Platelet Transfusion Toolkit

Ontario Regional Blood Coordinating Network

Inspiring and facilitating best transfusion practices in Ontario.

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DISCLAIMER

CHOOSING WISELY CANADA RECOMMENDATIONS

The **Choosing Wisely Canada** (CWC) campaign seeks to promote avoidance of wasteful or unnecessary tests, treatments and procedures.

An increasing weight of evidence from clinical trials is accumulating to support the clinical benefits of restrictive rather than liberal transfusion policies.

The following **Choosing Wisely** recommendations apply to the clinical use of platelet transfusion.

Don't routinely transfuse blood if other non-transfusion therapies or observation would be just as effective

Canadian Society for Transfusion Medicine, Choosing Wisely Canada Recommendation # 1.

Don't routinely transfuse platelets for patients with chemotherapy-induced thrombocytopenia if the platelet count is greater than 10 x 10^9/L in the absence of bleeding

Canadian Society for Transfusion Medicine, Choosing Wisely Canada Recommendation # 4.

For additional information on the Choosing Wisely Canada campaign and its associated recommendations, visit www.choosingwiselycanada.org

See also Pediatric "Choosing Wisely" Recommendation #2, similar to Choosing Wisely Canada's Recommendation # 4 (O'Brien et al., 2021).

INTRODUCTION

In 2017, an audit of platelet transfusion in Ontario hospitals was conducted over a three-month period, capturing information on 1903 platelet transfusions performed in 57 hospitals which together carry out about 90% of platelet transfusions in Ontario. Details of the conduct, audit criteria, findings and recommendations of this audit can be found in the Provincial Platelet Audit Report (www.transfusionontario.org) and in the published literature (Hill-Strathy et al., 2021).

The audit found that approximately 40% of platelet transfusions in adults and approximately 60% of platelet transfusions in children failed to meet the set criteria which were based on previously published guidelines (Kaufman et al., 2015; Nahirniak et al., 2015) and validated in a preliminary study (Etchells et al., 2018). The most frequent reasons for transfusions failing to meet criteria involved pre-transfusion platelet counts exceeding the designated threshold for appropriateness in the prophylactic prescribing of platelet transfusion in non-bleeding patients with hypo-proliferative thrombocytopenia, and in thrombocytopenic patients with different grades of bleeding complications.

The cost of these inappropriate transfusions in labor and materials has been estimated at $25 million and, if these inappropriate transfusions had not been given, several hundred adverse reactions would have been avoided.

This toolkit seeks to provide hospital Transfusion Services with guidance in optimizing the use of platelet transfusion by recommending threshold criteria for screening of platelet transfusion orders in various clinical situations, recognizing both the published guidelines and evidence supporting them, and that platelet transfusion, like any other, is not without potential and significant adverse effects.

The content of this toolkit includes a series of algorithms to assist hospital Transfusion Services in assessing individual requests for platelets for transfusion and in approaching questions of appropriateness arising from that assessment, covering both adult and pediatric practice.

In addition to new recommendations for evaluating orders for platelet transfusion, this toolkit includes, as in a previous edition, clinical practice recommendations for the use of non-ABO/RhD type-specific platelets and for the management of refractoriness to platelet transfusion.

Algorithms are included to assist in decision making in screening orders for platelets for transfusion. These are primarily directed to elective in-patient transfusion orders and exclude emergency service requests from operating rooms, trauma units, recovery rooms and post-anesthesia care units to avoid undue delay. They also exclude out-patient and medical day care units where the nature of the clinical practice dictates greater flexibility in the application of guidelines.

