, and » Patient has not been pregnant within the last 3 months • The Transfusion Medicine Service must have in place a process to determine whether the patient is pregnant or has been transfused since the date of collection of the pre-admission sample » If the patient has been transfused or pregnant in the interval, or the history is unknown, a group and screen must be performed on a sample collected within 96 hours of the intended transfusion
Electronic Crossmatch	• Requires second determination of the patient's ABO blood group, see Serologic examinations for details. • Electronic crossmatch is adequate to issue red blood cell containing component when there is: » No clinically significant antibody detected in current antibody screening and » No previous record of a clinically significant antibody » Confirmation of the ABO group of all red blood cell containing units involved » An appropriately validated computer system licensed for the provision of electronic crossmatching
Immediate spin crossmatch	• Immediate spin crossmatch is adequate to issue red blood cell containing component when there is: » No clinically significant antibody detected on antibody screening, and » No previous record of a clinically significant antibody » Relevant isohemaglutinins (anti-A, anti-B) demonstrate a 1+ or greater reaction • Requires second ABO determination, see Serologic examination for details.
Crossmatch examinations in emergency situations	• Emergency release policies, process and procedures apply when there is insufficient time before transfusion of a red blood cell containing component to: » Complete an antibody investigation » Source appropriate blood products » Perform a crossmatch

Crossmatch examinations with positive antibody screen	• If the antibody screen is positive, the antibody(ies) must be identified, with repeat investigations on subsequent samples from the same patient performed according to institutional policy • If the antibody(ies) is/are clinically significant: » Antigen negative units must be selected, if available » A full serological crossmatch must be completed and blood reserved for the patient
Antibody investigation and reporting	• All patient samples with positive antibody screen shall be investigated prior to transfusion unless clinical urgency requires immediate release of blood. » Issue indirect IgG antiglobulin test compatible units if possible » The Medical Director, Transfusion Medicine (or delegate) and ordering physician should be contacted prior to issue » Routine release of group O RhD negative units by emergency release is not an acceptable alternative • The interval between antibody detection examinations for patients with previously identified red blood cell antibodies who have been transfused or pregnant within the last 3 months should be 96 hours, to identify any new allo-antibodies. A policy establishing the interval between antibody investigation when antibody detection testing demonstrates no new detectable antibodies should be established • If antibody investigation services are not provided by the hospital Transfusion Medicine Service, samples may be referred to another Transfusion Medicine Service in an associated hospital or to an external reference laboratory such as CBS Laboratory Services • Results of the antibody investigation(s) must be forwarded to the patient's physician and the hospital Medical Records Service, and be recorded in the Transfusion Medicine Service files

REFERENCES

2. AABB, 2017.
31. CAN/CSA-Z902-15.
113. ORBCoN, OTTRM.
116. Reid ME, 2000.

Table 4.1 Clinical Significance of Antibodies and Provision of Red Blood Cells

Antibody Category	Antibodies to antigens as described	Is phenotyped antigen negative blood required	Full serological indirect antiglobulin XM required?
Common clinically significant antibodies	D,C,E,c,e,K,k,S,s,Jk^a,Jk^b,Fy^a, Fy^b,	Yes	Yes
Uncommon clinically significant antibodies	Kp^a,Wr^a,Js^a,Di^a,Co^a,C^w, M (if reactive at 37C) _____ Antibody to above + panreactive warm antibody	No. Serological crossmatch compatible only. _____ Yes, if antisera available	Yes _____ Yes
Common clinically in-significant antibodies	M (unreactive at 37oC). N,P_1,Le^a.Le^b,Lu^a,A_1, Bg	No. Crossmatch compatible only.	No if screen is negative _____ Yes if screen is positive
Passive anti-RhD (Recent RhIG documented)	Passive anti-D	Yes, as RhD negative	No
Warm auto- antibodies		Yes (requires Transfusion Medicine Consult)	Yes
Unidentified or inconclusive antibodies	Antibodies to common clinically significant blood groups are excluded	No. Crossmatch compatible only.	Yes

4.3 INVENTORY MANAGEMENT

Policy	The Transfusion Medicine Service has established an inventory management program appropriate to support the clinical programs delivered in the hospital. Inventory management is crucial to avoid unnecessary wastage due to overstocking and to support effective utilization of blood, blood components and products.
Reason	The objective is to provide adequate supplies of blood, blood components and products for routine and emergency situations while minimizing loss by outdating.
Responsibilities of the Medical Director, Transfusion Medicine	• To determine minimum and optimum hospital inventory levels and to review the inventory levels periodically, or in light of clinical program changes which may influence requirements • To implement measures that assist in improving inventory management • To provide the communication link between treating physicians and the Transfusion Medicine Service in critical shortage situations and to discuss alternatives or cancellation of elective procedures • Ensure that a hospital plan in place for the management of blood shortages is established in accordance with the Ontario Contingency Plan for the Management of Blood Shortages • Implement when necessary the measures laid out in the Ontario Contingency Plan for the Management of blood shortages
Responsibilities of Transfusion Medicine Service staff	• Maintain the inventory according to the guidelines and implement policies and procedures as required • Ensure that defined proper procedures are used in packing, shipping or receiving blood, blood components and products • Report inventory to CBS regularly

Components of an inventory/ conservation management system	An inventory management/conservation system should have: • Ability to select the oldest blood for transfusion, provided it is of an appropriate ABO and Rh group, and meets any necessary special requirements (e.g. irradiated) • Flexibility to use fresher blood when indicated (e.g. dedicated aliquots for neonates) • Where feasible, a blood redistribution program, especially for any components or products near expiry, as sender or receiver, at the discretion of the Medical Director, Transfusion Medicine • A policy regarding the issue of non-group specific platelets that are about to outdate • A mechanism to minimize inventory sequestered for specific patients (use of abbreviated crossmatch procedures; immediate spin, electronic) • A maximum surgical blood order (MSBOS) schedule based on local practices and patient population to provide screening guidelines to monitor requests, updated at scheduled intervals • A mechanism to review wastage data by patient location to identify process improvement strategies to minimize component and product loss • Monitoring crossmatch/transfusion ratios • Transfusion Committee review and audit of effectiveness and safety of inventory management and conservation measures
Critical shortages	The Transfusion Medicine Service shall have established policies processes and procedures to respond to shortages: • An approved, institution-specific contingency plan for the management of blood shortages that ensures conformity with the National and Provincial Contingency Plans for Blood Shortages • Procedures should detail circumstances under which the Medical Director, Transfusion Medicine will: » Convene the Hospital Emergency Blood Management Committee (HEMBC) » Activate the communication plan to clinical staff and patients regarding the cancellation of elective surgical procedures and transfusions » In conjunction with treating physicians, implement blood conservation strategies • Define steps to be taken when to: » Switch from ABO identical to ABO compatible units » Switch from RhD negative to RhD positive units » Initiate inter-hospital redistribution » Decrease platelet dose from 1 single donor (apheresis) unit or 1 pool of 4 buffy-coat derived platelets to “half-unit” platelet transfusions » Triage all blood component/product requests to ensure compliance with the Provincial Blood Shortage Contingency Plan

REFERENCES

2. AABB, 2017.
99. Ministry of Health and Long Term Care, Ontario Regional Blood Coordinating Network V3, 2016.
128. Stanger SHW, 2012.

5.0 APPROPRIATE USE OF BLOOD COMPONENTS FOR ADULTS

Policy	The Transfusion Medicine Service follows established guidelines for the appropriate use and administration of blood components and products to patients.
Reason	• Facilitate the efficacious and appropriate use of blood components and products • Facilitate compliance with hospital guidelines for product dosage • Enhance patient safety by the judicious use of blood components and products and reduction of inappropriate transfusion practices
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with available guidelines for the use of and indications for use of blood components and products • Be familiar with the appropriate use of and indications for use of blood component and products • Be available to consult with treating physicians and other staff in the appropriate use and administration of blood components and products • Initiate discussions with clinical staff when laboratory results and/or clinical circumstances suggest use of a blood component or product may, or may not, be indicated • Use such consultations and discussions to promote education in appropriate transfusion practices • Ensure availability of adequate educational material for physicians or other health professionals who prescribe blood components and products • Establish a mechanism to prospectively review orders for blood and blood components/products for appropriateness of indication and dosing Note: If prospective screening is not performed, a mechanism for periodic retrospective audit should be established.
Responsibilities of Transfusion Medicine Service staff	• Follow established process for prospective screening of orders for blood and blood components/products • Consult with the Medical Director, Transfusion Medicine or delegate when concern is raised that a blood component/product order (including indication, dose or timing) may not be compliant with the institution's guidelines (and cannot be directly resolved with clinical staff)

REFERENCES

25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.

5.1 TRANSFUSION OF RED BLOOD CELLS TO ADULTS

- Guidelines for transfusion of red blood cells have been published by several organizations [see www.transfusionontario.org/en].
- The decision to transfuse an individual patient is based on:
  - » Signs and symptoms of inadequate tissue oxygen delivery
  - » Ongoing blood loss
  - » Hemoglobin concentration
  - » Other patient factors e.g. coronary insufficiency, traumatic brain injury and patient preferences
- For an example of hospital specific guideline threshold and target hemoglobin levels for red blood cell transfusion – see table 5.1
- More detail is supplied in Table 5.2

Table 5.1 – An Example of Transfusion Guidelines for Red Blood Cells

HEMOGLOBIN g/L	Units	RECOMMENDATION
less than **60**	1 - 2	Transfusion highly recommended • Young patients may tolerate greater degrees of anemia • Patients with chronic iron deficiency can usually be treated with IV iron alone
less than **70**	1	Likely appropriate
less than **80**	1	Likely appropriate in patients with cardiovascular disease
less than **90**	1	Only if there are signs and symptoms of impaired tissue oxygen delivery
greater than **90**	none	Likely inappropriate Consult Blood Bank physician and document indication in patient chart

Table 5.2 Transfusion of Red Blood Cells to Adults

For adult patients	
Receiving transfusion for acute blood loss	• Maintain hemoglobin > 70g/L during active bleeding: » Consider rate of blood loss, hemodynamic factors, evidence of tissue ischemia, institutional speed of blood delivery and laboratory testing in decision about transfusion » Ensure prompt blood availability when hemoglobin is <80g/L • Consider maintaining hemoglobin at a higher level (>80 g/L) in patients with: » Unstable or acute coronary syndromes » Coronary artery disease » Uncontrolled/unpredictable bleeding
With anemia in coronary or critical care	• Recommend transfusion when patient's hemoglobin is <70g/L • In a patient with an acute coronary syndrome there is controversy over the desirable hemoglobin level: » Data are insufficient to recommend maintaining hemoglobin above an arbitrary level but a target of 80-90g/L is considered acceptable » Consider transfusing if there are clear signs of inadequate tissue oxygen delivery • Except for patients with unstable coronary syndromes, restrictive transfusion policy (trigger 70g/L) has proved at least as effective as a liberal transfusion policy for the critically ill • Unnecessary phlebotomy contributes significantly to anemia in the critically ill and strategies should be implemented to minimize blood draws
Peri-operative patients	• Manage patients undergoing elective surgery with approaches to minimize need for transfusion: » Hematological assessment and if needed appropriate non-transfusion therapy pre-operatively » Meticulous hemostasis intra-operatively » Consider alternatives such as erythropoietin, cell salvage, antifibrinolytic agents • Administer red blood cell transfusion one unit at a time in the non-urgent setting, assessing the need for further transfusion after each unit with repeat hemoglobin level and clinical assessment
With Chronic anemia	• Use transfusion **ONLY** when alternatives do not exist or have proven ineffective • Administer red blood cells at intervals to maintain the hemoglobin just above the lowest level necessary to prevent symptoms of anemia • Assess long-term transfusion recipients for iron overload and consideration of iron chelation treatment where organ toxicity from transfusion iron overload is anticipated
With hemoglobinopathies (eg. sickle cell disease, thalassemia) or autoimmune hemolytic anemia	• As goals and principles of transfusion in these patient populations differ significantly from other patients, a hematology consultation is advised prior to proceeding with transfusion
Selection order of ABO compatible donor red blood cells	• See table 5.3

Table 5.3 Selection Orders of ABO Compatible Donor Red Blood Cells

Recipient ABO group	1st Choice ABO identical	2nd Choice ABO compatible	3rd Choice ABO compatible	4th Choice ABO compatible
O	Group O	None	None	None
A	Group A	Group O	None	None
B	Group B	Group O	None	None
AB	Group AB	Group A	Group B	Group O

REFERENCES

25. Callum JL, 2016.
26. CBS, Circular of Information.
27. CBS, Clinical Guide to Transfusion, 2011.
32. Carson JL, 2016.
51. CMAJ, 1997.
65. BSH, 2017.

5.2 TRANSFUSION OF PLATELETS TO ADULTS

Guidelines for transfusion of platelets have been published by several organizations [see www.transfusionontario.org] includes commonly acceptable indications for platelet transfusion.

Table 5.4 Guidelines for Platelet Transfusion in Adults

PLT (x 10^9/L)	Clinical Setting	Suggest
<10	Non-immune thrombocytopenia	Transfuse 1 pool of platelets[45]
<10	Non-immune thrombocytopenia & HLA-alloimmunized	Transfuse 1 unit of HLA-matched apheresis platelets[45]
<20	Procedures not associated with significant blood loss (e.g., central line placement)	Transfuse 1 pool of platelets[15]
20-50	Procedures not associated with significant blood loss	1 pool of platelets on hold, transfuse only if significant bleeding[38]
<30	Patient on anticoagulants that should not be stopped	Transfuse 1 pool of platelets
<50	Epidural anesthesia and lumbar puncture	Transfuse 1 pool immediately before procedure[15,47]
<50	Procedures associated with blood loss or major surgery (>500 mL expected blood loss)	Transfuse 1 pool immediately before procedure[38,48]
<50	Immune thrombocytopenia	Transfuse platelets only with life-threatening bleeding[49]
<100	Pre-neurosurgery or head trauma	Transfuse 1 pool of platelets[50,51]
Any	Platelet dysfunction and marked bleeding (e.g., post cardiopulmonary bypass). **Exception: Transfusing platelets for intracranial hemorrhage not requiring surgical management in patients on antiplatelet agents leads to increased morbidity**	Transfuse 1 pool of platelets[38,52]

ABO/Rh-identical platelets are preferred, but ABO/Rh non-identical platelets may be transfused when ABO/Rh-identical platelets are not available. Rh negative females of child-bearing potential require Rh immunoglobulin (RhIG) when Rh positive platelets are transfused, to avoid formation of anti-D antibody. Each platelet pool contains up to 0.5 mL of RBCs. Each 120 ug of RhIG covers 6 mL RBC, with an effect lasting approximately 21 days.

Table 5.5 Relative Contraindications to Adult Platelet Transfusion

Condition	Platelet Transfusion
Heparin induced thrombocytopenia (HIT)	Is associated with arterial thrombosis
Thrombotic thrombocytopenic purpura/ hemolytic uremic syndrome (TTP/HUS)	Is associated with exacerbation
Immune thrombocytopenic purpura (ITP)	Will be ineffective; reserve for life-threatening bleeding

REFERENCES

20. British Committee for Standards in Haematology, 2017.
25. Callum JL, 2016.
26. CBS, Circular of Information.
27. CBS, Clinical Guide to Transfusion, 2011.
56. George JN, 1996.
137. Watson H, 2012.

5.3 TRANSFUSION OF FROZEN PLASMA TO ADULTS

The Ontario Clinical Practice Recommendations for the use of Frozen Plasma (FP)

SITUATIONS IN WHICH THE TRANSFUSION OF FP IS REASONABLE:

CLINICAL SETTING	INR	RECOMMENDATION
• Significant bleeding • Liver disease coagulopathy **AND** pre invasive procedure	greater than 1.8	3-5 units plasma Note: plasma is not required prior to procedures not associated with blood loss irrespective of INR e.g. paracentesis, thoracentesis, central line placement
• Microvascular bleeding • Extreme life threatening hemorrhage	Unable to wait for results	2 units plasma for every 4 units of RBCs Note: If massive transfusion required follow hospital Massive Hemorrhage Protocol
Plasma Exchange	any	Thrombotic thrombocytopenic purpura (TTP)

Note:
FP should ONLY be considered for warfarin reversal or vitamin K deficiency in the event PCCs are not available, and in the presence of serious bleeding or emergency surgery with INR > 1.5. See section 5.6.

SITUATIONS IN WHICH TRANSFUSION OF FP IS NOT USEFUL:

- INR less than 1.8 (including major or non-life-threatening bleeding)*
- Use of 1:1 or 2:1 (RBC:FP) replacement when patient is unlikely to require massive transfusion
- Coagulopathy in the absence of bleeding or need for major emergency surgery
- Minor procedures with any elevation in the INR*
- Elective reversal of warfarin where time allows for warfarin cessation and/or use of vitamin K
- Reversal of anticoagulants (eg: heparin/LMWH, rivaroxaban, dagbiatran,apixaban)**
- Volume expansion or “nutrition support”

* Note: Patients with an increased INR do not have an increased risk of bleeding with minor procedures and there is no evidence that transfusing plasma will prevent or reduce bleeding (Paracentesis, thoracentesis, central line insertion, PICC, bone marrow aspiration/biopsy)
** Note: FP has no effect in reversing or neutralizing heparins or thrombin inhibitors: FP should ONLY be used for warfarin reversal if PCC’s are not available
Note: Clinical Practice Recommendations for the use of FP and an order set template can be found at www.transfusionontario.org

5.4 TRANSFUSION OF CRYOSUPERNATANT PLASMA TO ADULTS

Uses include:

- In conjunction with plasma exchange in thrombotic thrombocytopenia or hemolytic-uremic syndrome

REFERENCES

19. British Committee for Standards in Haematology, Blood Transfusion Task Force, 2004
23. Callum JL, 2011.
25. Callum JL, 2016.
26. CBS, Circular of Information.
27. CBS, Clinical Guide to Transfusion, 2011.
81. Lin Y, 2004.
87. Michael M, 2009.
107. Pinkerton PH, 2010.
111. ORBCoN, 2013
117. Rock G, 2005.
132. Tinmouth A, 2012.
139. Yang L, 2012.

5.5 TRANSFUSION OF CRYOPRECIPITATE TO ADULTS

CLINICAL SETTING	FIBRINOGEN g/L	RECOMMENDATION
Microvascular bleeding	less than 1	4 grams of fibrinogen concentrate or 10 U of cryoprecipitate
Extreme life-threatening hemorrhage	less than 1.5 - 2	4 grams of fibrinogen concentrate or 10 U of cryoprecipitate
Acute promyelocytic leukemia • during acute presentation	less than 1.5	4 grams of fibrinogen concentrate or 10 U of cryoprecipitate
Intracranial hemorrhage secondary to treatment with Tissue Plasminogen Activator (TPA)	less than 2.0	4 grams of fibrinogen concentrate or 10 U of cryoprecipitate

- Treatment of bleeding in patients with von Willebrand disease or Hemophilia A only:
  - » when factor concentrates are unavailable (e.g. remote geographic region); and
  - » DDAVP is unavailable or ineffective
- Factor XIII deficiency when factor concentrates are not available

REFERENCES

19. BCSH, 2004.
24. Callum JL, 2009.
25. Callum JL, 2016.
26. CBS, Circular of Information.
27. CBS, Clinical Guide to Transfusion, 2011.

