NAC STATEMENT ON THE PROVISION OF RARE RED BLOOD CELLS

RARE BLOOD SUBCOMMITTEE

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TABLE OF CONTENTS

RARE BLOOD SUBCOMMITTEE 2
TABLE OF CONTENTS 3
ABBREVIATIONS 4
DEFINITIONS 4
1.0 BACKGROUND 5
2.0 RECOMMENDATIONS 5
2.1 General Principles 5
2.2 Indications 6
2.3 Additional Considerations 7
2.4 Inventory Management and Demand Forecasting 8
2.5 Outcomes Assessment 8
REFERENCES 9

ABBREVIATIONS

RBP	Rare Blood Program
RBC	Red blood Cell

DEFINITIONS

Extended Phenotype Matching – any form of matching of donor and recipient red cell antigens beyond ABO and RhD.

Red Cell Antigen Genotype – predicted blood group antigens detected using molecular genetic techniques.

High Prevalence Antigen – a blood group antigen present in more than 99% of a given population.

Patient Blood Management – a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment.[1]

Phenotype – profile of blood group antigens detected using serologic techniques.

Rare Blood – a phenotype (or combination of phenotypes) that occurs at a frequency of less than 1 in 1000, and by definition of the term "rare", is typically associated with limited available inventory and donors.

1.0 BACKGROUND

Individuals are defined as having a rare red cell phenotype (or combination) when that phenotype occurs at a frequency of less than 1 in 1000. The term “rare blood type” is associated with limited availability of red blood cell (RBC) inventory and donors.

The Rare Blood Program (RBP) at Canadian Blood Services functions to fulfill requests for rare RBC units through the testing and recruitment of donors and the maintenance and optimization of rare inventory. The RBP collaborates with the program at Héma-Québec (which is similar) and with the International Rare Donor Panel to obtain rare RBC units if none are available at Canadian Blood Services.

Because of limited availability, the provision of rare RBC units for a given patient must be balanced against the potential need for the same unit by other patients. This can be particularly challenging when there are multiple patient requirements at the same time. While requiring the same rare RBC units, these patients may have different transfusion risk profiles. For example, individuals undergoing a procedure with a minimal likelihood of transfusion need versus an individual requiring emergent exchange for sickle cell disease.

Currently, there is no standardized guidance on the clinical management and approach to patient needs for those with rare blood types in Canada. The absence of clinical management guidelines may place the RBP and the blood operator at odds with prescribing physicians in ensuring equitable access to rare RBC units. This situation may be further complicated when donor units are requested from international blood operators where guidelines are in place that do not support the clinical need for a particular situation as requested by Canadian prescribers.

The purpose of this guidance document is to align clinical care providers, hospital transfusion services and blood suppliers in the approach to transfusion management for those with rare blood types and to ensure equity in availability and utilization for patients. In addition, the documentation of this aligned approach is expected to facilitate the exchange of rare units with international blood suppliers, each of which may have different policies.

Basic assumptions of this guidance include that rare RBC units should only be issued after patient hemoglobin optimization strategies have been implemented, including management at a facility with an appropriate level of care such as specialized hematologic and/or surgical expertise, and when there is sufficient likelihood of transfusion to warrant issuing a rare RBC unit.

2.0 RECOMMENDATIONS

2.1 General Principles

2.1.1 Consultation

Ordering rare RBC units requires consultation between the hospital and the blood supplier RBP. Such consultation helps to ensure that there is a clear understanding of the timing and indication by the transfusion medicine service and the blood supplier and that there is a clear understanding of the inventory limitations by the prescribing health care provider.

From the hospital side, this consultation may include the ordering clinician, the transfusion service physician and/or the transfusion service laboratory staff. There should also be communication between the ordering physician and the hospital transfusion medicine laboratory prior to engaging the RBP. In some jurisdictions, consultation may occur directly between the RBP and the hospital patient blood management services, and/or hematology or transfusion consultants with awareness and support of the transfusion medicine laboratory. If a plan for ongoing transfusion management is in place, then repeat consultation may not be required for every recurring rare RBC unit order for the same patient and the same indication.

Additional important considerations include coordinated scheduling of planned surgery or delivery with the availability of rare RBC units intra- and post-operatively and liaison with surgical booking offices to prevent cancellations which could lead to wastage of precious units.

Triage of competing requests for limited rare inventory is the joint responsibility of the blood operator, the transfusion medicine physician and the most responsible physician for the patient. The principles used in a Red Phase blood shortage may apply, including additional considerations such as the likelihood of transfusion, when allocating rare RBC units.

2.1.2 Patient Optimization

Patient hemoglobin optimization is recommended in all rare blood patients and includes but is not limited to patient blood management principles such as:

- Hematinic supplementation;
- Avoidance of phlebotomy losses; and,
- Early pre-operative anemia management.