ONTARIO CLINICAL PRACTICE RECOMMENDATIONS FOR USE OF PLATELET TRANSFUSION IN ADULTS AND CHILDREN AGED OVER 4 MONTHS

Platelet Count x10^9/L	Clinical Indication*
< 10	Hypo-proliferative thrombocytopenia without bleeding
< 20	Minor procedure not associated with significant bleeding
< 30	Minor (Grade 2) bleeding; anticoagulation that cannot be stopped
< 50	Significant bleeding (Grade 3-4); major non-neuraxial surgery; major trauma; liver biopsy; lumbar puncture
< 80	Epidural anesthesia
< 100	Central nervous system bleeding; head trauma; neuraxial surgery; ocular surgery (excluding cataract)
Any	Platelet dysfunction with significant bleeding post cardiopulmonary bypass

*References to literature supporting these recommendations are provided in Appendix A.

Platelet Transfusion Not Useful or Not Appropriate
Platelet count greater than10x10^9/L, non-bleeding hypo-proliferative thrombocytopenia
Platelet counts above thresholds in circumstances defined above
Immune Thrombocytopenic Purpura in absence of life-threatening bleeding
Platelet transfusion for the sole purpose of meeting eligibility criteria for a clinical trial*

*Callum et al., 2010

ONTARIO CLINICAL PRACTICE RECOMMENDATIONS FOR THE USE OF PLATELET TRANSFUSION IN NEONATES AND CHILDREN UP TO AGE 4 MONTHS

Platelet Count x10^9/L	Clinical Indication*
< 25	Stable, non-bleeding
< 30	Neonatal Allo-immune Thrombocytopenia (NAIT) without severe bleeding**
< 50	Bleeding; non-neuraxial surgery/coagulopathy
<50 (raise to 100, maintain >50)	Neonatal Allo-immune Thrombocytopenia with intracranial hemorrhage (ICH) and/or previously affected sibling with ICH
<100	Major bleeding; major neuraxial or ocular surgery

* References to literature supporting these recommendations are provided in Appendix B.

** Platelet group selected

Platelet Transfusion Not Useful or Not Appropriate
Platelet count above 25x10^9/L in stable non-bleeding neonate
Platelet counts above thresholds in circumstances defined above

BACKGROUND AND SUMMARY OF AUDIT FINDINGS

Platelet transfusions are prescribed for the treatment or prevention of hemorrhage in patients with low platelet counts, and sometimes with abnormal platelet function. The shelf life is short, 5-7 days from collection depending on the particular product (pathogen-reduced product has the shorter 5-day shelf life, compared with conventional product), resulting in high wastage rates, and storage at room temperature predisposes to an increased risk of bacterial contamination leading to septic reactions in the non-pathogen reduced products.

Over the last 30 years the threshold for recommending platelet transfusion in uncomplicated hypo-proliferative thrombocytopenia has declined from $20x10^9$/L (Beutler, 1993) to $10x10^9$/L (Kaufman et al., 2015; Nahirniak et al., 2015) supported by randomized controlled trial data. Recently, evidence has emerged that the critical level of platelets at which spontaneous hemorrhage should be anticipated may be as low as $5x10^9$/L (Slichter et al., 2021).

Using criteria culled from the literature and validated in a preliminary study (as cited above) ORBCoN conducted an audit of platelet use in Ontario in 2017 reported in detail as the Provincial Platelet Audit Report at www.transfusionontario.org and in the peer-reviewed literature (Hill-Strathy et al., 2021).

AUDIT FINDINGS

The principal findings of the audit in adult patients were:

- Approximately 40% of platelet transfusions were outside the audit criteria guidelines.
- High rates of inappropriate use occurred across all hospital clinical services reporting platelet transfusions.
- The highest rates of inappropriate platelet transfusions were reported from more urgent care settings.
- The lowest rates of inappropriate use occurred in out-patient (oncology/ hematology) services, partly attributable to more flexible threshold criteria in the out-patient setting.
- Hospitals employing prospective order screening and pre-printed order sheets had significantly lower rates of inappropriate platelet transfusion than hospitals not using these measures.
- The most frequent reasons for inappropriate platelet transfusion were:
    - Prophylaxis for spontaneous bleeding in hypo-proliferative thrombocytopenia with platelet count $>10x10^9$/L.
    - Major non-neuraxial surgery or procedure associated with potential for major blood loss with platelet count $>50x10^9$/L.
    - Non-central nervous system bleeding, minor (WHO grade 1-2) with platelets $>20x10^9$/L or major (WHO grade 3-4) with platelet count $>50x10^9$L.
    - Immune thrombocytopenic purpura