Note: A comprehensive list of references to guidelines for transfusion medicine practice can be found at the ORBCoN website at www.transfusionontario.org

5.6 USE OF PROTHROMBIN COMPLEX CONCENTRATES (PCCs)

PCCs have replaced frozen plasma as the product of choice for emergency reversal of warfarin effect or vitamin K deficiency. Products available are Octaplex® and Beriplex®.

Indications for use of PCCs

- Emergency reversal of warfarin effect.
  - » For patients with INR ≥1.5 AND
  - » "Life or limb" threatening bleeding
  - » Emergency surgery within 6 hours

  Give:
  - » Vitamin K 10mg IV
  - » PCC according to INR (see below)
- PCCs should NOT be administered if:
  - » INR ≤1.5 as individual coagulation factors are not below the level needed to maintain hemostasis
  - » Patients with coagulopathies not related to warfarin or Vitamin K deficiency as they are deficient in coagulation factors not contained in PCCs (with the exception of the off-label uses described)
  - » Patients with known HIT (Beriplex® and Octaplex® both contain heparin)
  - » Patient has received or will receive recombinant Factor VIIa
- Its use should be limited to life-threatening hemorrhage and patients requiring emergency surgery.

Dosage

- The National Advisory Committee on Blood and Blood Products (NAC) Recommendations on dosing are based on the INR as detailed in the table to the right.
- If the INR is unknown and major bleeding is present, 2,000 IU (80mL) should be administered.
- The published NAC Recommendations include a table of detailed dosages based on a combination of INR and body weight, as an alternative dosing strategy.
- The maximum dose should not exceed 3,000 IU.
- Infusion rate should not exceed 3 mL/min for Octaplex® and 8 mL/min for Beriplex®.

INR	PCC DOSE
<3	1,000 IU
3-5	2,000 IU
>5	3,000 IU

Off-Label Uses of PCCs

- Reversal of anti-Xa inhibitors (Rivaroxaban and Apixiban).
- Currently specific reversal agents are in clinical trials and are not available outside of clinical trials
- PCCs at a dose of 2,000 IU (repeated in 1 hour if hemostasis is not achieved) is being used across Canada
- Data to support its use is limited to studies in animals and human volunteers
- A licensed antidote to dabigatran (Idarucizumab, Praxbind®) is available in Canada
- The dose of Idarucizumab is 5 g, administered in two 2.5 g bolus infusions each over 5 minutes, not more than 15 minutes apart

RESOURCES

1. Bloody Easy Coagulation Simplified, Second Version 2019.

REFERENCES

25. Callum JL, 2016.
28. CBS, Plasma Protein Products, 2011.
84. Majeed A, 2017.
94. NAC, Recommendations for use of Prothrombin Complex Concentrates, 2014.

6.0 SPECIAL PRODUCT SELECTION

6.1 PLATELET SELECTION

Policy	• The Transfusion Medicine Service will provide group-specific platelets whenever possible within the constraints of availability and urgency • Policies should be established for providing non-group specific platelets when group-specific component is not available. Such policies shall be incorporated into appropriate processes and technical procedures Note: Major or minor incompatible platelet component should not be issued to prevent outdate or wastage when group specific platelets are available, unless strategies are in place for prevention of hemolytic reactions
Reason	• Mitigate the risk of hemolytic reactions to high titre anti-A or anti-B alloantibodies when group O platelets are given to a non-group O recipient, and to prevent immunization of group RhD negative recipients by transfusion of RhD positive component, particularly those of child-bearing potential • The true incidence is difficult to quantitate due to under-recognition, but is in the order of magnitude of 1:100 to 1:9,000. Depending on the method used and the definition of high titre, approximately 10-40% of group O platelets contain high titres of isoagglutinins
Applies to:	• All patients receiving platelets for whom group specific platelets are not available within an acceptable time frame
Responsibilities of the Medical Director, Transfusion Medicine	• Establish policy, processes and procedures for: » Provision of non-group specific platelets when group specific platelets are not available informing the ordering MD and patient about signs and symptoms of hemolytic transfusion reactions » Consideration of the titration of anti-A and anti-B in situations when group O platelets are to be given to non-group O recipients » Reduction of risk of acute hemolytic transfusion reaction by plasma volume reduction or avoidance of high anti-A or anti-B titre component • Consult as required with clinical staff on individual cases
Responsibilities of Transfusion Medicine Service Staff	• Follow prescribed technical procedures • Consult with Medical Director, Transfusion Medicine (or delegate) as indicated in procedures, or by clinical circumstances

6.2 CLINICAL PRACTICE RECOMMENDATIONS FOR THE USE OF NON-ABO SPECIFIC PLATELETS

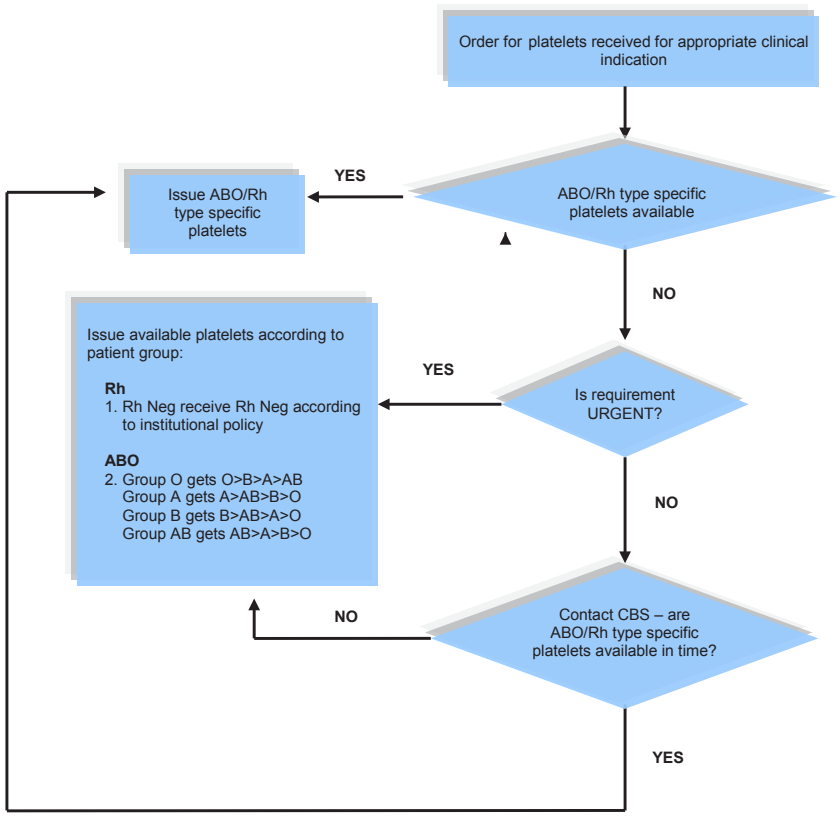
Purpose	These recommendations were developed by ORBCoN in collaboration with an expert working group to assist clinical decision making for the use of non-ABO or non-RhD type specific platelets when ABO/RhD type specific platelets are not readily available.
Guideline	Prior to use of these recommendations the following should be considered • There is evidence to suggest that ABO type specific platelets will result in higher platelet increment • There is no definitive evidence to suggest that adverse events or mortality are different with ABO type specific platelets or ABO non type specific, plasma compatible platelets • If ABO plasma compatible platelets are not available, group O platelets may be transfused to a non-O recipient so long as the ordering physician is informed to enable appropriate monitoring of the patient for signs of hemolysis • A trial of ABO type specific platelets should be given to patients who are refractory prior to screening for HLA antibodies • All institutions should have a policy to address the use of Rh positive platelets for Rh negative recipients including whether Rh Immune globulin (RhIG) will be administered
Recommendation	• ABO and Rh type specific platelets should be used when available • ABO plasma compatible platelets are a reasonable substitute when ABO type specific platelets are not available • Patients who require long term platelet support should ideally receive ABO type specific platelets • RhD positive platelets may be given to RhD negative recipients when RhD negative platelets are not available. RhD negative females of child bearing potential require Rh immunoglobulin (RhIG) when RhD positive platelets are transfused
Other Considerations	• There have been cases of hemolysis following transfusion of ABO plasma incompatible platelets containing high titre isohemagglutinins • Buffy coat platelets and apheresis single donor platelets contain approximately 250-300mL of plasma from one donor whose isohemagglutinin titre is unknown • Titration of ABO isohemagglutinins is of questionable value due to poor predictability between in vitro titres and red blood cell survival. The test is difficult to standardize and there is no reference to support the use of platelets beyond a certain level of titration • ABO plasma incompatible platelets can be volume reduced by centrifugation and removal of supernatant plasma

REFERENCES

47. Dunbar NM, 2012.
72. Josephson CD, 2004.
77. Larsson LG, 2000.
125. Shehata N, 2009.

Algorithm for the Use of Non-Group ABO/RhD Type Specific Platelets

Algorithm for the use of Non-ABO/Rh Type Specific Platelets



Each institution should have a policy to address use of RhIg when Rh Neg patients receive Rh Pos platelets, particularly when the patient is a female of child bearing potential

6.3 SPECIAL CIRCUMSTANCES

RhD positive platelets for RhD negative recipient	• When possible only RhD negative platelets should be given to RhD negative patients • RhD negative females with child-bearing potential should preferentially receive RhD negative platelets • If RhD positive platelets must be transfused to females of childbearing potential, post- transfusion treatment with RhIG is recommended (note that each platelet pool contains up to 0.5 mL of red cells and that each 120 ug of RhIG covers 6 mL red cells and lasts approximately 21 days)
ABO and HLA matched component required	• HLA/HPA match usually takes precedence over ABO match • If a group O, HLA/HPA matched component for a non-group O recipient is known to have a high titre anti-A or anti-B and plasma volume reduction is not possible, consultation with the Medical Director, Transfusion Medicine (or delegate) is required before release for transfusion • CBS should be informed so that an alternate ABO group HLA/HPA match donor can be sought

REFERENCES

20. British Committee for Standards in Haematology, 2017
25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
83. Lozano M, 2003.
125. Shehata N, 2009.

6.4 PLATELET REFRACTORINESS AND INDICATIONS FOR HLA MATCHED PLATELETS

Policy	• The Transfusion Medicine Service provides HLA matched platelets for appropriate patient populations whenever possible • The procedures for evaluation of requests for HLA matched platelets involves availability of information to identify patients who require these components, in case that information is not known to the ordering physician • The requirement for HLA matched platelets is placed on the Transfusion Medicine Service patient record, and these records are always to be checked as part of the evaluation of product request procedures
Reason	• Provision of specialized platelet component for thrombocytopenic alloimmunized patients, refractory to platelet transfusion
Responsibilities of the Medical Director, Transfusion Medicine	• Ensure a process is in place to identify patients who are refractory to platelet transfusion • Ensure there is a process in place to manage requests for HLA matched platelets • Establish hospital policy for screening of requests and appropriate communication with CBS • Be aware of HLA matched recipients and requests for HLA matched platelets • Ensure policies, processes and procedures are in place to confirm effectiveness of HLA-matched platelets and to discontinue their use if ineffective • Consult with and promote education of treating physicians in the management of platelet refractoriness
Responsibilities of Transfusion Medicine Service Staff	• Follow established written technical procedures • Consult with Medical Director, Transfusion Medicine (or delegate) as indicated in procedures or circumstances • Report any instances where HLA matched platelets were not given to a patient meeting criteria for HLA matched platelets

6.5 CLINICAL PRACTICE RECOMMENDATIONS FOR MANAGEMENT OF PLATELET REFRACTORINESS

Purpose	These recommendations were developed by ORBCoN in collaboration with an expert working group to assist clinical decision making regarding the appropriate use of HLA matched single donor platelets. The provision of HLA matched single donor platelets is resource intensive both from a blood supplier perspective, and that of the initiating institution, and should be reserved for HLA sensitized patients proven to be refractory to random donor platelets. *Note: when considering these guidelines, the following should be observed*: • *There is no evidence that any one patient group will benefit from the use of single donor platelets in the absence of HLA or HPA refractoriness* • *Leukoreduced (LR) buffy coat platelets and LR single donor apheresis platelets, should be used interchangeably for non-refractory patients*
Guideline	HLA matched platelets are exclusively indicated for refractory patients with demonstrated HLA antibodies. Criteria for determining platelet refractoriness in patients with HLA alloimmunization: • 10-60 minute increment $<10x10^9$ /L following at least two infusions of ABO-identical platelet transfusions **and** • Positive antibody screen for HLA-alloantibodies
Recommendation	• Single donor apheresis platelets should be released based on CBS supply and hospital demand for platelet products
Other considerations	**Other considerations:** • Other causes of non-immune refractoriness are identified and treated • Communication with clinical and CBS teams to make sure platelets only collected when needed is key to maintaining adequate supply/demand

REFERENCES

49. Dzik W, 2007.
74. Juskewitch JE, 2017.
105. Phekoo KH, 1997.

6.6 CMV SERONEGATIVE RED BLOOD CELLS AND PLATELETS

Policy	• Since October 2017 CBS has provided CMV seronegative components for intrauterine transfusion only
Reason	• Leukoreduced cellular components have a very low residual risk of transfusion-transmitted CMV • It is unknown if CMV seronegative units have any additional benefit to leukoreduction • Both CMV seronegative and leukoreduced cellular components are considered "CMV safe"
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the indications for CMV seronegative products • Establish a policy for the provision of CMV seronegative products • Consult with, and provide information to clinical and Transfusion Medicine Staff regarding the appropriate uses of CMV seronegative components • Discuss risks and benefits with treating physicians when CMV seronegative component is indicated but unavailable
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures • Consult Medical Director, Transfusion Medicine (or delegate) as indicated in procedures or by circumstances • Report all instances where a CMV seronegative component is not given to a patient who met criteria

6.7 INDICATIONS FOR USE OF CMV SERONEGATIVE RED BLOOD CELLS AND PLATELETS

Purpose	CBS provides CMV seronegative components for intrauterine transfusion only.
Guideline	If CMV seronegative components are not readily available and a delay in transfusion would compromise patient care, transfusion may proceed with CMV unscreened blood components at the discretion of the primary physician.
Recommendation	• Intrauterine transfusions
Other considerations	• All institutions shall have a policy for the appropriate use of CMV seronegative components

NAC's statement regarding appropriateness of use of Cytomegalovirus (CMV) sero negative vs "CMV safe" component	The NAC statement regarding CMV safe blood components can be seen at: http://www.nacblood.ca/resources/guidelines/CMV.html.

Unavailability of Leuko-Reduced Blood Products
In the event Canadian Blood Services cannot supply leuko-reduced products, CMV seronegative product will be provided and should be prescribed for patients in the following situations:

1. CMV seronegative allogeneic bone marrow transplant candidates and/or recipients of CMV seronegative donor marrow/stem cell recipients.
2. CMV seronegative autologous stem cell transplant candidiates.
3. CMV seronegative recipients of organs from CMV seronegative donors.
4. Pregnant women (except those imminently about to deliver).
5. Intrauterine transfusions.
6. Transfusion of infants of mothers who are CMV seronegative or unknown CMV serological status.
7. HIV positive patients who are CMV seronegative or of unknown CMV serological status.

REFERENCES

16. Blajchman, M, 2001.
25. Callum JL, 2016.
92. NAC, 2017.
110. Prokopchuk-Gauk O, 2017.
135. Vamvakas C, 2005.

6.8 IRRADIATED BLOOD COMPONENTS

Policy	• The Transfusion Medicine Service provides irradiated blood components for appropriate patient populations whenever possible • The procedures for evaluation of requests for blood components contains information to identify patients who require irradiated products, in the event it is not recognized by the ordering physician • The need for irradiated products is placed on the Transfusion Medicine Service patient record and these records are always checked as part of the evaluation of product request procedures
Reason	• Irradiating blood components reduces the risk of transfusion associated graft-versus-host disease (TA-GvHD), where donor cells mount an immune response in an immunologically compromised recipient • Prevention of TA-GvHD is particularly important in view of the high associated mortality • The Transfusion Medicine Service record check provides additional security that a patient receives the appropriate blood components
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the indications for irradiation of blood components. • Consult with, and provide information to, clinical and Transfusion Medicine staff on the appropriate uses of irradiated blood components • Ensure that an explanation is given to the patient of the reason for the use of irradiated component, and the possible consequences of not receiving irradiated component • Ensuring that the patient has, in writing, a statement of requirement for irradiated component (e.g. wallet card with essential information)
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures • Consult with Medical Director, Transfusion Medicine (or delegate) as indicated • Report all instances where irradiated blood components were not given to a patient who met criteria
Applies to:	• Specific populations of patients listed in table 6.1. Every attempt should be made to ascertain the patient's purine analogue drug status • Where there is doubt, irradiated blood components should be transfused • If irradiated blood components are not readily available and delay in transfusion could compromise patient care, transfusion may proceed **at the discretion of the patient's attending physician.** Consideration should be given to using components older than 14 days if irradiated components are not available and transfusion is urgently required

Table 6.1 Recommended Indications for the Use of Irradiated Components

PATIENTS REQUIRING IRRADIATED BLOOD

- Patients with severe T-cell congenital immunodeficiency states
- Intrauterine transfusions (IUT)
- Neonatal exchange transfusions for infants with prior IUT
- Neonatal top-up transfusion if there has been a previous IUT
- Patients with Hodgkin's lymphoma
- Patients undergoing bone marrow or stem cell transplants
  - » It is reasonable to continue providing irradiated products until immunosuppression discontinued
- Recipients of directed transfusions from family members
- Recipients of HLA-matched platelets
- Patients treated with purine analogs (e.g., fludarabine), purine antagonists (e.g., bendamustine), alemtuzumab and anti-thymocyte globulin

REFERENCES

25. Callum JL, 2016.
62. Gorlin B, 2011.
76. Kopolovic I, 2015.
119. Ruhl H, 2009.
133. Treleaven J, 2011.

6.9 WASHED RED BLOOD CELLS AND PLATELETS

Policy	• The Transfusion Medicine Service provides washed cells for appropriate patient populations, when possible • The procedure for evaluation of a request for washed red blood cells contains information to identify patients who require these components, in the event that it is not recognized by the ordering physician • The need for washed cells is placed on the Transfusion Medicine Service patient record, and these records are always checked as part of the evaluation of component request procedures • Orders for washed platelet components should be discussed with a medical expert in Transfusion Medicine
Reason	Red blood cell units and platelets are washed to remove plasma or additive solutions for patients identified in the indications section below
Applies to	Patients for whom contents in the plasma or additive solution have been shown to, or may, cause morbidity
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the indications for the need and use of washed red blood cells and platelets • Be familiar with the process to obtain washed red blood cells from CBS (washed platelets are not available through CBS) • Ensure a process is in place to handle requests • Consult with, and provide information to, clinical and Transfusion Medicine staff on appropriate uses of washed red blood cells and platelets • According to hospital policy, the Medical Director, Transfusion Medicine may need to screen all requests for washed components, or it may be appropriate for ordering physicians to consult directly with CBS physicians
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures • Consult with Medical Director, Transfusion Medicine (or delegate) as indicated in procedures or by circumstances • Report all instances where washed red blood cells or platelets were not given to a patient who met the criteria

6.10 INDICATIONS FOR WASHED RED BLOOD CELLS

Indications for washed red blood cells	For removal of plasma/platelets when transfusing red blood cells to recipients who are: • Known to have a history of severe or repeated allergic reactions to plasma contents, which are unresponsive to pre-medication • HPA-1 negative with anti-HPA-1 • History of anaphylactic transfusion reaction associated with anti-IgA antibodies, when IgA deficient blood products are not available Note: while IgA deficiency is common (1 in 700), only a fraction of these patients will make an anti-IgA antibody, and a smaller fraction again will develop anaphylactic transfusion reactions. Because IgA-deficient and washed blood products are difficult to source, investigation for anti-IgA antibodies is generally only advised for patients who have actually had an anaphylactic transfusion reaction. Testing for IgA deficiency is available through CBS (refer to www.blood.ca). As most patients with a history of anaphylactic transfusion reactions do not have anti-IgA antibodies, provision of IgA deficient blood products is not advised while awaiting results of testing For removal of additive solution: • Neonates undergoing exchange or massive transfusion • Repeated febrile non-hemolytic transfusion reactions despite adequate pre-medication • Repeated urticarial reactions despite adequate pre-medication

6.11 INDICATIONS FOR WASHED OR PLASMA DEPLETED PLATELETS

Indications for washed or "concentrated" platelets	• Orders for washed platelet components should be discussed with a medical expert in Transfusion Medicine • Washed platelets are **rarely** indicated • Washing platelets to remove incompatible plasma may result in significant loss of platelets in addition to promoting platelet activation. The resulting component is likely to have reduced effectiveness

REFERENCES

2. AABB, 2017.
26. CBS, Circular of Information.
42. Davenport RD, 2011.
88. Mollison's Blood Transfusion in Clinical Medicine, V12, 2014.

