

## Chapter 18: Platelet Transfusion, Alloimmunization and Management of Platelet Refractoriness

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Tanya Petraszko, MD, FRCPC and Michelle Zeller, MD, FRCPC, MHPE, DRCPSC

### BACKGROUND

Platelets are the smallest of the blood cells, with a diameter of two to three microns and no nucleus. Their main function is to mediate primary hemostasis, though they are involved in a number of other processes including primary immunity, tumour progression and inflammation.<sup>1</sup> Platelets circulate individually in the blood stream until they are exposed to the subendothelial matrix following an injury to a blood vessel, at which point the platelets activate and undergo morphologic changes. Once activated, platelets bind to the sites of injury and to each other to form a temporary hemostatic plug. This initiates the activation of additional plasma coagulation factors to form a more permanent fibrin hemostatic plug.

A normal platelet count is 150–400 x 10<sup>9</sup> per litre. Individuals with very low platelet counts are at increased risk of bleeding. The risk of clinically significant and/or spontaneous bleeding increases when the platelet count is less than 10 x 10<sup>9</sup> per litre. The risk of bleeding complications from surgery or other injury increases with platelet counts below 30–50 x 10<sup>9</sup> per litre. Individuals with congenital or acquired disorders of platelet function are also at increased risk of bleeding.

Platelet transfusions can be used to increase the number of functional platelets and therefore decrease the risk of bleeding problems. This chapter describes the process of collecting, manufacturing and storing platelets for transfusion, lists guidelines for administering platelet transfusions and provides further information on adverse reactions and platelet refractoriness.

### COLLECTION, PROCESSING AND STORAGE OF PLATELETS FOR TRANSFUSION

Canadian Blood Services produces platelet concentrates using two methods:

- 1. Buffy coat production method:** With this method, whole blood is collected and spun to separate the platelets from the plasma and the red blood cells (Figure 1). Following this separation, four units of platelets from group identical donors are pooled together and suspended in plasma from one of the male donors. This is often referred to as random donor or pooled platelets.
- 2. Apheresis method:** With this method, platelets are collected from a single donor using an apheresis machine. The machine extracts whole blood from the donor, spins it to separate the platelets and returns the rest of the blood components back to the circulating blood of the donor.

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**Table 1.** Platelet component characteristics at Canadian Blood Services\*

Platelet component	Volume (ml) Mean ± 1 SD	Platelet count (x10 <sup>9</sup> ) Mean ± 1 SD	Residual leukocytes (x10 <sup>6</sup> ) Mean ± 1 SD
<b>Pooled platelets LR CPD</b>	342 ± 15 (n=583)	298 ± 68 (n=583)	0.09 ± 0.54 (n=550)
<b>Apheresis platelets</b>	242 ± 8 (n=519)	370 ± 48 (n=519)	0.067 ± 0.208 (n=510)

\* Table reproduced from Canadian Blood Services Circular of Information.<sup>2</sup> Typical unit content is based on the number of units (n) tested from July 2016 to December 2016, inclusive.

**Quality criteria that must be met:**

**Pooled platelets LR CPD:** Volume: ± 10% labeled volume in all units tested; platelet count: >240 x 10<sup>9</sup> per unit in ≥75% of units tested; residual leukocytes: <5 x 10<sup>6</sup> in all units tested.

**Apheresis platelets:** Platelet count: ≥240 x 10<sup>9</sup> per unit in ≥75% of units tested; residual leukocytes: <5 x 10<sup>6</sup> in all units tested.

SD: standard deviation  
LR CPD: leukoreduced platelets collected with citrate phosphate dextrose (anticoagulant)

Both apheresis and buffy coat products are leukoreduced and tested for bacterial growth, and both are considered to be equally effective for most patients (Figure 2). See Table 1 for Canadian Blood Services platelet products characteristics. However, apheresis platelets may be associated with higher rates of adverse events (see Adverse Reactions section below).

Apheresis platelets offer the advantage of providing matched platelet products for specific indications (see Platelet Refractoriness section below).