The principal findings of the audit in children were:

- Approximately 63% of platelet transfusions were outside the audit criteria guidelines.
- High rates of inappropriate use occurred across all hospital clinical services reporting platelet transfusions.
- The most frequent reasons for inappropriate platelet transfusions were:
    - Prophylaxis for spontaneous bleeding in hypo-proliferative thrombocytopenia with platelet count $>10x10^9$/L.

- Immune thrombocytopenic purpura
- Minor non-central nervous system bleeding (WHO grade 1-2), platelet count >/=30x10^9/L.

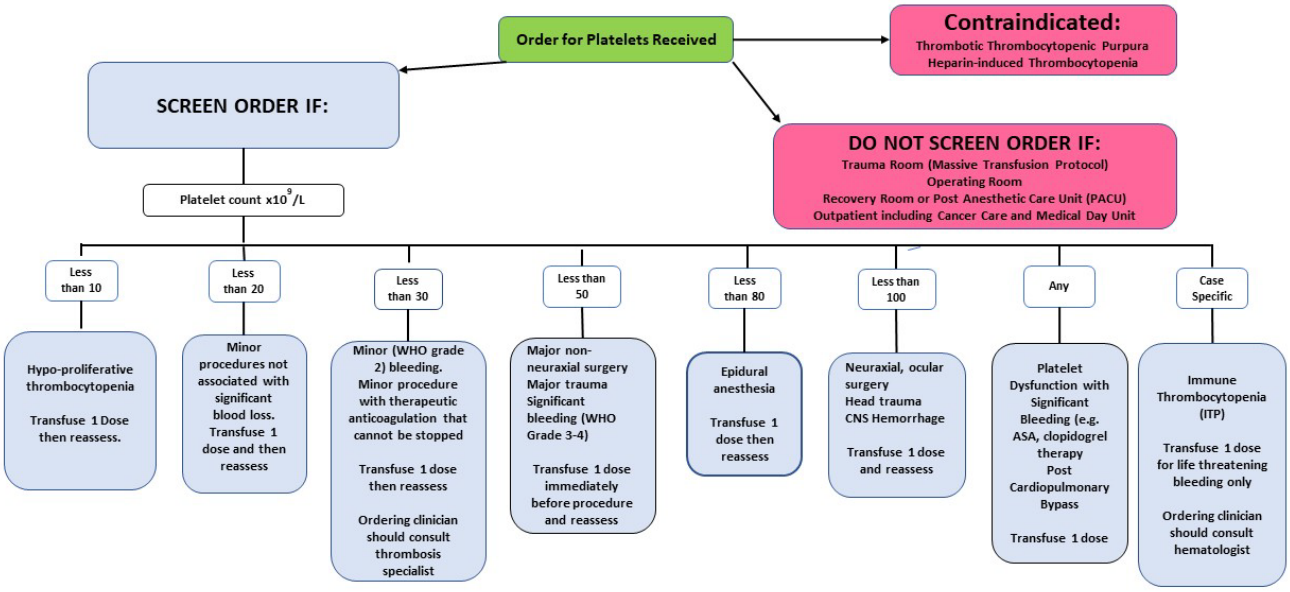
- Within the pediatric population there was a subgroup of 37 neonates for whom 24 transfusions were deemed inappropriate, all non-bleeding with platelet counts exceeding threshold.

Pre-transfusion platelet counts were reported for 1661/1693 (98%) of adult platelet transfusions and 207/210 (98.6%) of platelet transfusions in children. Corresponding figures for post-transfusion platelet counts were 1254/1693 (74.1%) and 152/210 (72.4%).