6.12 EMERGENCY RELEASE OF RED BLOOD CELL UNITS

Policy during regular working hours	• Transfusion Medicine staff will issue group O red blood cells in emergency situations when compatibility examinations cannot be done or results are not yet available, and the patient requires immediate red blood cell transfusion • RhD negative females of child bearing potential (each hospital should establish an age) should preferentially receive RhD negative components • If RhD negative red blood cells are not available the Medical Director, Transfusion Medicine (or delegate) should be contacted immediately • A policy should be in place to address the administration of RhIG when RhD positive platelets or red blood cells are transfused to an RhD negative recipient • The requesting physician must sign for the emergency release of red blood cells on the request or patient record, as provided for in CSA Standards • Group-specific red blood cells are **never** released on the basis of the blood group in the patient record, as provided for in CSA Standards, group O cells will be transfused until the patient's ABO and RhD group have been determined on two separate samples (see section 4.2)
Policy (outside of regular laboratory hours)	• Transfusion Medicine Service staff will establish a procedure for the Emergency release/issue of blood products by clinical personnel to include provision that: » Only trained and competent clinical personnel are approved to release/issue blood products from the laboratory or other specific locations where such units are stored within the facility » Clinical personnel who do this task will have their competence assessed at regular, defined intervals » Results of such competence assessment will be recorded as part of the employee record » Names and signatures of such clinical staff will be on record in the Transfusion Medicine Service
Reason	The clinical urgency of the emergency situation does not allow time to undertake or complete regular compatibility examinations.
Applies to:	Patients who require red blood cell transfusion before grouping and compatibility examinations are complete.
Responsibilities of the Medical Director, Transfusion Medicine	• Develop the policy, process and procedures for emergency release of blood, including the capability to: » Perform STAT examinations » Provide consultation to clinical staff » Avoid unnecessarily restrictive practices » Ensure timely or immediate availability of red blood cells to meet the needs of the requesting clinical service • Consult with Transfusion Medicine and clinical staff as needed • If a crossmatch completed during or after transfusion has occurred appears incompatible, immediately inform the treating physician(s) to minimize and manage any adverse reaction

Responsibilities of Transfusion Medicine staff	• Follow the procedures in the Emergency Release of Group O and Group Specific Red Blood Cells process • Provide component as promptly as possible during the emergency • Consult with supervisor or Medical Director, Transfusion Service (or delegate) as needed • It is recognized that documentation often occurs after transfusion, due to clinical urgency, but the Transfusion Medicine Service must insist upon: » Strict identification of donor units and patient samples even in the case of "unidentified" patients » Documentation of unit disposition » Documentation of the emergency status of the transfusion » Signature of the requesting physician that emergency release of component is required • If possible a serologic crossmatch should be performed on units transfused under Emergency Release procedures
Crossmatch	• The Transfusion Medicine Service should retain/obtain samples from the transfused uncrossmatched units and perform compatibility examinations when patient plasma/serum samples are available • Such compatibility testing should reflect the routine pre-transfusion methods, including an antibody screen, and proceeding to direct crossmatch versus bag segments only if antibody screen is positive • If the subsequent crossmatch is incompatible, the Medical Director, Transfusion Medicine (or delegate) must immediately inform the treating physician to minimize and manage any adverse reaction • Investigation of any blood transfused prior to arrival / testing should be done (prior hospital treatment or transfused en route to hospital) • If mixed field is detected in ABO/Rh testing and blood group cannot be clearly determined, group O red blood cells should be issued until the discrepancy can be resolved (RhD type should be determined based on age and gender of the recipient)
Responsibilities of the treating physician	• Ensure a blood sample is obtained prior to transfusion or as soon as possible after transfusion has commenced if transfusion has already begun • Ensure required procedures for positive patient identification and specimen labeling are followed • Sign the request for emergency release of red blood cell units
Responsibilities of treating nurse	• Trained and competent in the emergency issue of red blood cell units if the Transfusion Medicine laboratory is not staffed, or from a storage location other than the Transfusion Medicine laboratory • Dispatch the patient pre-transfusion sample to the Transfusion Medicine laboratory as soon as possible

Conditions	• RhD negative red blood cells should be used for females of child bearing potential • A switch to group-specific uncrossmatched blood should be possible within 15-30 minutes, provided appropriate pre-transfusion sample(s) has (have) been received and tested according to hospital policy, to conserve group O inventory • There is no threshold of units of group O RBCs above which a switch to group specific RBCs is prohibited • Cross-matched blood according to the routine procedures should be issued as soon as possible, subject to the immediately preceding policy statement • A policy should be established for the release of blood to transport personnel for both identified and unidentified patients and should include: » Instructions for packing, labeling and transport » Notification of the receiving facility when known » Contact information of the sending facility » Final disposition information including the patient ID and date/time of infusion of any blood prior to transfer

REFERENCES

2. AABB, 2017.
40. Dananayake T, 2011.

7.0 APPROPRIATE USE OF MANUFACTURED BLOOD PRODUCTS

Policy	The Transfusion Medicine Service follows established guidelines for use of all blood products.
Reason	• Assist in the efficacious use of blood products • Improve patient safety by providing the appropriate product at the right dosing schedule
Patient population	• As indicated in subsequent sections concerning individual products
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the appropriate use of these products • Assist in utilization management of these blood products by: » Developing policies, processes and procedures to screen requests for these products to ensure that the most appropriate product is used in the right dose » Promote education of clinical and other staff in the appropriate use of these products » Assist clinicians when orders deviate from established guidelines and dose recommendations
Responsibilities of the treating physician	• Obtain any necessary authorization or special product release
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures as written • Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated in procedures, as necessary based on technologist's skills and experience, or on the basis of available clinical or laboratory information • Report all instances where these products were not given to a patient who met criteria • Provide any required request forms and/or contact information needed to obtain appropriate authorization
Associated documents	Ontario guidelines have been developed for the following: • IVIG • Albumin Refer to: www.transfusionontario.org National guidelines have been developed for the following: • Prothrombin Complex concentrates (PCC) • Solvent/detergent-treated plasma • Recombinant FVIIa • Fibrinogen Concentrates Refer to: www.nacblood.ca

7.1 APPROPRIATE USE OF PLASMA FRACTIONATED PRODUCTS

Plasma fractionated products include:

- Albumin
- Intravenous immunoglobulin (IVIG)
- Subcutaneous immunoglobulin
- Specific immune globulins (RhIG, SCIG, HepBIG, VZIG)
- Human derived clotting factor concentrates (FEIBA ,PCC, FXI, fibrinogen concentrates)
- Recombinant clotting factors (FVII, VIII, IX,FXIII)

7.2 INDICATIONS FOR THE USE OF ALBUMIN

Refer to Bloody Easy 4: blood transfusions, blood alternatives and transfusion reactions, 4th ed, 2016.

7.3 INDICATIONS FOR THE USE OF INTRAVENOUS IMMUNOGLOBULIN (IG)

In April 2012 the Ontario Ministry of Health and Long Term Care launched their IVIG strategy. For a toolkit and the associated guidelines, refer to http://transfusionontario.org/en/download/immune-globulin-toolkit-for-ontario/

General Pre-requisites and indications for IVIG or SCIG Use:

1. A diagnosis must be confirmed for all orders.
2. For immune deficiency conditions, serum IgG levels must be clinically assessed to ensure optimum dosing.
3. For all other conditions, IVIG should only be used when other, less expensive, equally safe and efficacious alternatives have failed.
4. There must be regular clinical outcome assessment.
5. For all proposed treatments or course of treatments with IVIG and SCIG the MOHLTC IG Request Form (see below) shall be completed by the requesting physician.
6. All request forms must be reviewed for appropriate indication and dosage interval.
7. Detailed information on all aspects of IG Utilization Management can be found in the Immune Globulin Toolkit prepared by ORBCoN.

Special Requests for Use in Conditions not on the list of Approved Medical Conditions for IG Use:

- Subject to screening at the hospital level:
  - » IG user hospitals shall select the appropriate physician/committee to review, and where appropriate, approve requests for indications not listed on the MOHLTC IG Request Form
  - » The physician appointed to serve as the approving physician (or delegate) shall sign the request form
  - » On the request form under the heading “Other” the non-licensed indication shall be entered
- In the event of urgent treatment in a life-threatening situation, the request for IVIG shall be met immediately following verification of appropriate dose

Approved Indications for IG Treatment

The clinical indication, dose and duration of therapy must be in accordance with the Ontario IG Utilization Management Guidelines.
http://transfusionontario.org/en/documents/?cat=utilization-management-guidelines

Indications for which IG is NOT recommended nor indicated, or is ineffective:

Diagnosis	Efficacy/Comment
Rheumatoid Arthritis	Ineffective
Inclusion Body Myositis	Ineffective
Chronic Fatigue Syndrome	Ineffective
Recurrent Spontaneous Abortion	Ineffective
In Vitro Fertilization/Implantation Procedures	Ineffective
Sepsis In Critical Care Patients	No large randomized controlled trials to confirm benefit
Autologous Bone Marrow/Stem Cell Transplant	No benefit
Epilepsy	Ineffective
Amyotrophic Lateral Sclerosis	Ineffective

IVIG dose calculation:

- An IVIG Dose Calculator based on adjusted body weight is available to determine the appropriate dose for each individual patient.
- Available at http://ivig.transfusionontario.org and as an application for installation on hand-held electronic devices.
- Based on patient height and weight.
- For IVIG for immunoglobulin replacement, use dose calculator for 1st dose and determine subsequent doses based on the IgG trough level.
- Preparations of immunoglobulin are available from Canadian Blood Services. Dosage is individualized, consult package insert.

REFERENCES

5. Anderson D, 2007.
12. Berger M, 2011.
25. Callum JL, 2016.
34. Chow S, 2012.
36. United Kingdom Department of Health, Clinical Guidelines for Immunoglobulin, 2nd ed. 2011
53. Feasby T, 2007.
70. ORBCoN, Immune Globulin Toolkit for Ontario, 2018.
71. BC PBCO, Intravenous Immune Globulin.
85. Martin A, 2013.
123. Shehata N, 2010.
124. Shehata N, 2010.

Table 7.1: Use of Recombinant* and Plasma Derived Products that Do Not require a Special Access program (SAP) Approval

<table>
<tr><th>Product</th><th>Clinical Indication</th><th>Standard Dose
(Always refer to the product insert for most current information)</th></tr>
<tr><td>Antihemophiliac factor/ Von Willebrand Factor complex
Humate P®
Wilate®</td><td>VonWillebrand’s disease when unresponsive to DDAVP</td><td>Minor Bleed: either product
Humate® P 40-50 IU/kg 1 or 2 doses
Wilate® 20-40 IU/kg q 12-24 hours

Major Bleed:
Humate P® 40–80 IU/kg q 12–24 hours
Wilate® 40–60 IU/kg q 8–12 hours</td></tr>
<tr><td>Factor VIII concentrate*

Refer to the hemophilia centre to determine the appropriate product as this is usually patient specific</td><td>Hemophilia A</td><td>• 1 U/kg produces 2% increase in factor VIII level
• Half life variable depending on product

<table><tr><th>Category of Bleed</th><th>Activity Goal</th></tr><tr><td>mild</td><td>30%</td></tr><tr><td>major</td><td>50-100%</td></tr></table></td></tr>
<tr><td>Factor IX concentrate*</td><td>Hemophilia B (Christmas disease)</td><td>• 1 U/kg produces 1% increase in factor IX level
• Half life variable depending on product

<table><tr><th>Category of Bleed</th><th>Activity Goal</th></tr><tr><td>mild</td><td>30%</td></tr><tr><td>major</td><td>50-100%</td></tr></table></td></tr>
<tr><td>Factor XIII Concentrate*</td><td>Congenital factor XIII deficiency</td><td>Consult package inserts</td></tr>
<tr><td>Antithrombin III</td><td>Antithrombin deficiency
• Congenital deficiency
• Heparin resistance in association with cardiovascular surgery</td><td>Refer to package insert.</td></tr>
</table>

Rh Immune Globulin (RhIG) **Note: Following any event at 20 weeks gestation or thereafter, feto-maternal testing should be performed to determine if additional doses of RhIG are required**	For prevention of RhD alloimmunization in at-risk RhD negative females _____ Pregnancy • At 28 weeks gestation and post-partum with RhD positive infant _____ Obstetrical ** Abortion-- therapeutic, spontaneous or threatened _____ Amniocentesis or chorionic villus sampling (CVS) <34 weeks gestation _____ Amniocentesis, CVS or other manipulation >34 weeks gestation _____ Additional sensitizing events (e.g. trauma, fall) _____ Post-transfusion of Rh D positive red blood cells or platelets	_____ Dose at 28 weeks, 1,500 IU or 300ug Dose post-partum 1,500 IU or 300ug, (may require additional doses as calculated following quantitation of feto-maternal hemorrhage) _____ 1,500 IU or 300ug _____ 1,500 IU or 300ug _____ 600 IU or 120ug _____ <12 weeks : 600 IU or 120ug ≥ 12 weeks: 1500 IU or 300ug _____ 1,500 IU or 300ug for each 15mL red blood cells or 30 mL whole blood
Varicella-Zoster Immune Globulin (VZIG)	Passive immunization to chickenpox in high risk exposed patients	125 U/10kg to maximum of 625U, within 96 hours of exposure
Hepatitis B Immune Globulin (HBIG)	Passive immunization of exposed patients	Dose 0.06ml/kg immediately Repeat in 1 month if not vaccinated
Tetanus Immune Globulin (TIG)	Passive immunization of exposed patients	For dose, refer to package insert
Prothrombin Complex Concentrates (Octaplex® and Beriplex®)	Treatment of major bleeding or in anticipation of urgent surgery in acquired deficiency of the prothrombin complex coagulation factors due to vitamin K antagonists or deficiency (for use in pediatric patients - see section 8.4)	Effective half life is only about 6 hours INR <3 – 1,000 IU INR 3-5 – 2,000 IU INR >5 (adults only) 3,000 IU Adjust for patients with extremes of body weight (<50kg, >90 kg) For details of INR and weight-based dosing see chart available at www.nacblood.ca
C1 esterase inhibitor	Treatment of hereditary angioedema in C1 esterase deficiency	Refer to product insert
Fibrinogen concentrate (riaSTAP™)	Acquired hypofibrinogenemia	Refer to product insert and www.nacblood.ca

Table 7.2: Use of Products that Require approval through Health Canada Special Access Program or SAP
https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs/special-access-programme-drugs-1.html

Plasma Fractionated Product	Clinical Indication	Dose Information
Factor VII concentrate	Congenital FVII deficiency	Refer to product insert
Factor XI concentrate	Congenital FX deficiency	Refer to product insert
Factor XIII concentrate	Congenital FXI deficiency	Refer to product insert
Protein C concentrate	Congenital or acquired deficiency of Protein C	Refer to product insert

REFERENCES

25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
54. Fung Kee Fung K, 2003.
81. Lin Y, 2004.
94. NAC, 2014.
95. Canadian Immunization Guide, 7th ed, 2006.
127. Speiss B, 2008.

7.4 USE OF RECOMBINANT FACTOR VIIA, ERYTHROPOIETIN

Policy	The Transfusion Medicine Service follows established guidelines for use and dosage of recombinant products for the purposes outlined below. The Medical Director, Transfusion Medicine has established a process to screen requests for recombinant products. This process includes creation and maintenance of a record of the patient response to therapy and outcome. All first time requests for recombinant factors must be approved by the Medical Director, Transfusion Medicine to address the issue of "off-label" use of recombinant factor VIIa.
Applies to	• Recombinant Factor VIIa: » Control of bleeding in congenital factor VII deficiency » Patients with hemophilia A and B with coagulation factor inhibitors » Patients with acquired coagulation factor inhibitors refractory to medical therapy » Not recommended for treatment of bleeding in patients without the disorders listed above

Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the availability and use of recombinant products and be aware that: » NAC guidelines recommend against off label use » Random controlled trials do not support off label use » Risk of adverse event is doubled over age 65 and tripled over age 75 • Understand the indications for and use of erythropoietin in the management of peri-operative patients and for patients who refuse blood transfusion • Ensure effective use of recombinant products by: » Screening requests for recombinant products » Promoting education of treating physicians and other health care professionals in the appropriate use of recombinant products • Manage the inventory by: » Determining if the patient population served warrants holding a supply of these products as part of regular inventory, or should be requested from Canadian Blood Services on an *ad hoc* basis » Ensuring recirculation for expiring products in a timely fashion
Responsibilities of Transfusion Medicine Staff	• Follow associated technical procedures as written • Respond promptly to requests where there life-threatening hemorrhage • Insist that proper documentation is followed • Order, receive and issue recombinant products • Contact the Medical Director, Transfusion Medicine on receiving first-time requests for recombinant products • Be aware that for all off-label requests for refractory bleeding: » NAC guidelines recommend against off label use » Random controlled trials do not support off label use » Risk of adverse event is doubled over age 65 and tripled over age 75
Conditions	• Recommended dosing for recombinant factor VIIa for: » Inhibitor patients - 70-90u/kg 2 hourly » Congenital factor VII deficiency – 15-30u/kg 4-6 hourly
Erythropoietin	Although erythropoietin is not distributed through the Transfusion Medicine Service, the Medical Director, Transfusion Medicine should be familiar with the drug and its indications for use in the peri-operative period and for patients who refuse blood transfusion.

REFERENCES

17. Bodnaruk M, 2004.
25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
28. CBS, Plasma Protein Products, 2011.
82. Lin Y, 2012.
89. Moltzan CJ, 2008.