Patient referral to a center with expertise in transfusion medicine and bloodless surgical techniques should be considered.

Patients with rare blood needs may be best served in centres close to the blood supplier in order to facilitate use of rare frozen inventory prepared immediately prior to anticipated transfusion and/or which may facilitate transportation from supplier to hospital while minimizing risk of component outdates due to delays in shipments to remote locations.

2.1.3 Management of Frozen Units

Once thawed, rare RBC units must be transfused within a specified time and cannot be re-frozen. Hospitals should work with the blood operator RBP to avoid thawing of frozen rare RBC units that have a low probability of being transfused.

2.2 Indications

Decisions on use of rare RBC units for a planned transfusion require both donor and patient considerations.

From the blood supplier perspective, the accessibility of liquid units, the number of donors available for recruitment, the capacity to import (Héma-Québec or international suppliers),

estimated transport time and ability of the hospital to return unused liquid units to Canadian Blood Services are considered.

Factors that increase the likelihood of transfusion of the rare RBC units must also be considered. For example, the type of procedure, presence of anemia, iron levels, coagulopathy, obesity and/or other comorbidities may contribute to the requirement for rare RBC units to be on hand at a hospital.

Established indications for release of rare RBC units to the hospital transfusion service include:

- Patients with clinically significant antibodies to high prevalence antigens who have an active transfusion indication or are scheduled for a procedure with moderate to high risk of transfusion; and,
- Patients with multiple antibodies to common antigens which in combination result in a requirement for a rare RBC unit and who have an active transfusion indication or a scheduled procedure with a moderate to high risk of transfusion.

Circumstances where rare RBC units **are not required** include:

- Prophylactic matching for rare antigens (or rare combinations) to which the patient has not yet made a specific antibody, even when the patient is alloimunized against other common antigens, including sickle cell disease patients;[2] and,
- Patients with clinically significant antibodies to high prevalence antigens when the likelihood of transfusion is low.

2.3 Additional Considerations

2.3.1 Obstetrics

For routine low risk deliveries including those where routine pre-transfusion type and screen testing is not recommended,[3] there is no requirement for on hand availability of rare RBC units.

Cases where a pre-delivery type and screen and rare RBC unit availability is recommended, include (but may not be limited to) the following:

- Abnormal placentation including placenta accreta spectrum;
- Preeclampsia/hemolysis, elevated liver enzymes and low platelets syndrome;
- Hemoglobin <100g/L;
- History of prior hemolytic disease of the fetus and newborn;
- Known bleeding disorder;
- History of postpartum hemorrhage;[4] and,
- Other conditions with high risk for hemorrhage.[5]

When rare blood availability is deemed necessary, consultation with the RBP will help to determine whether that availability includes on site liquid units versus a frozen units at the blood center.

2.3.2 Neonatal

For cases where blood is on hand for use at delivery, the same rare RBC unit may be appropriate for neonatal transfusion if required. Additional risk factors for neonatal

transfusion may also be considered when determining the need for on site availability of rare RBC units. For example:

- Known fetal anemia;
- Prior intrauterine transfusion; and/or,
- Fetal or neonatal anemia with anticipated need for urgent post natal transfusion.

In situations involving intrauterine or neonatal transfusion with rare RBCs, prophylactic matching for other antigens such as RhD and or Kell may not be possible.

In neonates with the potential need for ongoing transfusion support, consideration of blood sparing techniques including limited blood draws, iron and erythropoietin therapy[6-8] are strongly recommended.

If a rare RBC unit is for pediatric, neonatal or fetal transfusion and not for exchange, the unit(s) must be aliquoted to maximize use of the total volume of the donor unit. Consideration should be given to transporting patients to a site where aliquoting can be performed or transporting rare RBC units to a hospital site where aliquots can be prepared and shipped to the transfusing site.

2.4 Inventory Management and Demand Forecasting

The following elements must be discussed in conjunction with the RBP:

- Estimating the likelihood of future transfusion requirements;
- The potential for future donation as a rare allogenic donor;[9]
- Family member/sibling assessment; and,
- Disposition management of any un-transfused units.

For patients who are expected to have ongoing transfusion requirements, a management plan is required.

2.5 Outcomes Assessment

Documentation of patient outcomes in rare blood transfusion cases is important to help establish guidance for future cases as published literature is currently limited. Considerations for extra counseling and guidance are as follows:

- Assessment of hemolytic disease of the fetus and newborn future risk;
- Assessment of sibling and offspring risk; and,
- Outcomes reporting for antigen-positive transfusions, including working with the RBP to report to the International Society of Blood Transfusion Rare Donor database with patient consent.

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