Recommendations in the Audit Report relevant to this Toolkit are addressed through the following considerations:

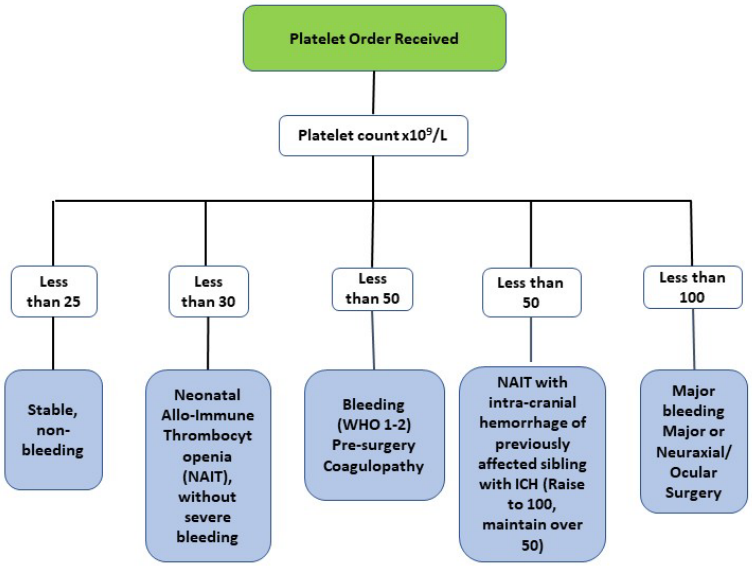
- Dissemination of clinical practice recommendations to assist in monitoring orders for the clinical use of platelet transfusion, endorsed by Ontario Transfusion Medicine specialists, as a general guide to transfusion practice.
- These clinical practice recommendations may form the basis for development of hospital transfusion policy by Transfusion Committees with a view to formal hospital approval.
- The use of prospective order screening and pre-printed order sheets have demonstrated that, in this audit, they can contribute significantly to enhanced appropriateness of platelet transfusions. The clinical practice guidelines and algorithms to assist platelet transfusion order evaluation in this Toolkit can also provide the basis for individual hospital development of such aids to improve transfusion practices.

ALGORITHM FOR EVALUATION OF PLATELET TRANSFUSION ORDERS FOR ADULTS/CHILDREN GREATER THAN 4 MONTHS



If order is outside these guidelines, inform patient care area that the request is outside recommendations and the case should be referred to the TM physician
For an adult 1 dose equals one unit as supplied by Canadian Blood Services. For a child, 1 dose equals 10mL/kg body weight up to adult dose.

ALGORITHM FOR THE EVALUATION OF PLATELET ORDERS FOR NEONATES (LESS THAN 4 MONTHS)



Give one dose (10mL/kg) and reassess. Platelet group selected for NAIT.
For orders outside guidelines, recommend review/consultation with pediatric TM physician

PEDIATRIC PLATELET DOSAGES

Product	Dose
Pathogen-reduced buffy coat platelets	8mL/kg
Pathogen-reduced apheresis platelets	10mL/kg
Non-pathogen-reduced buffy coat platelets	10mL/kg
Non-pathogen-reduced apheresis platelets	10mL/kg

CLINICAL PRACTICE RECOMMENDATIONS FOR THE USE OF NON-ABO/RH TYPE SPECIFIC PLATELETS

Purpose: This guideline was developed to assist clinical decision making regarding the use of non-ABO or non-RhD type specific platelets when ABO/RhD type specific platelets are not readily available.

Note: Prior to use of these guidelines the following should be considered:

1. There is evidence to suggest that ABO type specific platelets will result in higher platelet increments.
2. There is no definitive evidence to suggest that adverse events or mortality are different with ABO type specific or ABO non-type specific, plasma compatible platelets.
3. If ABO plasma compatible platelets are not available, ABO plasma incompatible platelets may be transfused provided the ordering physician is informed to enable appropriate monitoring of the patient for signs of hemolysis, or the patient provided with platelets either with low-titre ABO isohemagglutinins or, in the case of non-group-O recipients, volume reduced group O platelets.
4. A trial of ABO type specific platelets should be given to patients who are refractory, prior to screening for HLA antibodies (see section on refractoriness to platelet transfusion below).
5. RhD negative platelets should be prioritized for females of child-bearing potential (age <45years).
6. All institutions should have a policy to address use of RhD positive platelets for RhD negative recipients including whether Rh Immune Globulin (RhIG) will be administered in females of child-bearing potential (age <45 years).