8.0 APPROPRIATE USE OF BLOOD COMPONENTS IN NEONATES AND PEDIATRIC PATIENTS

Policy	The Transfusion Medicine Service follows established guidelines for the appropriate use and administration of blood products in neonates and pediatric patients.
Reason	Aid in the efficacious use of blood components and products. Improve patient safety through judicious use of blood components and products.
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the use of and indications for the use of blood components and products in neonates and pediatric patients • Be available to consult with treating physicians and other staff on the appropriate use and administration of blood products for neonates and pediatric patients • Promote education of treating physicians and other staff in the appropriate use of blood components and products in neonates and pediatric patients including appropriate dosing/monitoring for effectiveness and reporting of transfusion reactions • Initiate discussions with clinical staff when laboratory results and/or clinical setting suggest blood component or product use may, or may not, be indicated • If applicable to hospital population, ensure guidelines for neonates and children are available
Responsibilities of Transfusion Medicine Service staff	• Perform all steps of applicable Transfusion Medicine Service procedures as written • Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated in technical procedures, or as necessary based on technologist's skills and experience, or additional clinical or laboratory information

REFERENCES

19. British Committee for Standards in Haematology, 2004.
25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
118. Roseff SD, 2002.

8.1 NEONATAL RED BLOOD CELL AND PLATELET TRANSFUSION

Policy	The Transfusion Medicine Service follows established policies, processes and procedures for transfusion of blood components and products to neonatal patients.
Reason	Indications for transfusion and specific requirements for neonates are different from transfusion requirements for those over 4 months of age.
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with indications for neonatal transfusion and be available for consultation with treating physicians • Ensure guidelines are readily available in institutions with neonates
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures as written • Consult with the Medical Director, Transfusion medicine (or delegate) as indicated by procedures or circumstances • Ensure requests for blood products meet hospital guidelines for indications and dosage

8.2 NEONATAL PATIENT MANAGEMENT

General considerations	• A neonate is considered to be an infant up to 4 months of age • There is conflicting evidence for restrictive transfusion practices and for an effect on the long-term neurodevelopmental outcome in preterm infants exposed to severe anemia • Desirable hemoglobin levels vary with clinical circumstances (see table 8.1) • Transfusion solely to replace blood removed for laboratory tests is not recommended • All neonates should receive CMV-safe components
Red Blood Cell Dosage and Type	10-15mL/kg body weight packed red blood cells that are: • Compatible with mother and neonate » ABO group specific where possible » Irradiated if previous intrauterine transfusion up to 40 weeks gestational age, exchange transfusion, complex cardiac abnormality until congenital immunodeficiency has been ruled out, massive transfusion (not necessary for low volume transfusion).
Massive Transfusion in a neonate (including exchange transfusion)	• In addition to meeting the criteria in section above, units should be negative for hemoglobin S.
Compatibility testing – initial pre-transfusion examination	• Cord blood should not be used for pre-transfusion examinations • Required examinations include determination of ABO/RhD and • Antibody screen on a sample from the neonate or mother » If clinically significant antibody(ies) are identified, the neonate must receive antigen negative units, compatible by antiglobulin crossmatch, until the antibody is no longer detectable in the infant's serum/plasma
Compatibility testing – subsequent pre-transfusion examinations	• If the initial antibody screen is negative, repeat examination for unexpected antibodies may be omitted during the current hospital admission, up to 4 months of age. (Alloimmunization in a neonate is unlikely) • If a non-group O neonate needs to receive non-group O red blood cells that are incompatible with the maternal ABO group, the neonate's serum/plasma should be examined for anti-A or anti-B by antiglobulin testing, and compatible blood should be used

Table 8.1: Threshold and Target Hemoglobin Levels for Neonatal Red Blood Cell Transfusion

Transfuse neonate	If the hemoglobin result is	And the neonate is
With acute blood loss	Any hemoglobin level	Hypotensive and ill.
Weaned off mechanical ventilation	<100g/L	Requiring supplemental oxygen
With anemia	<80g/L	Showing signs of anemia with: • Significant unexplained apnea • Persistent unexplained heart rate >165-180 bpm or respiratory rate > 80 per minute lasting >24 hours • Unexplained poor weight gain, 10g/day over 4-7 days despite adequate caloric intake (100-120 kcal/kg/day) • Unexplained lethargy
On ECMO or cyanotic heart disease	120g/L	

Table 8.2: Indications for Neonatal Platelet Transfusion

Transfuse if Neonate is	And the platelet count is	And clinical condition is
Any age up to 4 months	<20x10^9/L ——————————— <50x10^9/L ——————————— <100x10^9/L	**any** ——————————— bleeding or invasive non-neuraxial procedure ——————————— invasive neuraxial procedure
Premature	<30x10^9/L	stable, or Neonatal Alloimmune Thrombocytopenia

REFERENCES

21. British Committee for Standards in Haematology, 2016.
78. Lau W, 2017.
101. Pediatric Transfusion: A Physician's Handbook, 2014.
118. Roseff SD, 2002.
120. Sacher RA, 1989.
130. Strauss R, 2004.

8.3 PEDIATRIC BLOOD COMPONENT TRANSFUSION

Policy	The Transfusion Medicine Service follows established guidelines for the appropriate use and administration of blood components and products to pediatric patients.
Reason	• Indications for transfusion and specific blood component and product requirements differ between children and adults • Aid in the efficacious use of blood components and products • Improve patient safety through the judicious use of blood components and products
Applies to	Patients greater than 4 months of age up to patients of adult size or weight (e.g. >50kg)
Responsibilities of the Medical Director Transfusion Medicine	• Be familiar with the use of and indications for the use of blood components and products in the pediatric population • Where appropriate, ensure guidelines are in place for pediatric patients • Be available to consult with treating physicians and other staff in the appropriate use and administration of blood components and products for pediatric patients • Promote education of clinical and other staff in the appropriate use of blood components and products in pediatric patient including appropriate dosing/ monitoring for effectiveness and reporting of transfusion reactions • Initiate discussion with clinical staff when laboratory results and/or clinical setting suggest blood component or product use may, or may not, be indicated for a pediatric patient
Responsibilities of Transfusion Medicine Service staff	• Follow appropriate technical procedures as written • Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated in technical procedures, or as necessary based on the technologist's skills and experience, additional laboratory examination results or the clinical situation • Consult Medical Director, Transfusion Medicine (or delegate) for requests not meeting hospital guidelines for indication and dosage

REFERENCES

25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
67. Hume H, 1997.
78. Lau W, 2017.
118. Roseff SD, 2002.

Table 8.3: Pediatric Red Blood Cell Transfusion Guidelines

Transfuse pediatric	Hemoglobin	And the child is or has
Surgical patient	<60-70g/L _____ <80g/L	Pre-operative and alternate therapy is not available _____ Post-operative and showing symptoms or signs of anemia
Severe cardiopulmonary disease	120g/L	Ongoing transfusion requirements
Chemotherapy or irradiation	<70g/L	Ongoing transfusion requirements
Chronic anemia	<70g/L	Symptomatic anemia unresponsive to medical therapy and not bleeding
Complications of sickle cell disease	Target 100 – 110g/L	Treatment or presentation of cerebro-vascular accident, acute chest syndrome, aplastic crisis, splenic sequestration, or pre-operative preparation. Refer to section 9.5
Thalassemia syndrome	Maintain at 90 – 100g/L	Chronic transfusion regimen
Hemorrhage	Maintain >70g/L	Suspected acute blood loss of 15% or more of blood volume

8.4 TRANSFUSION OF FROZEN PLASMA TO PEDIATRIC PATIENTS

Appropriate uses include:

- In conjunction with vitamin K for emergency reversal of warfarin effect in a patient requiring an urgent operative procedure or with life-threatening bleeding if Prothrombin Complex Concentrates are not available*.
- Active bleeding or major surgery with PT/aPTT results >1.5 x mid-range of age-related reference range
  - » In the absence of heparin, LMWH, lepirudin, hirudin, or other FXa inhibitor, or lupus inhibitor
- Massive transfusion and clinical status precludes waiting for PT/aPTT results
- Acute DIC with bleeding
- Cardiopulmonary bypass procedures with hemorrhage and PT/PTT > 1.5 x mid-range of age-related reference range
- Preparation of reconstituted whole blood for exchange transfusion in neonates
- Hepatic failure with INR >1.5 and major bleeding or invasive procedure (other than para or thoracocentesis)
- Single coagulation factor deficiencies when alternative specific factor concentrates are not available (e.g. factor V, patient at remote location)
  - » Specific factor concentrates should be made available as soon as possible, if necessary by transferring the patient to a centre where appropriate concentrates are available
- Rare plasma protein deficiencies for which alternative therapy is not immediately available (e.g. C1 esterase deficiency)
- Thrombotic thrombocytopenic purpura
  - » Slow continuous transfusion while awaiting access to exchange transfusion

Inappropriate uses include:

- Hypovolemia
- Treatment of immunodeficiency states

*Note added in proof: "Dosage schedule for Prothrombin Complex Concentrate based on patient weight over 35 kg is provided in the National Advisory Committee Recommendations[115]

For children under 35kg anecdotal evidence suggests that Prothrombin Complex Concentrate is dosed as follows[98]:

- <10 kg INR <3, 250 IU; INR ≥ 3, 500 IU
- 10-25 kg INR <3, 500 IU; INR ≥ 3, 750 IU
- 25-35 kg INR <3, 750 IU; INR ≥ 3, 1,000 IU

REFERENCES

21. British Committee for Standards in Haematology, 2016.
25. Callum JL, 2016.
78. Lau W, 2017.
98. Noga T, 2016.
115. NAC, 2011.
118. Roseff SD, 2002.

8.5 TRANSFUSION OF PLATELETS TO PEDIATRIC PATIENTS MORE THAN 4 MONTHS OF AGE

Dose:

- Body weight <10kg: 5-10ml/kg apheresis or buffy coat platelets should increase platelet count 50 – 100 X 10^9/L
- Body weight ≥10kg: 1 unit/10kg of apheresis or buffy coat platelets should increase platelet count 50 – 100 X 10^9/L

Table 8.4 Indications for Pediatric Platelet Transfusion (other than neonate)

Transfuse when platelet count is	And the child has
<10 X 10^9/L	Failure of platelet production with: • active bleeding • invasive procedure
<50 X 10^9/L	• serious bleeding • major surgery • invasive procedure with risk of major bleeding
<100 X 10^9/L	• Peri-neurosurgery • Head injury • Post operative cardiac surgery with significant bleeding
Any count	Platelet dysfunction with major bleeding

REFERENCES

21. British Committee for Standards in Haematology, 2016.
25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
118. Roseff SD, 2002.

8.6 MANAGEMENT OF CONGENITAL ANEMIAS (see also section 9, Special Transfusion Situations)

Policy	The Transfusion Medicine Service has established policies, processes and procedures to assist in the management of patients with congenital anemias that include the provision of phenotypically matched units when appropriate.
Reason	Transfusion thresholds and indications for transfusion in patients with sickle cell syndromes, congenital hemolytic anemias or thalassemia syndromes may be different from those with other causes of anemia.
Responsibilities of the Medical Director, Transfusion Medicine	• Be familiar with the management of transfusion in patients with congenital anemias • Work in consultation with clinical staff in individual cases • Work in consultation with clinical staff to determine patient blood group phenotypes and decide on the optimal phenotype of units chosen for ongoing transfusion support • Establish policies and procedures for the provision of special products including: irradiated components, Hg S negative red blood cells • and phenotypically matched red blood cells
Responsibilities of Transfusion Medicine Service staff	• Where possible, ensure full red blood cell phenotype (Rh, Kell, Duffy, Kidd, MNS) is performed prior to the first transfusion in a patient who will require ongoing transfusion support (refer to section 9.8 for list of antigens) • If the Transfusion Medicine Service does not have the capacity to perform these investigations, send samples to a regional reference laboratory or CBS requesting a full phenotype determination • Record results of phenotype determinations in the patient record • Provide phenotype compatible blood as determined by the Medical Director, Transfusion Medicine and appropriate clinical staff for subsequent transfusions • Check with CBS for availability of phenotype information
Patient Management	• Patients with inherited red blood cell membrane disorders should be transfused for the symptomatic relief of anemia • Non-alloimmunized patients with sickle cell syndromes should receive blood that is of the same Rh (D, C, c, E, e) and Kell phenotype • Sickle cell syndrome patients with detectable alloantibody should receive antigen negative blood and extended phenotype matched units when possible • Red cell units for children with sickle cell syndromes undergoing exchange transfusion should be negative for HbS if possible, because the post-transfusion hemoglobin S level is often measured to monitor the effectiveness of the exchange

8.7 MANAGEMENT OF TRANSFUSION IN PEDIATRIC PATIENTS WITH AUTOIMMUNE HEMOLYTIC ANEMIA

Refer to section 9.6

REFERENCES

25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
67. Hume H, 1997.
101. Pediatric Transfusion: A Physician's Handbook, 2014.
130. Strauss R, 2004.

9.0 SPECIAL TRANSFUSION SITUATIONS

Some clinical situations may present particular challenges to hospital Transfusion Medicine Services, for which it is useful to have, in advance, defined policies, processes and procedures for dealing with these situations. These special situations include:

- Support of a patient with signed refusal of consent for transfusion
- Management of a patient requiring massive transfusion
- Management of a patient with auto-immune hemolytic anemia requiring transfusion
- Transfusion support of patients who are recipients of solid organ, bone marrow or stem cell transplant
- Transfusion support in sickle cell syndromes

9.1 SUPPORT OF A PATIENT WITH SIGNED REFUSAL OF CONSENT FOR TRANSFUSION

Policy	The Medical Director, Transfusion Medicine and appropriate medical/surgical staff jointly establish programs to support patients who ordinarily would require transfusion, but have refused consent for transfusion of blood components or products. Where hospital resources cannot adequately support such patients, a procedure should be established for referral to a facility where the necessary resources are available.
Reason	Pre-planned support for patients who refuse transfusion is necessary for safety of the patient.
Applies to	Patients who have refused transfusion.
Responsibilities of the Medical Director, Transfusion Medicine	• Work with clinical staff to develop policies, processes and procedures to support patients who have refused consent to transfusion • Ensure that any blood salvage techniques and equipment used to support such patients meet the standards (CAN/CSA) for collection, labeling, storage, reinfusion and staff training • Work with surgical and anesthetic staff to assess the perioperative risks of morbidity and mortality of any elective procedure in a patient who refuses transfusion • In cases with prohibitive risk, ensure that the surgical and anesthetic staff are fully aware of the level of risk, and have advised the patient accordingly • Provide support/consultation to physicians caring for non-surgical, anemic or bleeding medical patients who refuse transfusion • Ensure a mechanism is in place to document discussion of risks and options
Responsibilities of Transfusion Medicine service staff	• Record refusal of consent in the Transfusion Medicine Service patient record • Notify the Medical Director, Transfusion Medicine (or delegate) if an order is received that is not consistent with advance directive
Responsibilities of Treating Medical Staff	• Work with the Medical Director, Transfusion Medicine to: » Develop programs to support patients who have refused transfusion » Assess the perioperative risks of morbidity and mortality of any proposed elective surgical procedure in a patient who has refused transfusion • The role of these physicians is to: » Advise the patient if prohibitive risk exists » Assist in the application of available blood alternatives

Patient Management	Alternatives to blood component and product transfusion include: • Minimization of iatrogenic blood loss (e.g. limit laboratory testing, use of low volume collection containers) • Meticulous surgical technique • Maintenance of circulating volume with crystalloid or colloid • Where acceptable to the patient: » Pre-surgical autologous blood donation (through CBS or hospital based autologous collection program) » Intraoperative cell salvage procedures • Preoperative optimization of hemoglobin level: » Iron, folate, vitamin B12, erythropoetin • Pharmacological agents that minimize bleeding » DDAVP, antifibrinolytic agents, vitamin K • Anesthetic techniques to reduce blood loss (regional anesthesia)

REFERENCES

3. AABB, 2014.
7. Aubuchon JP, 2011.
17. Bodnaruk ZM, 2004.
25. Callum JL, 2016.
60. Goodnough LT, 2003.

9.2 MANAGEMENT OF PATIENT REQUIRING MASSIVE TRANSFUSION

"Massive transfusion" is generally defined as requiring transfusion sufficient to replace one full circulating volume in less than 24 hours, or, in an adult, transfusion of 10 units or more in less than 24 hours.

Policy	The Transfusion Medicine Service has established guidelines for the management of patients requiring massive transfusion, including the administration of blood components and products and selection of red blood cells.
Reason	Patients receiving massive transfusion are at risk for developing coagulopathies that increase blood loss and contribute to morbidity and mortality. Such patients may also deplete the Transfusion Medicine Service of specific components, requiring changes to be made in blood group of components provided or incompatible blood given to patients with alloantibodies.
Applies to	Patients with severe blood loss requiring large volume, rapid transfusion, replacing at least one total blood volume in less than 24 hours.
Responsibilities of the Medical Director, Transfusion Medicine	• Work with clinical staff to establish a massive hemorrhage protocol to guide the general conduct of massive transfusion events and periodically test the protocol through simulation exercises • Ensure that the equipment for blood warming and cell salvage, and the training and continuing assessment of competency of staff operating the equipment, meet the required standards (CAN/CSA) • Establish the requirements for appropriate laboratory monitoring • Be informed of any patients requiring massive transfusion • Be available to treating medical staff, to consult as required on transfusion measures in individual cases
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures • Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated in procedures or by circumstances
Patient Management	• Clinical transfusion decisions must often be made before Transfusion Medicine Service examinations have been completed. • However, these examinations should be completed as promptly and frequently as required by the clinical circumstances • In general, the bleeding patient should be transfused to maintain the following parameters: » Platelet count >50x10^9/L (with head injury >100x10^9/L) » INR < 1.8 » aPTT < 1.5 x normal » Fibrinogen >1.5g/L » Hemoglobin > 80g/L • Application of blood conservation strategies » Antifibrinolytics » Cell salvage » Prompt surgical intervention » Uterotonic agents in obstetrical hemorrhage » Interventional radiology » Avoidance of hypothermia and acidosis • In setting of massive uncontrolled hemorrhage, component therapy should be administered according to the agreed protocol (see above)

RESOURCES

Ontario's Recommendations for Massive Hemorrhage Protocol available at http://transfusionontario.org/en/documents/?cat=massive-hemorrhage-protocol

9.3 SWITCHING ABO GROUP IN MASSIVE TRANSFUSION OR DURING INVENTORY SHORTAGE

- Selection order of ABO compatible donor red blood cells is shown in table 9.1
- Selection order of ABO group of platelets or frozen plasma is shown in table 9.2
- It is not necessary to provide group specific cryoprecipitate because of the low volume of plasma (<10mls) in each unit. Non-group specific cryo is satisfactory for all blood groups. Pooling a mixture of blood groups together in one dose is not advised
- Urgent platelet transfusion should not be delayed in the event plasma compatible platelet units are not immediately available

Table 9.1. Selection Order of ABO Compatible Donor Red Blood Cells

Recipient ABO Group	1st Choice ABO identical	2nd Choice ABO compatible	3rd Choice ABO compatible	4th Choice ABO compatible
O	Group O	None	None	None
A	Group A	Group O	None	None
B	Group B	Group O	None	None
AB	Group AB	Group A	Group B	Group O

Table 9.2. Selection Order of ABO Group for Platelets or Frozen Plasma

Recipient ABO Group	Component Group 1st Choice	Component Group 2nd Choice	Component Group 3rd Choice	Component Group 4th Choice
AB	AB	A*	B*	O*
A	A	AB	B*	O*
B	B	AB	A*	O*
O	O	A	B	AB

** Choices with incompatible plasma, listed in "least incompatible" order*

9.4 SWITCHING FROM RHD NEGATIVE TO RHD POSITIVE RED BLOOD CELLS IN MASSIVE TRANSFUSION

It may not be possible to provide RhD negative blood for an RhD negative patient with massive transfusion. The following policies should be implemented for switching from RhD negative to RhD positive red blood cells:

- Prior to switching, if possible, confirm that the patient's plasma does not contain anti-D
- If a continuing transfusion requirement is expected to exceed the available supply of RhD negative blood, or if the patient is likely to require >4-8 units of red blood cells, the switch to RhD positive blood should be made early to conserve RhD negative stock for other recipients
- In general, patients expected to receive <4 units of packed cells in a single transfusion episode should not be switched unless RhD negative stocks are critically low
- RhD negative females of child bearing potential should only be switched to RhD positive blood under extraordinary circumstances. RhIG is **not recommended** when RhD positive red blood cells are given intentionally
- If RhD positive platelets must be transfused to an RhD negative female of child bearing potential, post-transfusion treatment with RhIG **is recommended**

References:

14. Bhella S, 2012.

9.5 MASSIVE TRANSFUSION IN A PATIENT WITH ALLOANTIBODIES

- Provision of antigen negative units to patients with alloantibodies may not be possible during massive transfusion due to the volume of blood required
- If antigen positive units were transfused during active bleeding, subsequent transfusion should be with antigen negative units wherever possible
- The Medical Director, Transfusion Medicine (or delegate) must advise the treating physicians that incompatible units were transfused, advise of the risk of a delayed hemolytic transfusion reaction, and recommend the appropriate laboratory parameters to be monitored

REFERENCES

25. Callum JL, 2016.
27. CBS, Clinical Guide to Transfusion, 2011.
48. Dzik WH, 2011.
59. Goodnough LT, 2011.
142. Young PP, 2011.

9.6 TRANSFUSION MANAGEMENT OF AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA)

Policy	The Transfusion Medicine Service has established policies and guidelines to assist in the management of patients with AIHA.
Reason	Patients with auto-antibodies requiring transfusion may pose difficulties with compatibility testing, and may be at risk for hemolytic transfusion reactions and/or developing alloantibodies. The Transfusion Medicine Service may be asked to determine whether the autoantibody exhibits blood group antigen specificity or, in the presence of cold autoantibodies, whether it shows a clinically significant thermal amplitude and titre.
Responsibilities of the Medical Director, Transfusion Medicine	• Be aware of such patients and oversee the laboratory investigations, and provide guidance to Transfusion Medicine Service Staff, and consultative advice to attending physicians • Advise treating physicians of the likely duration of delay in obtaining compatible blood, and where appropriate discuss possible transfer of the patient to specialized centre with the necessary range of pre-transfusion testing ability • Establish the policies, processes and procedures for release of incompatible blood in medical emergencies when complete pre-transfusion testing is not possible ***Note: the term "least incompatible" should never be used as there is no clinical evidence to support that the survival of transfused red blood cells can be predicted based on the strength of a serological reaction***
Responsibilities of Transfusion Medicine Service staff	• Perform appropriate technical procedures • Expedite investigations to obtain compatible blood as promptly as possible, or to exclude the possibility of underlying alloantibodies when compatible blood cannot be obtained • Consult with the technical supervisor and/or the Medical Director, Transfusion Medicine (or delegate) as indicated in technical procedures, or as necessary based on the technologist's skills and experience, additional clinical information or results of laboratory examination • Be prepared to send appropriate blood samples to a reference centre or Canadian Blood Services for investigation when testing is beyond the scope of the hospital laboratory

Pre-transfusion examination	• Preliminary antibody investigation to determine whether the autoantibody exhibits any blood group antigen specificity • Examinations to determine whether there are any underlying alloantibodies, using additional technical devices such as autoadsorption, differential alloadsorption, pre-warming methods • So far as technically possible, determine the patient's red blood cell phenotype for clinically significant antigens using a pre-transfusion sample, or when not available by genotyping
Phenotype specificity	So far as possible, red blood cells provided for transfusion should not express clinically significant antigens which the patient lacks (at minimum, red blood cells should be matched for Rh and Kell antigens).
Patient management	• In a patient in stable condition, hemoglobin levels as low as 60 g/L may be tolerated, to try to avoid exposing the patient to transfusion and possible alloantibody development • In a symptomatic patient, blood transfusion should not be withheld even if the pre-transfusion investigation has not been completed • Patients failing to respond to RBC transfusion with an adequate post-transfusion rise in Hb or who show evidence of hemolysis post-transfusion should be investigated for incompatibility • Patients must be monitored closely for signs and symptoms of acute hemolysis and for response to each unit with a Hb estimation • If autoantibody demonstrating 'e' like specificity and patient is E negative, blood selected for transfusion should be E negative rather than e negative

REFERENCES

2. AABB, 2017.
10. Barros MMO, 2010.
15. Blackall DP, 2011.
55. Garratty G, 2010.
97. Ness PM, 2006.
103. Petz LD, 2003.

9.7 TRANSFUSION SUPPORT FOR PATIENTS FOLLOWING SOLID ORGAN OR ALLOGENEIC BONE MARROW OR STEM CELL TRANSPLANT

Policy	The Transfusion Medicine Service in Centres performing transplant procedures shall have policies, processes and procedures to address the special needs of transplant patients for blood transfusion. In hospitals that are not transplant centres, the Transfusion Medicine Service providing post-transplant care will be guided by the transfusion policies and practices of the Transplant Centre where the transplant procedure was carried out.
Reason	Recipients of non-identical ABO/Rh organs or stem cells may demonstrate blood typing anomalies and may be at risk for hemolytic events. Transplant patients may be discharged to their community prior to complete recovery. Transfusion policies may not be identical for all transplant centres.
Responsibilities of the Medical Director, Transfusion Medicine	**Transplant Centre:** • Establish policies, processes and procedures to address the particular problems of post-transplant blood transfusion practice in patients receiving non-identical ABO/Rh group organs/stem cells • When such patients are discharged to the community, establish a mechanism to ensure that the Transfusion Medicine Service and the treating physician in that community are informed as to how the patient's particular transfusion requirements should be met • Patients should be informed in writing of their transfusion requirements **Receiving hospital**: • Be aware of post-transplant patients and their particular needs as communicated by the transplant centre staff • Liaise with the treating physician to accommodate the patient's particular requirements • Inform Transfusion Medicine Service staff of the patient's particular requirements and ensure they are entered in the patient's Transfusion Medicine Service record
Responsibilities of Transfusion Medicine Service staff	• Follow associated technical procedures • Check the patient record for specific instructions regarding irradiation and blood group requirements • Consult with the Medical Director, Transfusion Medicine (or delegate) as indicated by procedures or circumstances

REFERENCES

38. Cohn CS, 2015.
41. Daniel-Johnson J, 2011.
104. Petz LD, 1987
126. Slichter SJ, 1998.

9.8 TRANSFUSION SUPPORT OF PATIENTS WITH SICKLE CELL SYNDROMES

Policy	The Medical Director, Transfusion Medicine and appropriate medical/surgical staff jointly establish policies, processes and procedures for the management of patients with sickle cell syndromes requiring blood transfusion.
Reason	Patients with sickle cell syndromes (homozygous sickle cell disease, hemoglobin S/C disease, hemoglobin S/beta-thalassemia) have particular transfusion requirements because of: • Increased blood viscosity due to presence of high concentrations of HbS • Increased liability to allo-immunization and risk of hemolytic transfusion reactions as a result of frequent red blood cell transfusion and genetic differences between sickle cell patients and the general blood donor pool
Responsibilities of the Medical Director, Transfusion Medicine	• Ensure that patients with sickle cell syndromes are so identified in the Transfusion Medicine Service records • Ensure that information on the patient's extended red blood cell phenotyping test results are recorded in the Transfusion Medicine Service records • This information may be obtained: » By referring appropriate samples to a reference laboratory or CBS » By contacting Central Ontario CBS Registry of patients with sickle cell syndromes. (Central Ontario only 416-313-4675) • Establish policies, processes and procedures to optimize the extended phenotypic matching of donor red blood cells to patients requiring transfusion • Establish guidelines for red blood cell transfusion in sickle-cell patients because of significant differences in transfusion indications in different clinical situations in this patient population • Where appropriate, consult with an expert in transfusion medicine in cases presenting challenges in clinical decision-making regarding transfusion support • Consult with the treating physician regarding the provision of suitable donor red blood cells in a clinically appropriate time frame • Ensure that any equipment used for exchange transfusion and the competency of staff operating the equipment meets Canadian Standards Association requirements (CAN/CSA)
Responsibilities of Transfusion Medicine Service staff	• Follow policies and procedures as written • Notify the Medical Director, Transfusion Medicine when informed of a request for red blood cells for transfusion, or otherwise, of the presence of a sickle cell syndrome patient in the hospital if unable to obtain appropriate red blood cells and/or order is outside of sickle cell transfusion guidelines
Responsibilities of the treating physician	• To work with the Medical Director, Transfusion Medicine to arrange the optimal red blood cell transfusion regime in a clinically timely fashion. This may involve: » Simple red blood cell transfusion » Exchange transfusion of red blood cells » Transfer to a centre experienced in management of transfusion in patients with sickle cell syndromes

Special considerations	• In the absence of symptoms (e.g. heart failure, dyspnea, hypotension, severe fatigue) transfusion should be avoided unless the hemoglobin level is decreased to <50 g/L in the setting of uncomplicated vaso-occlusive crisis • In the treatment or prevention of sickle cell complications the hemoglobin level should never be increased above 100 g/L • Improvement in tissue oxygen delivery is better achieved through decreasing the HbS percentage than simply by raising the hemoglobin concentration • Blood matched for extended blood group phenotype is desirable to reduce allo-immunization in individuals liable to require frequent transfusion » Non-immunized, Rh/Kell only » Allo-immunized, extended (Rh, Kell, Duffy, Kidd, MNS) • Sickledex® positive red blood cells should not be used for exchange transfusion if possible, as this complicates calculation of its effectiveness • For recommendations in particular cases, the literature or a medical centre specializing in care of sickle cell syndromes should be consulted

REFERENCES

25. Callum JL, 2016.
73. Josephson CD, 2007.
96. National Institutes of Health, 2014.
136. Vichinsky EP, 2012.
138. Winkler AM, 2012.
140. Yawn BP, 2014.
141. Yazdanbakhsh K, 2012.

10.0 DISASTER AND CONTINGENCY PLANS

Policy	The Transfusion Medicine Service has written plans for internal and external disasters and for contingency situations occasioned by blood shortages. These plans are stored centrally, updated as required and include up-to-date contact information.
Reason	The Transfusion Medicine Service is a vital function in the case of internal or external disasters and critical blood shortages. The CSTM and CSA Standards require the establishment of a Disaster Plan and a Contingency Plan for blood shortages in respect of Transfusion Medicine Services consistent with suppliers' contingency plans and health authority requirements. The Ontario Ministry of Health and Long Term Care requires all health care facilities within Ontario to establish a hospital based contingency plan for the management of blood shortages in alignment with the Ontario Provincial Contingency Plan for the Management of Blood Shortages as well as the National Plan for the Management of Shortages of Labile Blood Components.
Applies to	External and internal disasters and critical blood shortages as defined by the Ontario Ministry of Health and Long Term Care: Contingency Planning for Blood Shortages and the National Advisory Committee on Blood and Blood Products: National plan for the management of shortages of labile blood components.
Responsibilities of the Medical Director, Transfusion Medicine	• Cooperate with other departments or organizations to develop plans appropriate to the level and nature of services provided by the Transfusion Medicine Service • Ensure that the hospital is aware of and includes the Transfusion Medicine Service in its own disaster plans • Ensure that the hospital meets the provisions of the National and Provincial Contingency Plans for Management of Blood Shortages including the establishment of a hospital based plan and a Hospital Emergency Blood Management Committee (HEMBC). • Cooperate with other departments and/or other organizations to plan and execute mock exercises to ensure the Transfusion Medicine Service can respond appropriately in case of a disaster or critical blood shortage.
Responsibilities of Transfusion Medicine Supervisor	• Review the plans annually, and update contact information as required • Ensure staff are trained appropriately to respond to a disaster or notification of a blood shortage • Update inventory levels as appropriate for hospital activities
Responsibilities of Transfusion Medicine Service staff	• Be familiar with and follow the provisions of the plan when it is implemented • Participate in disaster and critical blood product shortage contingency exercises • Cooperate with other departments and/or organizations as needed in disaster or critical blood product shortage situations
Scope of Disaster Plan	• The following basic information is included in the plan: » Communication with hospital and regional disaster teams » Communication with other hospital transfusion medicine services » Communication with CBS » Communication with patients and hospital staff » Call list for all staff » Roles and responsibilities of staff. » Management of current inventory if applicable (e.g. moving to safe and accessible storage) » Ability to obtain and store new inventory from suppliers or other centres » Optimal use of limited inventory

	• Where the disaster involves a large number of local casualties, provision for the following is also included in the plan: » Triage of limited inventory » Recipient identification and examination » Specific group O RhD negative requirements » Staffing of the Transfusion Medicine Service » Computer downtime processes
Scope of the Contingency Plan for Management of Blood Product Shortages	• Types of Shortages (as defined by CBS inventory levels): "Green" phase (optimal) >3-4 days of average daily use "Green Advisory" phase (minimal decrease) more than 3 successive days of < 2-3 days of average daily use of selected red cell groups "Amber" phase (serious) 2-3 days of average daily use "Red" phase (critical) < 2 days of average daily use "Recovery" phase – gradual resumption of normal transfusion activity in keeping with increasing inventory levels • Preparedness for responding to blood shortages » Develop hospital contingency plan for shortages » Define inventory levels by blood shortage phase and reduce target levels to reduce amount of blood requested from CBS » Identify blood conservation opportunities » Identify surgeries with high blood loss that require to be postponed » Define stepwise reduction of blood use to occur on activation of plan » Identify key stakeholders to be identified on activation of the plan » Develop communication protocol to be used for notification » Ensure plan for managing blood shortages is integrated into the Disaster Plan and/or hospital wide pandemic plan » Provide training on the contents of the plan and communication measures related to blood shortages » Prepare detailed procedures to be followed should an "Amber" or "Red" phase shortage level be identified » For details of desirable measures, consult the Ontario Contingency Plan for Management of Blood Product Shortages and the National Advisory Committee on Blood and Blood Products Plan for the Management of Shortages of Labile Blood Components (see references below) • Establishment of an Emergency Blood Management Committee (EBMC) » Each hospital should establish an Emergency Blood Management Committee to decide on strategies and measures to be implemented when the hospital is notified of impending shortages » Committee may include Medical Director, Transfusion Medicine, Manager responsible for the Transfusion Service, an anesthetist, surgeon, hematologist/oncologist, ER staff physician, chair of the Transfusion Committee, Transfusion Nursing Specialist, Risk Manager and other members deemed appropriate » For "Red phase" alerts, the EBMC may be expanded to include senior hospital management and senior medical and nursing staff » Principal features of the terms of reference for an EBMC are outlined in the Ontario Contingency Plan and Toolkit » One of the important duties of the EBMC will be the triage of blood order requests to optimize use of available inventory to meet the most urgent needs. Identification of a triage officer/team to perform triage of blood order requests is required in "red" phase shortages

REFERENCES

30. CSTM, version 4, 2017
45. AABB, 2008.
93. NAC, National Plan for the Management of Shortages of Labile Blood Components.
99. Ministry of Health and Long Term Care, Ontario Regional Blood Coordinating Network V3, 2016.

11.0 TRANSFUSION REACTIONS

Policy	The Transfusion Medicine Service has established policies, processes and procedures for the identification, investigation and management of suspected transfusion reactions. All transfusion reactions should be reported according to Health Canada requirements. All transfusion reactions should also be reported to the national surveillance programs to which the hospital is a reporting participant.
Reason	While the care of the recipient is primarily the responsibility of the attending physician(s), some immediate and delayed transfusion reactions are sufficiently uncommon that physicians and nurses may be unfamiliar with their recognition and management. Thus, the Medical Director, Transfusion Medicine has an important role in the education of clinical staff in the diagnosis and management of transfusion reactions. Transfusion safety, transfusion practice and accreditation standards all require that facilities detect, manage, investigate and report such reactions.
Applies to	Recipients with suspected adverse reactions to blood components or products. The Public Health Agency of Canada (PHAC) defines an adverse reaction as: ***"An undesirable and unintended occurrence during or after the administration of blood, blood components, or blood products (plasma derivatives) whether or not considered to be related to the administration of these products."***
Responsibilities of the Medical Director, Transfusion Medicine	• Liaise with, communicate with, and promote the education of, clinical staff regarding the recognition, management, investigation and reporting of transfusion reactions • Determine the extent of investigation required on possible adverse reactions as defined above • Provide direction as necessary to technologists regarding the examinations to be performed • Report the final conclusion regarding the type of reaction in a timely manner • Sign off on all required documentation • Review the clinical and laboratory information on all transfusion reactions, assess the probability of a causal relationship between transfusion and the signs and symptoms, and if applicable categorize the reaction according to PHAC definitions (see users manual at PHAC website) • Advise the treating physician, when appropriate, on the investigations, possible management and strategies to avoid future adverse reactions • Ensure that CBS or the plasma protein product manufacturer is immediately informed in cases where a component/product-attribute issue (e.g. bacterial contamination) is linked to a transfusion and another recipient may be at risk • Ensure that CBS or the plasma protein product manufacturer is contacted promptly, and in any case within 24 hours, if a death is linked to transfusion • Report the result of assessment of the putative adverse reaction to the required surveillance programs. There are currently two national surveillance programs: The Transfusion Transmitted Injury Surveillance System (TTISS) and the Transfusion Error Surveillance System (TESS). Not all hospitals report through these systems. Contact PHAC for more information if your hospital does not currently report to these systems and would like to do so • Engage clinical staff in the development of clinical practice documents for reporting transfusion reactions

Responsibilities of clinical staff	• Recognize and manage the signs and symptoms of a transfusion reaction • Confirm all unique identifiers for recipient and component/product to determine whether the transfused component/product was intended for the recipient • Complete a transfusion reaction report form and submit to the Transfusion Medicine Service • With any signs and symptoms for which the transfusion is to be terminated (i.e. other than urticaria/pruritis or mild non-hemolytic febrile reaction controlled with antipyretics) including IVIG-related reactions not resolved by ongoing transfusion care, send the following to the Transfusion Medicine Service: » The blood component/product with the remaining contents, sealed to avoid contamination » The attached administration set » Recipient post-reaction blood samples or a request for their collection » Recipient blood culture samples or request for their collection, if indicated by the nature of the reaction » Epinephrine should be readily available wherever transfusion is carried out (see also section 11.1) » First post-transfusion voided urine sample • Collaborate with laboratory staff in the development of clinical practice documents for reporting transfusion reactions
Responsibilities of Transfusion Medicine Service staff	• Based on the clinical information provided, complete an investigation in accordance with the policies, processes and procedures, and the guidelines laid out in sections 11.8 below • Send copies of completed transfusion reaction investigations to the required surveillance agencies (TTISS/TESS; CBS, Plasma protein product manufacturers) • At the request of the Medical Director, participate in the development of clinical practice and laboratory documents for the investigation and reporting of transfusion reactions. With Health Canada regulations, hospitals are required to report any reaction to a component where the hospital has modified it (washed, plasma reduced etc).