Guidelines:

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

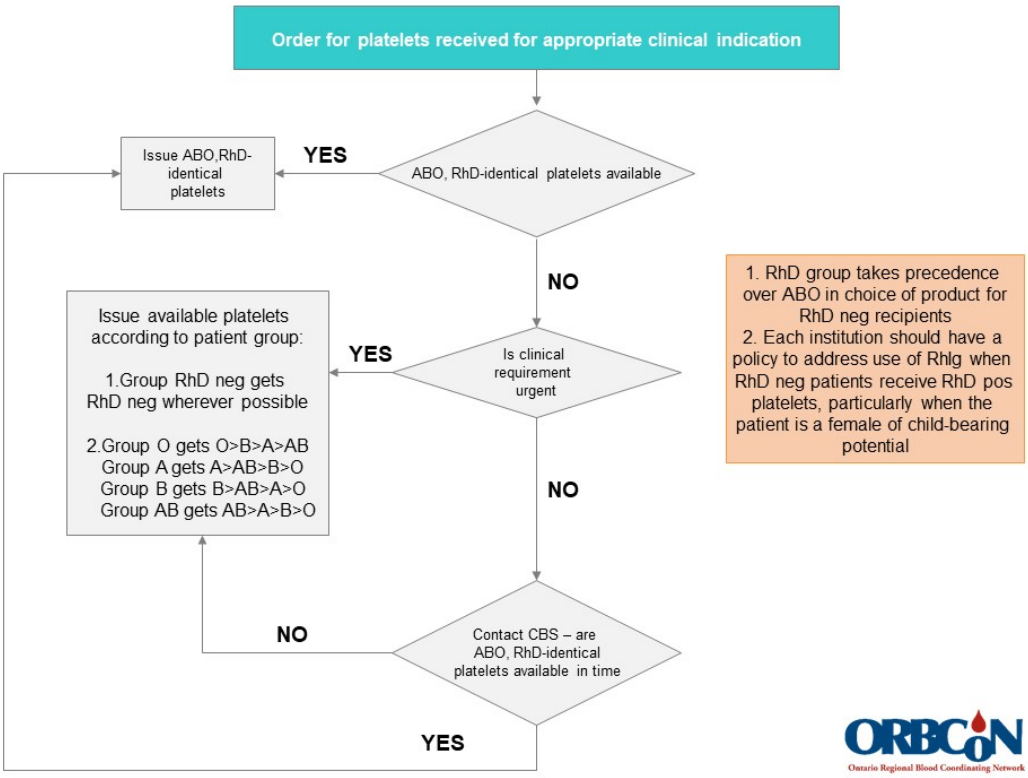
NB. RhD negative males, and females age >45, may receive RhD positive platelets with extremely low risk of alloimmunization (<1%).

Other considerations:

- There have been cases of hemolysis following transfusion of ABO plasma incompatible platelets containing high titre isohemagglutinins
- Buffy coat pooled and apheresis single donor platelets contain approximately 250-300mL of plasma from one donor whose isohemagglutinin titre is not known
- Titration of ABO isohemagglutinins is of questionable value due to poor predictability between in vitro titres and red cell survival. The test is difficult to standardize and there is no reference to support the use of platelets beyond any particular titre level
- ABO plasma incompatible platelets may be volume reduced by centrifugation to reduce isohemagglutinin exposure
- Pathogen reduced platelets have partial plasma replacement with additive and present less risk of ABO isohemagglutinin induced hemolysis.