General Policies		
Clinical and Laboratory Teams	Every effort should be made to create and maintain a transfusion leadership team with clinical, technical and transfusion medicine physician representation that coordinates information in regard to transfusion practice and develops detailed documents that inform all staff involved in transfusion care on standardized optimal practice.	
Immediate contact – clinical staff with the Transfusion Medicine Service	The nursing staff in the clinical area will immediately contact the Transfusion Medicine Service to report reactions when: • A recipient identity check error is found in relation to a transfused recipient or • A transfused recipient shows any of the following; » Sudden spike in fever >1.5 C from pre-transfusion temp » Sudden onset of hypoxemia/dyspnea » Sudden onset of hypotension » New onset of red/brown urine	
Immediate contact – Transfusion Medicine Service staff with Medical Director, Transfusion Medicine (or delegate):	The Transfusion Medicine Service staff will immediately contact the Medical Director, Transfusion Medicine or delegate if they receive a report of a transfusion reaction with the following: • Recipient or component/product identity check error • Suspected bacterial contamination of the component/product • Sudden onset of hypoxemia/dyspnea • Sudden onset of hypotension • Hemoglobinuria reported in recipient's post-transfusion urine sample • If and when, the transfusion reaction investigation shows: » Abnormal results after completion of the primary investigation » Component/product is requested before the investigation is completed	
Premedication of recipient	• Premedication of recipients with anti-histamines or anti-pyretics is NOT recommended in the absence of a history of repeated allergic or febrile reactions • "Fever" is defined as a temperature ≥ 38°C AND an increase of ≥ 1°C above recipient's baseline temperature (oral temperature)	
Restarting transfusions	**Signs & Symptoms**	**Ongoing transfusion care**
	Urticaria/pruritis with any component/product: • Minor allergic reaction. • Absence of clerical error, anaphylaxis, serious symptoms. Medical assessment indicates transfusion may proceed.	• Close monitoring of vital signs
	• Fever » Temperature <39°C or fever is a consequence of an underlying condition. » Absence of clerical error, serious symptoms. » Medical assessment indicates transfusion may proceed.	• Close monitoring of vital signs
Use of surveillance data	• Track changes in reaction patterns for the institution and assess reactions in the wider hospital population for comparison • Provide information for the institution's Transfusion Committee to facilitate: » Identification of opportunities for improvement in clinical or laboratory transfusion practice » Initiation of process improvement projects	

<table>
<tr><td rowspan="4">Recipient assessment and monitoring</td><td colspan="3">The recipient is directly observed during initiation of the transfusion, and for the first 15 minutes of the transfusion. Vital signs are recorded as indicated below</td></tr>
<tr><td>Recipient category</td><td>Frequency of Vitals/Observation</td><td>Vital signs include</td></tr>
<tr><td>ALL</td><td>• Vital signs within 30 minutes prior to transfusion
• Observe for first 15 minutes, starting the transfusion slowly if clinical circumstances permit
• Vital signs 15 minutes after start of transfusion
• Vital signs at end of transfusion of each unit
• Vital signs and observation if a transfusion reaction is suspected</td><td>• Temperature
• Blood pressure
• Pulse rate
• Respiratory rate</td></tr>
<tr><td>High Risk:
Those with risk of cardiac overload, history of previous transfusion reaction, or clinically unstable recipients</td><td>• All of the above plus:
» Oxygen saturation
» Auscultation for recipients at risk for circulatory overload (TACO), e.g. elderly, pediatric, cardiac disease
• More frequent monitoring and observation as prescribed by the ordering physician</td><td></td></tr>
<tr><td>Unconscious</td><td>• Continuous monitoring</td><td></td></tr>
<tr><td>Laboratory investigation of suspected transfusion reactions</td><td colspan="3">• Laboratory investigation of transfusion reactions will depend on the type of reaction and the differential diagnostic possibilities
• All laboratories should have an algorithm and process for determining the investigation that is required</td></tr>
<tr><td>Retention of records of transfusion reactions</td><td colspan="3">• 10 years for recipients who have had serious transfusion complications or reactions
• Minimum of 5 years for all other recipients with transfusion reactions</td></tr>
<tr><td>Reporting of reactions to external agencies</td><td colspan="3">• All serious transfusion reactions must be reported within 24 hours to:
» Fresh blood and blood components: CBS
» Manufactured blood products: report to the individual manufacturer
» It is the manufacturer's responsibility to report all serious adverse reactions to Health Canada within 24 hours
• Preliminary report with full investigation to follow and complete report within 15 days. If fatality report must be complete within 24 hours</td></tr>
</table>

RESOURCES

1. TTISS-ON Ontario Guide for Reporting Transfusion Reactions, March 2017.
2. Health Canada regulations Guidance Document: Blood Regulations (mod Mar 2016) Health Products and Food Branch, Health Canada.

REFERENCES

25. Callum JL, 2016.
30. CSTM, version 4, 2017
31. CAN/CSA-Z902-5.
80. Lima A, 2015.
112. Transfusion Transmitted Injuries Surveillance System User's Manual, 2007.
122. Serious Hazards of Transfusion (SHOT), 2017.
131. Tinegate A, 2012.

TTISS-ON Transfusion Reaction Chart

Immediate Actions!

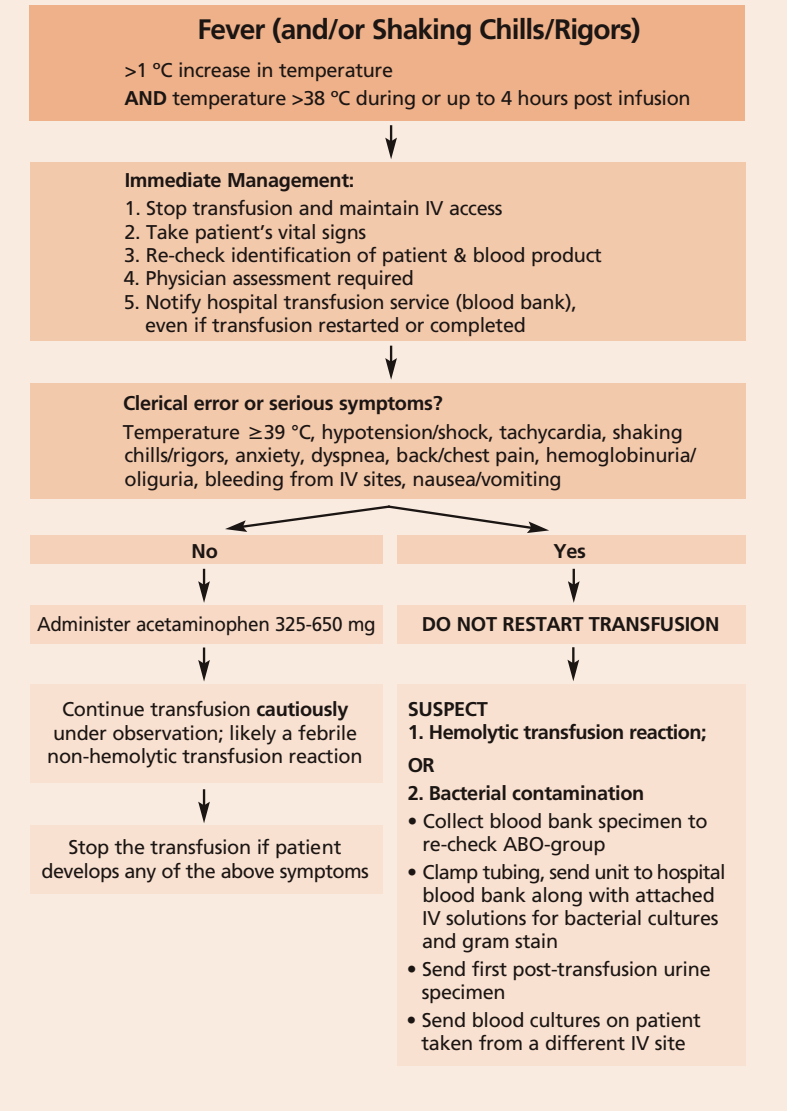
1. STOP the transfusion
2. Maintain IV access
3. Check vital signs
4. Re-check patient ID band and product label
5. Notify physician
6. Notify Transfusion Laboratory

Signs & Symptoms		Usual Timing	Possible Etiology	Recommended investigations	Suggested Treatment and Actions
Fever (at least 38° C and an increase of at least 1° C from baseline) **and/or** Shaking Chills/ Rigors	38°C to 38.9°C but **NO** other symptoms	During or up to 4 hours post transfusion	Febrile non-hemolytic transfusion reaction	No testing required	▲ Antipyretic ▲ With physician approval transfusion may be resumed cautiously if product still viable
	Less than 39°C but with other symptoms (e.g. rigors, hypotension) **or** 39° C or more	Usually within first 15 minutes but may be later	Febrile non-hemolytic transfusion reaction Bacterial contamination Acute hemolytic transfusion reaction	▲ Group & Screen, DAT ▲ Patient blood culture(s) ▲ Urinalysis If hemolysis suspected (e.g. red urine or plasma) ▲ CBC, electrolytes, creatinine, bilirubin, LDH, aPTT, INR, fibrinogen, haptoglobin, plasma Hb	**Do not restart transfusion** ▲ Antipyretic ▲ Consider Meperidine (Demerol®) for significant rigors ▲ If bacterial contamination suspected, antibiotics should be started immediately ▲ Monitor for hypotension, renal failure and DIC ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact_____
Urticaria (hives) Itching **or** Rash	Less than 2/3 body but **NO** other symptoms	During or up to 4 hours post transfusion	Minor allergic	No testing required	▲ Antihistamine ▲ With physician approval transfusion may be resumed cautiously if product still viable
	2/3 body or more but **NO** other symptoms	Usually early in transfusion	Minor allergic (extensive)	No testing required	**Do not restart transfusion** ▲ Antihistamine ▲ May require steroid
	Accompanied by other symptoms (e.g. dyspnea hypotension)	Usually early in transfusion	Anaphylactoid reaction/Anaphylaxis	▲ Group & Screen, DAT ▲ Chest X-Ray (if dyspneic) ▲ Blood gases (if dyspneic) ▲ Haptoglobin ▲ Anti-IgA testing	**Do not restart transfusion** ▲ Epinephrine ▲ Washed/plasma depleted blood products pending investigation ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact_____
Dyspnea **or** Decrease in SpO_2% to 90% or less (and change of at least 5% from baseline)	Typically with Hypertension	Within several hours of transfusion	Transfusion associated circulatory overload (TACO)	▲ Group & Screen, DAT ▲ Chest X-Ray ▲ Blood gases ▲ Urinalysis If sepsis suspected: ▲ Patient blood culture(s) If hemolysis suspected: ▲ CBC, electrolytes, creatinine, bilirubin, LDH, aPTT, INR, fibrinogen, haptoglobin, plasma Hb If anaphylaxis suspected: ▲ haptoglobin, Anti-IgA	**Do not restart transfusion** ▲ Diuretics, oxygen, High Fowler's position ▲ Return blood product to Transfusion Laboratory ▲ Slow transfusion rate with diuretics for future transfusions
	Typically with Hypotension	Within 6 hours of transfusion	Transfusion related acute lung injury (TRALI)		**Do not restart transfusion** ▲ Assess chest X-Ray for bilateral pulmonary infiltrates ▲ If TRALI may require vasopressors and respiratory support ▲ If bacterial contamination suspected, antibiotics should be started immediately ▲ Monitor for hypotension, renal failure and DIC ▲ If anaphylaxis suspected, epinephrine ▲ Return blood product to Transfusion Laboratory ▲ For additional assistance, contact_____
		Usually within first 15 minutes but may be later	Bacterial contamination Acute hemolytic transfusion reaction Anaphylaxis		

* Ontario Transfusion Transmitted Injuries Surveillance System (TTISS-ON)

version 2.1 January 2016 *Originally printed in Bloody Easy Blood Administration*

Table 11.2 Algorithm for management of transfusion – associated fever



REFERENCES

4. AABB, 2012.
18. Brecher ME, 2015.
23. Callum JL, 2011.
37. Cohen, 2017.
44. Delaney M, 2016.
80. Lima A, 2015.
102. Perotta PL, 2001.
134. Vamvakas EC, 2009.

11.1 URTICARIA AND OTHER ALLERGIC REACTIONS

Minor allegic reaction – urticaria/pruritus	• Etiology: • Unclear, but relates to factors in plasma portion of component or in the product
Clinical features	• A single to widespread urticarial lesions • May be associated with pruritus, erythema, mild upper respiratory symptoms, nausea, diarrhea
Management	• Interrupt the transfusion • Give diphenhydramine 25-50 mg po or IV depending on severity of the reaction • Transfusion may be restarted slowly if the urticarial rash involves less than 2/3 of body surface and no associated symptoms suggesting severe allergic reaction

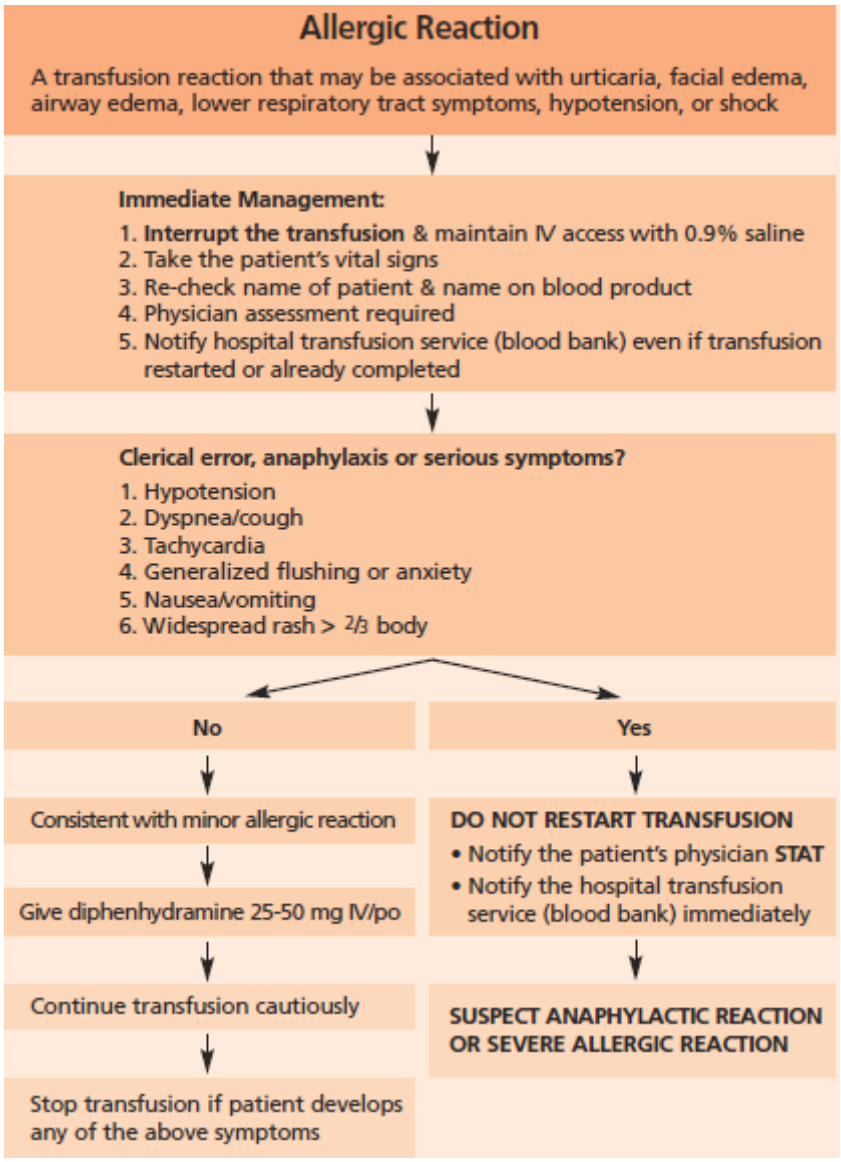
Prevention	• For recurrent urticarial reactions, the following measures (of uncertain efficacy) may be used:
	  » Premedication with diphenhydramine and/or corticosteroids
	  » Plasma depletion of red blood cells or platelets
	  » Washing red blood cells or platelets (see section 6.9)

Severe Allergic Reaction/ Anaphylaxis	• Usually unexplained • Sensitivity to IgA or haptoglobin in a patient with deficiency of these • Sensitivity to polymorphic forms of plasma proteins • Sensitivity to allergens or drugs in donor plasma
Clinical features	• Immediate to 45 minutes after start of transfusion • Severe urticaria - >2/3 body area • Upper or lower airway obstruction, may be severe • Hypotension • Gastrointestinal symptoms • Potentially life-threatening

Management	• Stop the transfusion. Do not restart
	• Severe allergic reaction – urticaria >2/3 of body area
	  » 25-50 mg diphenhydramine IV
	• Anaphylaxis
	  » Promptly administer epinephrine, corticosteroids, diphenhydramine, vasopressors and supportive care as required
	  » Ventilatory support as required
	  » Epinephrine should be readily available wherever transfusion is carried out

Prevention	• Premedication with intravenous steroids and diphenhydramine
	• Determine IgA status of the patient
	• Test for anti-IgA regardless of status
	• Where the patient is IgA deficient with anti IgA the following products may be recommended:
	  » IgA deficient components available from CBS
	  » Washed red blood cells or platelets (see section 6.9)
	  » If patient is of Asian extraction, test for haptoglobin deficiency

Table 11.3 Management Algorithm for Allergic Reactions



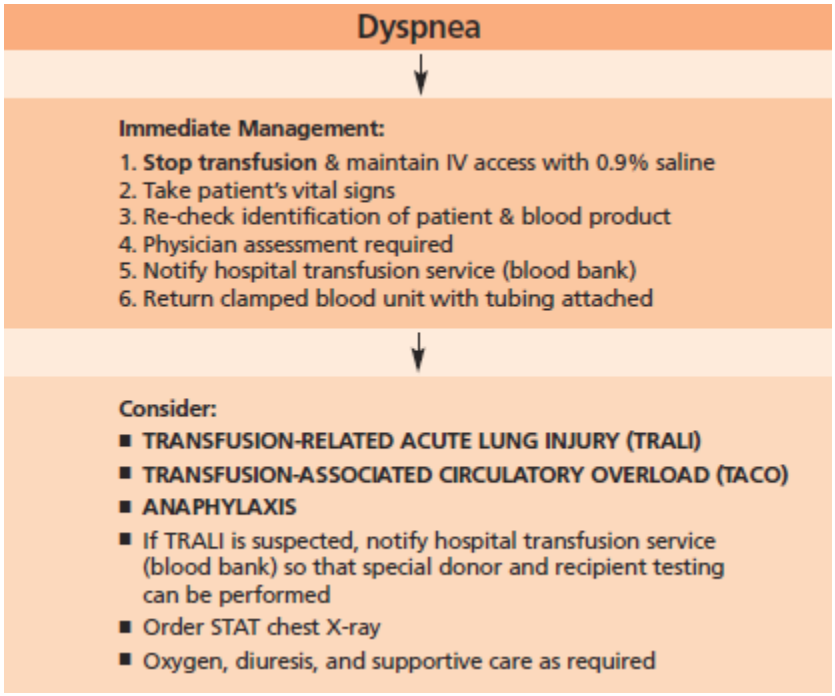
REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
57. Gilstad CW, 2003.
102. Perotta PL, 2001.

11.2 DYSPNEA

Transfusion-related acute lung injury (TRALI)	**Etiology** Two mechanisms have been postulated: • Passive transfer of HLA or granulocyte antibodies to recipient from a donor sensitized by previous pregnancy or transfusion • Biologic response modifiers in the transfused component with a susceptible recipient
Clinical features	• Acute onset of dyspnea during or within 6 hours of transfusion. • Hypoxemia • Bilateral lung infiltrates on radiograph • No evidence of circulatory overload (see 11.3) • Predisposing factors include direct lung injury (e.g. aspiration, pneumonia, toxic inhalation) and indirect lung injury (e.g. severe sepsis, multiple trauma, burn injury)
Investigation	• Accurate diagnosis and reporting to the hospital Transfusion Medicine Service is essential to identifying implicated donors • Patient and donor testing for implicated antigens/antibodies should be arranged through CBS
Management	• Stop the transfusion and check vital signs • Check identification of patient and component label • Return residual component and clamped tubing to the Transfusion Service laboratory • Supportive care, including mechanical ventilation as necessary • Diuretics and steroids are not believed to be useful
Prevention	• Deferral of donors confirmed to be implicated in an episode of TRALI • Component strategies to reduce the risk of TRALI include: » Plasma for transfusion from male donors only » Buffy coat platelet pools re-suspended in male plasma » Apheresis single donor platelets collected only from male and never pregnant females

Table 11.4 Management Algorithm for Dyspnea



REFERENCES

4. AABB, 2012.
11. Benson AB, 2009.
25. Callum JL, 2016.
58. Goldman M, 2005.
109. Popovsky MA, 2010.
134. Vamvakas EC, 2009.

11.3 TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD (TACO)

TACO	Etiology • Impaired cardiac or renal function • Excessively rapid rate of transfusion • Elderly patients, infants and euvolemic severely anemic patients • Common and under-diagnosed
Clinical features	• Dyspnea and orthopnea • Cyanosis • Increased venous pressure • Tachycardia, hypertension
Investigation	• Cardiac assessment • Chest X-ray
Management	• Interrupt the transfusion • Administer diuretics intravenously and oxygen as needed • Consider restarting transfusion at reduced rate if clinical status allows and component is still within standard time limits
Prevention	• Pre-transfusion assessment to identify patients at risk • Measures at time of transfusion include: » Transfuse only one unit at a time and over longer time period up to 3.5 hours from time of issue from Transfusion Medicine Service » Pre-emptive diuretics » Oral furosemide in low risk patients » IV furosemide in high risk patients » Transfuse components in smaller (“split”) aliquots
Anaphylaxis	See section 11.1

REFERENCES

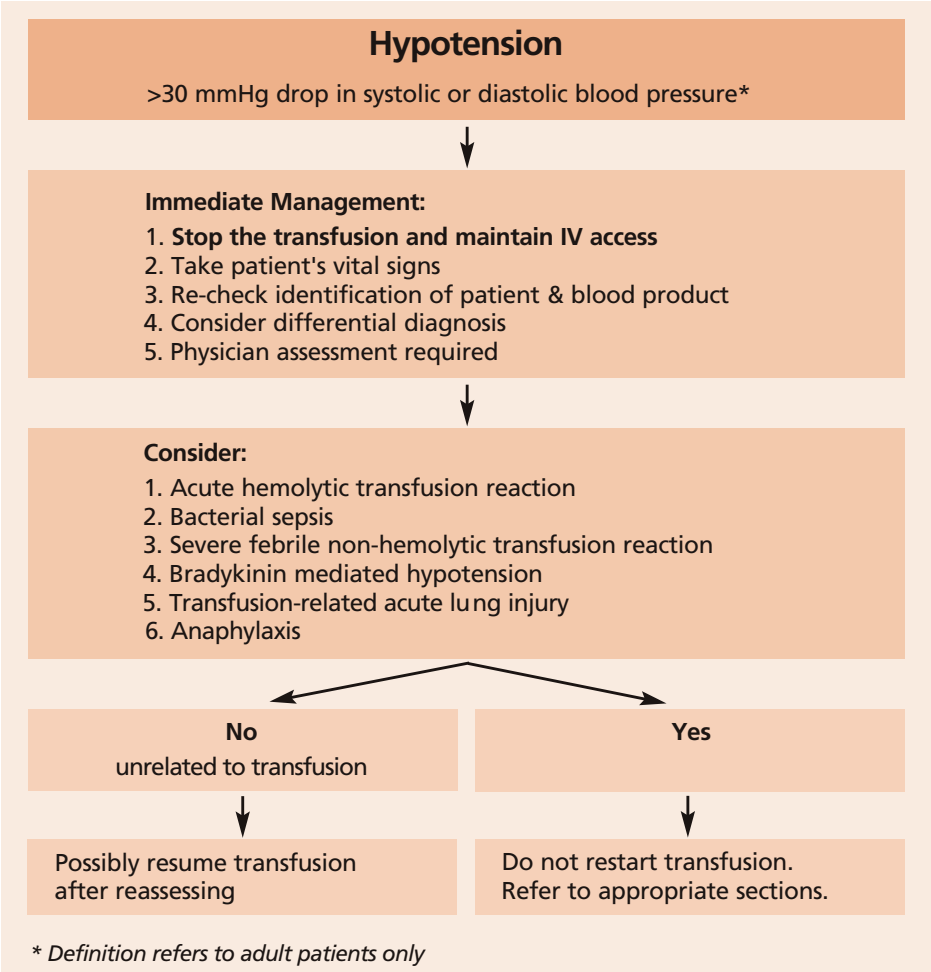
25. Callum JL, 2016.
35. Clifford L, 2017.
79. Lieberman L, 2013.
91. Narick C, 2012.
102. Perotta PL, 2001.
109. Popovsky MA, 2010.

11.4 HYPOTENSION (BRADYKININ MEDIATED)

Defined as a >30 mmHg fall in systolic or diastolic blood pressure (in adults only).

Hypotension	**Etiology** • Genetic polymorphism leading to decrease in bradykinin degradation • Use of angiotensin converting enzyme inhibitors » Hypotension may be a part of the constellation of signs in other transfusion reactions, including acute hemolytic reactions, bacterial sepsis, severe febrile non-hemolytic transfusion reactions, TRALI or anaphylaxis
Clinical features	• Majority occur with platelet transfusions • Often associated with use of ACE inhibitors • Other symptoms may include nausea, vomiting, dyspnea and urticaria • Rarely associated with significant morbidity
Investigation	• Consider other potential causes of hypotension listed above
Management	• Detect early, during the monitoring of transfusion in the first 15 minutes • Stop the transfusion and do not restart • Provide supportive care including IV fluids • Consult with an expert in transfusion medicine if further transfusion is required
Prevention	• Where ACE inhibitors have been implicated, consider alternative anti-hypertensive agents

Table 11.5 Management Algorithm for Hypotension



** Definition refers to adult patients only*

REFERENCES

4. AABB, 2012
6. Arnold DM, 2004.
25. Callum JL, 2016.
39. Cyr C, 2001.
50. Eastland T, 2007.

11.5 CYTOPENIAS AFTER TRANSFUSION

Post-transfusion purpura (PTP)	**Etiology** • Transfusion of a platelet antigen positive component to a patient who lacks that antigen • 75% of cases involve HPA-1a positive platelets transfused to an HPA-1a negative recipient • Autologous platelet destruction occurs but the mechanism is unclear
Clinical features	• Occurs 1-24 days (median 9 days) after transfusion • Female:male ratio 5:1 as a consequence of sensitization in pregnancy • Platelet count <10 x 10^9/L in 80% of cases • Mortality about 8%, mainly intra-cranial hemorrhage • Thrombocytopenia lasts about 2 weeks if untreated with IVIG
Investigation	• Test patient plasma for platelet-specific antibodies (refer to CBS)
Management	• IVIG 1g/kg daily for 2 days; response expected within 4 days • Patients with PTP should be warned that they (and possibly relatives) are at risk for neonatal immune thrombocytopenia
Prevention	• Transfuse only with components negative for the appropriate antigen

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
86. McFarland JG, 2007.
102. Perrotta PL, 2001.

11.6 TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE (GVHD)

GVHD	**Etiology** • Due to an immune response mounted by donor lymphocytes against the recipient's HLA determinants • Occurs in immuno-compromised recipients, and • Immuno-competent recipients receiving a haplo-identical product
Clinical features	• Fever, rash, hepatic dysfunction and diarrhea 1-2 weeks post-transfusion • Overwhelming infections with mortality >90%
Investigation	• Diagnosis can be confirmed by skin, liver or bone marrow biopsy • Confirmation requires documentation of presence of donor lymphocytes (HLA typing or DNA analysis)
Management	• Treatment mostly ineffective • Survival is rare, and is attributed to immunosuppressive therapy
Prevention	• For patients at risk, irradiation of cellular components (red blood cells and platelets) is critical • Pre-storage leukoreduction does not completely eliminate the risk of GvHD • Indications for irradiation are detailed in section 6.8 • Patient at risk should have a card indicating the requirement for irradiated cellular components

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
76. Kopolovic I, 2015.
102. Perrotta PL, 2001.
119. Ruhl H, 2009.
134. Vamvakas EC, 2009.

11.7 RARE CAUSES OF TRANSFUSION-ASSOCIATED CYTOPENIA

- Transfusion-associated alloimmune thrombocytopenia:
  - Due to platelet-specific donor antibodies to recipient platelet antigens
- Transfusion-associated alloimmune neutropenia:
  - Due to neutrophil-specific donor antibodies to recipient neutrophil antigens

11.8 HEMOLYSIS AFTER TRANSFUSION

Delayed hemolytic transfusion reactions (DHTR)	**Etiology** • Results from formation of antibodies in the recipient to red blood cell allo-antigens from transfusion or exposure during pregnancy • Concentrations of antibody are below the level of detectability of antibody screen testing • Incidence is about 1 in 7000 units of red blood cells transfused
Clinical features	• Appear 3 – 14 days post-transfusion • Fall in hemoglobin, spherocytosis, reticulocytosis, elevated bilirubin, hemoglobinuria, elevated LDH • Positive DAT and antibody screen • Most are relatively benign, but occasional DHTRs present with severe hemolysis and renal failure may occur
Investigation	• Identification of the offending allo-antibody • Confirmation of the presence of the corresponding antigen on one or more of donor red blood cell units transfused • Confirmation of the absence of the corresponding antigen on the recipient's red blood cells
Management	• Supportive therapy as needed • Select only red blood cells "negative" for the antigen involved for subsequent transfusions
Prevention	• Avoid transfusion if possible • Use antibody screening methods with maximal sensitivity • Notify the patient and supply a wallet card and recommend medical alert bracelet with antibody information
Other possible causes of hemolysis after transfusion	• Transfusion-transmitted malaria or babesiosis • Use of hypotonic IV solutions with red blood cell transfusion • Medical device (warmer, cell saver) malfunction • Freezing or overheating of red blood cells • Transfusion of outdated red blood cells • Transfusion through small bore needle under pressure

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
42. Davenport RD, 2011.

11.9 ADVERSE REACTIONS TO INTRAVENOUS IMMUNOGLOBULIN (IVIG)

General policy	• In the event of an adverse reaction, stop the transfusion and assess the patient • If the reaction is minor, the transfusion may be continued at a reduced infusion rate • Report all adverse reactions to the Transfusion Medicine Service
Clinical features and management of reactions to IVIG	

Table 11.6 Adverse Reactions to IVIG

Reaction	Severity	Frequency**	Comment/Treatment
Anxiety, chills/fever, rash, flushing, headache, chest, back or abdominal pain, nausea/vomiting, tachycardia, hypo- or hypertension	Mild-moderate	Common	Slow or pause IVIG treatment. Symptomatic treatment. Recurrent reactions – pre-medicate and/or change to another manufacturer's IVIG product
Aseptic meningitis	Moderate	7 in 10,000[272]	Stop infusion. Administer analgesics. Usually resolves spontaneously in 24-48 hours
Anaphylaxis	Severe	Rare	Stop infusion. **May require epinephrine promptly.** Consider testing for IgA and anti-IgA (see page 63)
Acute renal failure	Severe	Rare (120 cases reported to FDA in 13 years)	Usually with sucrose-containing product (none currently licensed in Canada). Predisposing factors: age >65, diabetes mellitus, pre-existing renal insufficiency
Hemolysis	Mild-Severe	10%[273,274]	More common in non-group O patients
Thrombo-embolic events	Severe	0.5-1%[275]	Causative relationship not clearly established. Possibly related to increases in viscosity
Infectious disease transmission	Severe	No reported case since HCV in 1995.[276] No known case of transmission of HIV or HBV	Modern viral reduction measures are robust. Prion (vCJD) transmission remains an entirely theoretical risk

** Reactions are more likely with faster rates of infusion.

REFERENCES

4. AABB, 2012.
25. Callum JL, 2016.
33. Cherin P, 2016.
106. Pierce LR, 2003.
129. Stiem ER, 2013.

REFERENCES

1. American Association of Blood Banks. Guidelines for Informed Consent for Transfusion Medicine. AABB Press, Bethesda, MD, 2006.
2. American Association of Blood Banks. Technical Manual, 19th Ed. Fung, MK. AABB, Bethesda, MD, 2017.
3. American Association of Blood Banks. The evolving paradigm of patient blood management. Transfusion 2014;54:2581-2790.
4. American Association of Blood Banks. Transfusion Reactions 4th Ed. Popovsky MA. AABB Press, Bethesda, MD, 2012.
5. Anderson D, Ali K, Blanchette V et al. Guidelines on the Use of Intravenous Immune Globulin for Hematologic Conditions. Transfus Med Rev 2007; 21 (Suppl 1): S9-S56.
6. Arnold DM, Molinaro G, Warkentin TE et al. Hypotensive Transfusion Reactions can Occur with Blood Products that are Leukoreduced before Storage. Transfusion 2004; 44: 1361-1366.
7. Aubuchon JP, Puca K, Saxena S et al. Getting Started in Patient Blood Management. AABB, Bethesda, MD, 2011. Web. <www.aabb.org/pbm/Documents/112024.pdf>
8. Aubuchon, JP. Managing Change to Improve Transfusion Safety. Transfusion 2004; 44.9: 1377-1383.
9. Aubuchon, JP. The Role of Transfusion Medicine Physicians. Arch Path Lab Med, 1999; 123.8: 663-667.
10. Barros MMO, Blajchman MA, Bordin JO. Warm Autoimmune Hemolytic Anemia: Recent Progress in Understanding the Immunobiology and the Treatment. Transfus Med Rev 2010; 24:195-210.
11. Benson AB, Moss M, Silliman CC. Transfusion-Related Acute Lung Injury (TRALI): A Clinical Review with Emphasis on the Critically Ill. Br J Haematol 2009; 147: 431-443.
12. Berger M. Choices in IgG Replacement Therapy for Primary Immune Deficiency Diseases: Subcutaneous IgG vs. Intravenous IgG and Selecting an Optimal Dose. Curr Opin All Clin Immunol 2011;11: 532-538.
13. Berte LM, Nevalainen DE. Quality Systems for the Laboratory. ASCP Press. Chicago, IL, 2000.
14. Bhella S, Gerard L, Lin Y et al. Obstetric and Trauma Database Review at a Single Institution Finds the Optimal Maternal Age Restriction for the Transfusion of D Negative Blood to Women Involed in Trauma to be 45 Years. Transfusion 2012; 52.11: 2488-2489.
15. Blackall DP. How Do I Approach Patients with Warm-Reactive Antibodies?. Transfusion 2011; 51.1: 14-17.
16. Blajchman M, Goldman MA, Freedman J, Sher GD. Proceedings of a Consensus Conference: Prevention of Post-transfusion CMV Infection in the Era of Universal leukoreduction. Transfus Med Rev 2001; 15.1: 1-20.
17. Bodnaruk ZM, Wong CJ, Thomas MJ. Meeting the Clinical Challenge of Care of Jehovah's Witnesses. Transfus Med Rev 2004;18: 105-116.
18. Brecher ME, Hay SN. Bacterial Contamination of Blood Components. Clin Microbiol Rev 2015;18:195-204.
19. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant. Br J Haematol 2004; 126:11-28.
20. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the Use of Platelet Transfusions. Br J Haematol 2017; 176: 365-394.
21. British Committee for Standards in Haematology. Guidelines on Transfusion for Fetuses, Neonates and Older Children. Br J Haematol 2016;175: 784-828.

22. Callum JL et al. Reporting of Near-miss Events for Transfusion Safety. Transfusion 2001;41.10: 1204-1211.

23. Callum JL, Dzik WH. The Use of Blood Components Prior to Invasive Bedside Procedures: A Critical Appraisal In Transfusion Therapy: Clinical Principals and Practice, 3rd Ed. Mintz PD. AABB, Bethesda, MD, 2011; 1-35.

24. Callum JL, Karkouti K, Lin Y. Cryoprecipitate: the current state of knowledge. Transfus Med Rev 2009;23.3: 177-188.

25. Callum JL, Pinkerton PH, Lima A et al. Bloody Easy 4: Blood Transfusions, Blood Alternatives and Transfusion Reactions. A Guide to Transfusion Medicine, 4th ed. Ontario Regional Blood Coordinating Network, 2016.

26. Canadian Blood Services. Circular of Information for the Use of Human Blood and Blood Components. Web. <http://blood.ca/en/hospitals/circular-information>

27. Canadian Blood Services. Clinical Guide to Transfusion. Web. <http://professionaleducation.blood.ca/en/transfusion

28. Canadian Blood Services. Plasma Protein Products. Canadian Blood Services, 2011.Web. <https://blood.ca/en/hospitals/plasma-protein-products>

29. Canadian Society of Transfusion Medicine. Informed Consent: Position Paper. Web. <http://www.transfusion.ca>

30. Canadian Society of Transfusion Medicine. Standards for Hospital Transfusion Services. Version 4. 2017. Web. <http://www.transfusion.ca/Resources/Standards>

31. Canadian Standards Association. Standards for Blood and Blood Components. CAN/CSA-Z902-15.

32. Carson JL, Guyatt G, Heddle N et al. Clinical Practice Guidelines from the AABB. Red Blood Cell Transfusion Thresholds and Storage. JAMA 2016; 316: 2025-2035.

33. Cherin P, Marie I, Michallet EP et al. Management of adverse events in the treatment of patients with immunoglobulin therapy. Autoimm Rev 2016;15: 71-81.

34. Chow S, Salmasi G, Callum JL, Lin Y. Trimming the Fat with an IVIG Approval Process. Transfus Aph Sci 2012;46: 349 – 352.

35. Clifford L, Jia Q, Subramanian A et al. Anesthesiology. Risk factors and clinical outcomes associated with perioperative transfusion-associated circulatory overload. Anesthesiology 2017; 126:409-418.