Reference: Dunbar et al., 2020.

ALGORITHM FOR USE OF NON-ABO/RH TYPE-SPECIFIC PLATELETS



CLINICAL PRACTICE RECOMMENDATIONS FOR THE MANAGEMENT OF REFRACTORINESS TO PLATELET TRANSFUSION

Purpose: This Guideline was developed to assist clinical decision making regarding the appropriate use of HLA/HPA matched single donor platelets. The provision of matched single donor platelets is resource intensive both from the perspective of the blood supplier and the initiating institution, and should be reserved for sensitized patients proven to be refractory to random donor platelets, defined as failure of ABO-identical platelet transfusion to raise the post-transfusion count by more than $7.5x10^9$/L on at least two occasions.

Note: When considering these guidelines, the following should be observed:

1. Possible causes of non-serological refractoriness should be considered
2. There is no evidence that any particular patient group will benefit from the use of single donor platelets in the absence of HLA or HPA antibodies
3. Leuko-reduced (LR) buffy coat platelets and LR single donor apheresis platelets should be used interchangeably for non-refractory patients

Guideline:

HLA/HPA matched platelets are indicated exclusively for refractory patients with demonstrated HLA/HPA antibodies

Managing platelet refractoriness in patients with HLA or HPA alloimmunization:

- Refractoriness is confirmed if the 10-60 minute post-transfusion platelet increment is <7.5x10^9/L following at least two transfusions of ABO-identical platelets
- Screen for HLA antibodies and, if positive, request HLA selected platelets
- If HLA-selected platelets fail to correct refractoriness, screen for HPA antibodies; If positive request HPA selected platelets
- If HLA and HPA immunization as the basis of refractoriness are excluded, seek expert transfusion medicine opinion.

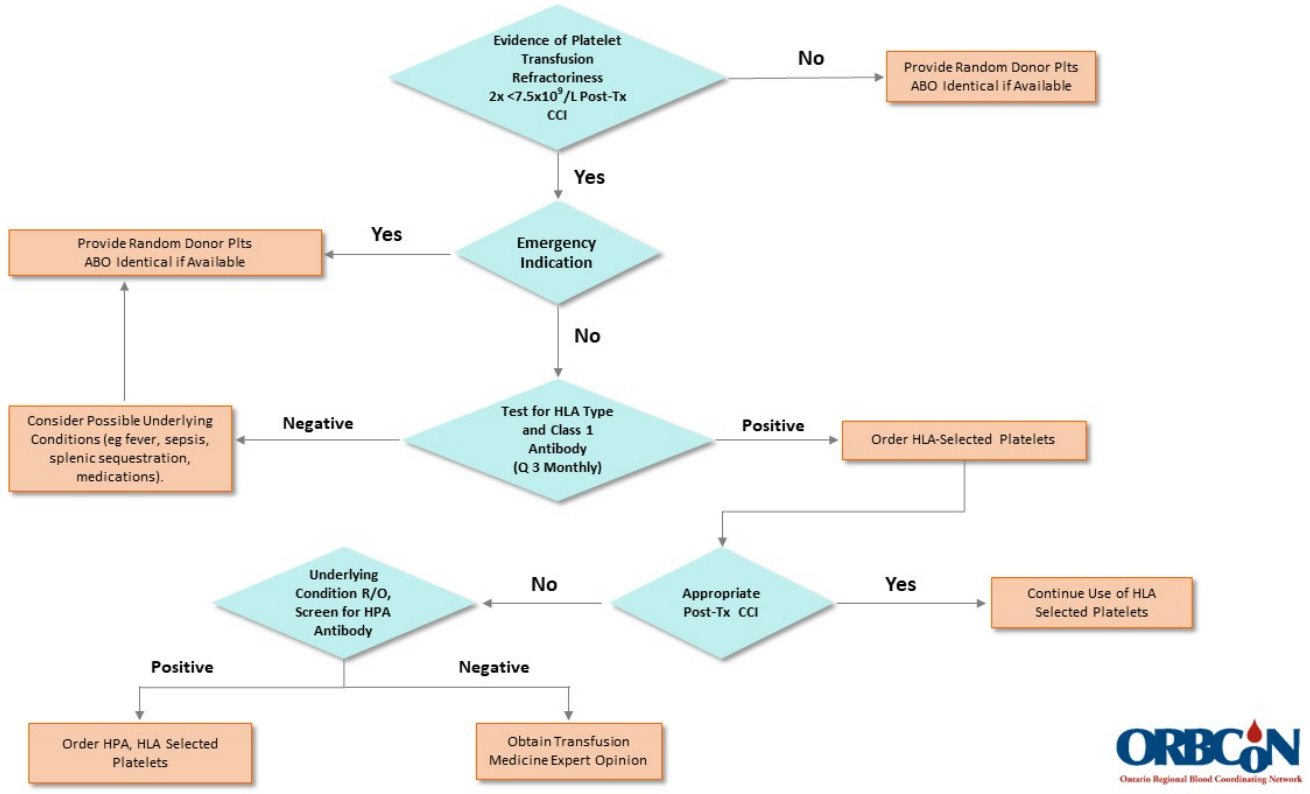
Other considerations:

- Other (non-immune) causes of refractoriness should be identified and treated
- Communication with clinical and CBS teams to ensure HLA/HPA selected platelets are only collected when needed is important to maintain appropriate ordering and adequate supply (each unit requires particular donor selection and donation).

References:

Juskewitch et al., 2017; Belizaire et al., 2020; Saris and Pavenski, 2020.

PLATELET REFRACTORINESS MANAGEMENT ALGORITHM:



APPENDIX A. REFERENCES TO CRITERIA FOR DEFINING THRESHOLDS FOR PLATELET TRANSFUSION IN ADULTS AND CHILDREN AGED 4 MONTHS TO 18 YEARS.

Clinical Indication	Platelet Count $x10^9/L$	References
Hypo-proliferative Thrombocytopenia	<10	Kaufman et al., 2015; Nahirniak et al., 2015; New et al., 2016; Schiffer et al., 2018.
Minor procedure not associated with significant bleeding	20	Kaufman et al., 2015; New et al., 2016; Schiffer et al., 2018; Patel et al., 2019; Estcourt et al., 2020.
Minor bleeding (Grade 2), anticoagulant therapy that cannot be stopped	30	Alaniz, 2010: Estcourt et al., 2017.
Significant bleeding (Grade 3-4), major non-neuraxial surgery, major trauma, liver biopsy, lumbar puncture	50	Kaufman et al., 2015; Etchill et al., 2017; New et al., 2016; Schiffer et al., 2018; Patel et al., 2019.
Epidural anesthesia	80	Estcourt, 2020.
Neuraxial surgery, head trauma, central nervous system bleeding, ocular surgery (not including cataract)	100	New et al., 2016; Etchil et al., 2017.
Platelet dysfunction from cardiopulmonary bypass with significant bleeding	Any	Kaufman et al., 2015.

APPENDIX B. REFERENCES TO CRITERIA FOR DEFINING THRESHOLDS FOR PLATELET TRANSFUSION IN NEONATES UP TO 4 MONTHS OF AGE.

Clinical Indication	Platelet Count $x10^9/L$	References
Stable, non-bleeding	<25	New et al., 2016; Curley et al., 2019; Estcourt, 2019.
Neonatal allo-immune thrombocytopenia without severe bleeding*	30	Lieberman et al., 2019.
Bleeding, pre-surgery, coagulopathy	50	New et al., 2016.
Neonatal allo-immune thrombocytopenia with intra-cranial hemorrhage and/or previously affected sibling with ICH*	50 (raise to 100 and maintain over 50)	Lieberman et al., 2019.
Major (WHO 3-4) bleeding, major neuraxial or ocular surgery	100	New et al., 2016.

* Platelet group-selected preferred.

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