36. Clinical Guidelines for Immunoglobulin Use. 2nd ed. United Kingdom Department of Health, 2011. Web. <http://www.gov.uk/government/publications/clinical-guidelines-for-immunoglobulin-use-second-edition-update>

37. Cohen R, Escorcia A, Tasmin F et al. Transfusion. Feeling the burn: the significant burden of febrile nonhemolytic transfusion reactions. Transfusion 2017;57:1674-1683.

38. Cohn CS. Transfusion support issues in hemopoietic stem cell transplantation. Cancer Control 2015;22:52-59.

39. Cyr C, Eastland T, Blais C et al. Bradykinin Metabolism and Hypotensive Transfusion Reactions. Transfusion 2001; 41: 136-150.

40. Dananayake T, Sime PJ, Phipps R, Blumberg N. Transfusion Therapy in Critical Care. In Transfusion Therapy. Clinical Principles and Practice, 3rd Ed. Mintz PD. AABB Press, Bethesda, MD, 2011; 323-337.

41. Daniel-Johnson J, Schwartz J. How Do I Approach ABO-Incompatible Hemopoietic Progenitor Cell Transplantation?. Transfusion 2011; 51: 1143-1149.

42. Davenport RD. Management of Transfusion Reactions. Transfusion Therapy. Clinical Principles and Practice, 3rd Ed. Mintz PD. AABB Press, Bethesda, MD, 2011;1-35.

43. Davis RE, Vincent CA, Murphy MF. Blood Transfusion Safety: The Potential Role of the Patient. Transfus Med Rev 2011;25: 12-23.

44. Delaney M, Wendel S, Bercovitz RS et al. Transfusion reactions: prevention, diagnosis, and treatment.

45. Disaster Operations Handbook, Version 2. American Association of Blood Banks, October 2008. Web. <www.aabb.org>

46. Domen RE. The Transfusion Medicine Service is an Integral and Important Component of the Hospital and Should Not be Outsourced. Transfus Sci 1997; 18: 565-573.

47. Dunbar NM, Ornstein DL, Dumont LJ. ABO incompatible platelets: risks vs. benefit. Curr Opin Hematol 2012;19:475-479.

48. Dzik WH, Blajchman MA, Fergusson D et al. Clinical review: Canadian National Advisory Committee on Blood and Blood Products – Massive Transfusion Consensus Conference 2011: Report of the Panel. Criti Care 2011;15.6: 242.

49. Dzik WH. How I do it: platelet support for refractory patients. Transfusion 2007; 47.3: 374-378.

50. Eastland T. Vasoactive Mediators and Hypotensive Transfusion Reactions. Transfusion 2007;47: 369-372.

51. Expert Working Group Guidelines for Red Blood Cell and Plasma Transfusion for Adults and Children. CMAJ 1997;156: S1-S24.

52. Farrell AM, Brazier M. Consent for Blood Transfusion. Brit Med J 2010;341: 539-541.

53. Feasby T, Banwell B, Benstead T et al. Guidelines on the Use of Intravenous Immune Globulin for Neurologic Conditions. Transfus Med Rev 2007; 21 Suppl 1: S57-S107.

54. Fung Kee Fung K, Eason E, Crane J et al. Prevention of Rh Alloimmunization. J Obst Gyn Can 2003;25: 765-673.

55. Garratty G. Advances in Red Blood Cell Immunology 1960 to 2009. Transfusion 2010; 50.3: 526-535.

56. George JN, Woolf SH, Raskob GE et al. Idiopathic Thrombocytopenic Purpura: A Practice Guideline Developed by Explicit Methods for the American Society of Hematology. Blood 1996; 88: 3-40.

57. Gilstad CW. Anaphylactic transfusion reactions. Curr Opin Hematol 2003; 10: 419-423.

58. Goldman M, Webert KE, Arnold DM et al. Proceedings of a Consensus Conference: Towards an Understanding of TRALI. Transfus Med Rev 2005;19: 2-31.

59. Goodnough LT, Daniels K, Wong AE et al. How We Treat: Transfusion Medicine Support of Obstetric Services. Transfusion 2011; 51: 2540-2548.

60. Goodnough LT, Shander A, and Spence R. Bloodless Medicine: Clinical Care Without Allogeneic Blood Transfusion. Transfusion 2003; 43.5: 668-676.

61. Goodnough LT. What is a Transfusion Medicine Specialist?. Transfusion 1999; 39.9: 1031-1033.

62. Gorlin JB, Mintz PD. Transfusion Associated Graft vs. Host Disease. Transfusion Therapy 3rd Ed. Mintz PD. AABB, Bethesda, MD, 2011;1-35.

63. Government of Canada. [Commission of Inquiry on the Blood System in Canada, final report] Commissioner, Horace Krever 1997.

64. Guideline for Implementation of Informed Consent for Blood and Blood Products. Provincial Blood Coordinating Office, British Columbia, 1999. Web. <http://www.pbco.ca/>

65. Guideline on the Administration of Blood Components. British Society of Haematology 2017. Web <http//:www.b-s-h.org.uk/guidelines/guidelines/administration-of-blood-components/>

66. Hamrock DJ. Adverse events associated with intravenous immunoglobulin therapy. Int Immunopharmacol 2006;6: 535-542.

67. Hume H, Kronkick JB, Blanchette VS. Review of the Literature on Allogeneic Red Blood Cell and Plasma Transfusions in Children. CMAJ 1997; 156.11: S41-S49.

68. Informed Consent Card and Mobile Application. Ontario Regional Blood Coordinating Network. 2014. Web. <http://www.transfusionontario.org/>

69. Institute for Quality Management in Healthcare. The IQMH Requirements and Guidance Information for Medical Laboratories, 2018 Web. <https://iqmh.org>

70. Immune Globulin Toolkit for Ontario. Ontario Regional Blood Coordinating Network. 2018. Web. <www.transfusionontario.org>

71. Intravenous Immune Globulin. Provincial Blood Coordinating Office, British Columbia. Web. <www.pbco.ca>

72. Josephson CD et al. Significant numbers of apheresis-derived group O platelet units have “high titre” anti-A/A,B: implications for transfusion policy. Transfusion 2004;44:805-808.

73. Josephson CD, Su LL, Hillyer KL, Hillyer CD. Transfusion in the Patient with Sickle Cell Disease: A Critical Review of the Literature and Transfusion Guidelines. Transfus Med Rev 2007; 21: 118-133.

74. Juskewitch JE, Norgan AP, De Goey SR et al. How do I...manage the platelet-refractory patient? Transfusion 2017;57:2828-2835.

75. Kaplan HS, Callum JL, Rabin Fastman B, Merkley LL. The Medical Event Reporting System for Transfusion Medicine: Will it Help Get the Right Blood to the Right Patient. Transfus Med Rev 2002; 16.2: 86-102.

76. Kopolovic I, Ostro J, Tsubota H et al. A systematic review of transfusion-associated graft-versus-host disease. Blood 2015;126:406-414.

77. Larsson LG, Welsh VJ, Ladd DJ. Acute intravascular hemolysis secondary to out-of-group platelet transfusion. Transfusion 2000;40: 902-906.

78. Lau W. Neonatal and Pediatric Transfusion. Clinical Guide to Transfusion. Canadian Blood Services, 2017. Web. <https://professionaleducation.blood.ca/en/transfusion/clinical-guide/neonatal-and-pediatric-tr

79. Lieberman L, Maskens C, Cserti-Gazdewich C et al. A retrospective review of patient factors. transfusion practices, and outcomes in patients with transfusion-associated circulatory overload. Transfus Med Rev 2013;27:206-212.

80. Lima A. Bloody Easy Blood Administration: A Handbook for Health Professionals, 2nd Ed. Ontario Regional Blood Coordinating Network. 2015

81. Lin Y, Callum JL. Emergency Reversal of Warfarin Anticoagulation. CMAJ 2004; 182: 2004.

82. Lin Y, Moltzan CJ, Anderson DR. The Evidence for the Use of Recombinant Factor VIIa in Massive Bleeding: Revision of the Transfusion Policy Framework. Transfus Med 2012; 22: 383-394.

83. Lozano M, Cid J. The Clinical Implications of Platelet Transfusions Associated with ABO or Rh(D) Incompatibility. Transfus Med Rev 2003;17: 57-68.

84. Majeed A, Agren A, Holmstrom et al. Management of rivaroxaban- or apixaban-associated major bleeding with prothrombin complex concentrates: a cohort study. Blood 2017; 130: 1706-1712.

85. Martin A, Lavoie L, Goetghetbeur M, Schellenberg R. Economic Benefits of Subcutaneous Rapid Push Versus Intravenous Infusion Therapy in Adult Patients with Primary Immune Deficiency. Transf Med 2013;23:55-60.

86. McFarland JG. Post transfusion purpura. In Transfusion Reactions 3rd Ed. Ed. Popovsky MA. AABB Press, Bethesda, MD. 2007;275-299.

87. Michael M, Elliot EJ, Craig JC et al. Interventions for Hemolytic Uremic Syndrome and Thrombotic Thrombocytopenic Purpura: a systematic Review of Randomized Controlled Trials. Amer J Kid Dis 2009;53: 259-272.

88. Mollison's Blood Transfusion in Clinical Medicine, 12th Ed. Klein HG. Blackwell Scientific Publications, 2014:432-433.

89. Moltzan CJ, Anderson DA, Callum JL et al. The Evidence for the Use of Recombinant Factor VIIa in Massive Bleeding: Development of a Transfusion Policy Framework. Transf Med 2008;18: 112-120.

90. Murphy MF, Stanworth SJ, Yazer M. Transfusion Practice and Safety: Current Status and Possibilities for Improvement. Vox Sang 2011;100: 46-59.

91. Narick C, Triulzi DJ, Yazer MH. Transfusion-Associated Circulatory Overload after Plasma Transfusion. Transfusion 2012;52.1: 160-165.

92. National Advisory Committee on Blood and Blood products. NAC statement regarding appropriateness of use of Cytomegalovirus (CMV) Seronegative Versus CMV safe product(February 14, 2017) Web. www.nacblood.ca/resources/guidelines/CMV.html.

93. National Advisory Committee on Blood and Blood Products. National Plan for the Mangement of Shortages of Labile Blood Components and the Emergency Framework for Rationing of Blood for Massively Bleeding Patients During a Red Phase Blood Shortage. Web. <www.nacblood.ca/resources/shortages-plan/index.html>

94. National Advisory Committee on Blood and Blood Products. Recommendations for use of Prothrombin Complex Concentrates in Canada. 2014. Web. www.nacblood.ca/resources/guidelines/PCC-recommendations-final-2014-05-16.pdf.

95. National Advisory Committee on Immunization. Canadian Immunization Guide, 7th ed. The Public Health Agency of Canada, 2006. Web. <https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html>

96. National Institutes of Health. Evidence-based management of sickle cell disease: expert panel report, 2014. US Department of health and Human Services, National Heart, Lung and Blood Institute. Web. <https://www.nhlbi.nih.gov/guidelines>

97. Ness PM. How do I encourage clinicians to transfuse mismatched blood to patients with autoimmune hemolytic anemia in urgent situation? Transfusion 2006;46: 1859-1862.

98. Noga T, Bruce AAK, Blain H et al. Four-factor prothrombin complex concentrates in paediatric patients- a retrospective case series. Vox Sang 2016;110:253-257.

99. Ontario Contingency Plan for Management of Blood Shortages and Contingency Planning Toolkit. Ministry of Health and Long Term Care, Ontario Regional Blood Coordinating Network V3, 2016. Web. <http://transfusionontario.org/en/download/ontario-hospital-toolkit-for-emergency-blood-management/ >

100. Ontario Regional Blood Coordinating Network. Transfusion Committee Handbook V2, 2016. Web. <http://transfusionontario.org/en/download/transfusion-committee-handbook-version-2/ >

101. Pediatric Transfusion: A Physician's Handbook, 4th Ed. Rosoff SD. AABB Press, Bethesda, MD. 2014.

102. Perrotta PL, Snyder EL. Non-infectious Complications of Transfusion Therapy. Blood Rev 2001; 15: 69-83.

103. Petz LD, Garratty G. Immune Hemolytic Anemias. Churchill Livingstone, Philadelphia, PA. 2003.

104. Petz LD. Immunohematologic Problems Associated with Bone Marrow Transplantation. Transfus Med Rev 1987; 1:85-100.

105. Phekoo KH, Hambly H, Sehey SA et al. Audit of Practice in Platelet Refractoriness. Vox Sang 1997; 73: 81-86.

106. Pierce LR, Jain N. Risks Associated with the Use of Intravenous Immunoglobulin. Transfus Med Rev 2003;17: 241-251.

107. Pinkerton PH, Callum JL. Rationalizing the Clinical Use of Frozen Plasma. CMAJ 2010;182: 1019-1020.

108. Popovsky MA, Triulzi D. The Role of the Transfusion Medicine Consultant. Amer J Clin Path 1996;105: 798-801.

109. Popovsky MA. To Breathe or Not to Breathe – That is the Question. Transfusion 2010; 50.9: 2057-2062.

110. Prokopchuk-Gauk O, Solhz. CMV seronegative, irradiated and washed blood components. Canadian Blood Services: Clinical Guide to Transfusion. 2017; chapter 15.

111. Provincial Frozen Plasma and Prothrombin Complex Concentrate Audit Report. Ontario Regional Blood Coordinating Network, 2013. Web. <http://transfusionontario.org/en/documents/?cat=frozen-plasma-audits-blood-utilizati

112. Public Health Agency of Canada. Transfusion Transmitted Injuries Surveillance System. User's Manual, V3.0. Minister of Health, Ottawa, November 2007. Web. <www.phac-aspc.gc.ca>

113. Reading and Recording Gel Reactions using MTS Columns. Ontario Regional Blood Coordinating Network. Doc. GM.001. 2014. Web. < http://transfusionontario.org/en/download/gm-001-reading-and-recording-gel-reactions-using-mts-columns/

114. Reading and Recording Hemagglutination Reactions, OTTRM. Ontario Regional Blood Coordinating Network. Doc. RT.001. 2014 Web. http://transfusionontario.org/en/download/rt-001-reading-and-recording-hemagglutination-reactions/

115. Recommendations for use of Prothrombin Complex Concentrates in Canada. National Advisory Committee on Blood and Blood Products, 2011. Web. <www.nacblood.ca/resources/guidelines/nac-pcc-recommendations-june-2011-final.pdf>

116. Reid ME, Oyen R, Marsh WL. Summary of the Clinical Significance of Blood Group Alloantibodies. Sem Hematol 2000;37: 197-216.

117. Rock G, Anderson D, Clark W et al. Does Cryosupernatant Plasma Improve Outcome in Thrombotic Thrombocytopenic Purpura? No answer yet. Br J Haematol 2005; 129: 79-86.

118. Roseff SD, Luban NL, Manno CS. Guidelines for Assessing Appropriateness of Pediatric Transfusion. Transfusion 2002;42: 1398-1413.

119. Ruhl H, Bein G, Sachs UJH. Transfusion-associated graft-vs-host disease. Transfus Med Rev 2009; 23:62-71.

120. Sacher RA, Luban NLC, Strauss RG. Current Practice and Guidelines for Transfusion of Cellular Components in the Newborn. Transfus Med Rev 1989;3: 39-54.

121. Saxena S, Shulman IA. The Transfusion Committee: Putting Patient Safety First. AABB Press. Bethesda, MD, 2006.

122. Serious Hazards of Transfusion (SHOT). 2016 Annual SHOT Report, 2017. Web. <https://www.shotuk.org/2016-annual-shot-report-published-12-july-2017/>

123. Shehata N, Palda V, Bowen T et al.The Use of Immunoglobulin Therapy for Patients with Primary Immune Deficiency: An Evidence-Based Practice Guideline. Transfus Med Rev 2010; 24 (Suppl 1): S28-S50.

124. Shehata N, Palda VA, Meyer RM et al. The Use of Immunoglobulin Therapy for Patients Undergoing Solid Organ Transplantation: An Evidence-Based Practice Guideline. Transfus Med Rev 2010; 24 (Suppl 1): S7-S27.

125. Shehata N, Tinmouth A, Naglie G et al. ABO-identical versus non-identical platelet transfusion: a systematic review. Transfusion 2009; 49: 2442-2453.

126. Slichter SJ. Transfusion and Bone Marrow Transplantation. Transfus Med Rev 1998; 2: 1-17.

127. Speiss BD. Treating Heparin Resistance with Antithrombin or Fresh Frozen Plasma. The Ann Thor Surg 2008;85: 2153-2160.

128. Stanger SHW, Yates N, Wilding RJ, Cotton S. Blood Inventory Management: Hospital Best Practice. Transfus Med Rev 2012;26: 153-163.

129. Stiem ER. Adverse effects of human immunoglobulin therapy. Transfus Med Rev 2013; 27: 171-178.

130. Strauss R. Handbook of Pediatric Transfusion Medicine. Elsevier Academic Press, San Diego CA, 2004.

131. Tinegate A, Birchall J, Gray A et al. Guideline on the Investigation and Management of Acute Transfusion Reactions Prepared by The BCSH Blood Transfusion Task Force. Br J Haematol 2012;159: 143-153.

132. Tinmouth A. Evidence for a Rational Use of Frozen Plasma for the Treatment and Prevention of Bleeding. Transfus Aph Sci 2012;46: 293-298.

133. Treleaven J, Gennery A, Marsh J et al. Guidelines on the Use of Irradiated Blood Components Prepared by the British Committee for Standards in Haematology Blood Transfusion Task Force. Br J Haematol 2011; 152.1 : 35-51.

134. Vamvakas EC, Blajchman MA. Transfusion-Related Mortality: The Ongoing Risks of Allogeneic Blood Transfusion and the Available Strategies for their Prevention. Blood 2009; 113: 3406-3417.

135. Vamvakas EC. Is white blood cell reduction equivalent to antibody screening in preventing transfusion transmission of cytomegalovirus? A review of the literature and a meta-analysis. Transfus Med Rev 2005; 19: 181-199.

136. Vichinsky EP. The Prevention and Management of Alloimmunization in Sickle Cell Disease: The Benefit of Extended Phenotypic Matching of Red Blood Cells. Immunohematology 2012; 28.1: 20-23.

137. Watson H, Davidson S, Keeling D. Guidelines on the diagnosis and management of heparin induced thrombocytopenia, 2nd ed. Br J Haematol, 2012;159:528-540.

138. Winkler AM, Josephson CD. Transfusion Practices for Patients with Sickle Cell Disease at Major Academic Medical Centers Participating in the Atlanta Sickle Cell Consortium. Immunohematology 2012; 28: 24-26.

139. Yang L, Stanworth S, Hopewell S et al. Is Fresh-Frozen Plasma Clinically Effective? An Update of a Systematic Review of Random Controlled Trials. Transfusion 2012; 52: 1673-1686.

140. Yawn BP, Buchanan G, Afenyi-Annan AN et al. manage,ent of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014; 312: 1033-1048.

141. Yazdanbakhsh K, Ware RE, Norzat-Pirenare F. Red Blood Cell Alloimmunization in Sickle Cell Disease: Pathophysiology, Risk Factors and Transfusion Management. Blood 2012; 120.3: 528-537.

142. Young PP, Cotton BA, Goodnough LT. Massive Transfusion Protocols for Patients with Substantial Hemorrhage. Transfus Med Rev 2011; 25.4: 293-303.