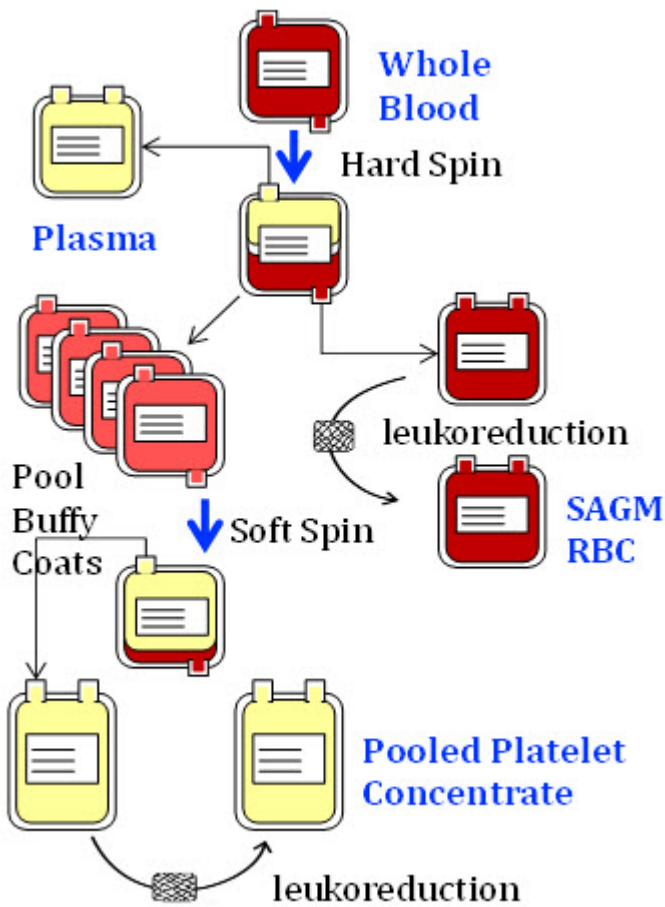
As such, the only absolute indication for apheresis platelets is the provision of specific platelets for patients with documented antibodies targeting human leukocyte antigen (anti-HLA) or human platelet antigen (anti-HPA) and alloimmune platelet refractoriness, or in the setting of post-transfusion purpura or neonatal alloimmune thrombocytopenia.

Platelets manufactured by Canadian Blood Services and Héma-Québec are stored at room temperature and have a seven-day shelf life.

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**Figure 1:** Buffy coat platelet production at Canadian Blood Services (additional details are available in Chapter 2 of this [Guide](#)).

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**Figure 2:** Apheresis platelet (left) and pooled platelet (right) concentrates prepared by Canadian Blood Services.

### INDICATIONS

Platelets are transfused into individuals with thrombocytopenia or platelet dysfunction for two indications:

- to stop bleeding (therapeutic platelet transfusions)
- to prevent bleeding (prophylactic platelet transfusions)

One unit or dose of platelets is expected to increase the platelet count by an average of  $15\text{--}25 \times 10^9$  per litre;<sup>3</sup> however, the increment may be more or less depending on the underlying cause of the thrombocytopenia, comorbidities and patient size.

### Therapeutic Platelet Transfusions

There is limited high-quality evidence to guide the use of platelet transfusions to treat bleeding. There is general agreement that the following patients should receive platelet transfusions:

1. Patients with non-immune thrombocytopenia and clinically significant bleeding with platelet count below  $50 \times 10^9$  per litre.
2. Head trauma or life-threatening hemorrhage with a platelet count below  $100 \times 10^9$  per litre.
3. Platelet dysfunction from congenital or acquired causes (e.g. cardiopulmonary bypass surgery) and clinically significant bleeding.
4. Immune-mediated thrombocytopenia with severely reduced platelet count (less than  $20 \times 10^9$  per litre) and severe bleeding.
5. As part of a massive transfusion protocol in bleeding trauma patients.

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It is important to consider the underlying etiology of the thrombocytopenia and to consider additional hemostatic agents where appropriate (e.g. antifibrinolytics, tranexamic acid). Thrombocytopenia can be caused by decreased production or by increased destruction, consumption or sequestration of platelets. In the case of thrombotic thrombocytopenic purpura (TTP) and heparin-induced thrombocytopenia (HIT), platelet transfusions are generally avoided as they may increase the risk of thrombotic events.

### Prophylactic Platelet Transfusions

Both AABB and the International Collaboration for Transfusion Medicine Guidelines (ICTMG) conducted separate systematic reviews and used the GRADE method to assess evidence quality. The resulting clinical practice guidelines on platelet transfusion<sup>4,5</sup> make a number of recommendations for the use of platelet transfusions to prevent bleeding (Table 2).

**Table 2:** Summary of recommendations on platelet transfusion

Recommendation for platelet transfusions	Quality of Evidence	Strength of Recommendation
Hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia <sup>††</sup> - Transfuse with a platelet count of $\leq 10 \times 10^9$ cells/l - Single standard apheresis or equivalent	Moderate	Strong
Patients having elective central venous catheter placement with platelet count $< 20 \times 10^9$ cells/l <sup>†</sup>	Very low	Weak
Patients having elective diagnostic lumbar puncture with platelet count $< 50 \times 10^9$ cells/l <sup>†</sup>	Very low	Weak
Patients having major elective non-neuroaxial surgery with a platelet count $< 50 \times 10^9$ cells/l <sup>†</sup>	Very low	Weak
Consider platelet transfusion for patients undergoing cardiopulmonary bypass who exhibit perioperative bleeding with thrombocytopenia and/or evidence of platelet dysfunction <sup>†</sup>	Very low	Weak
Cannot recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage <sup>‡</sup>	Very low	Weak
<sup>†</sup> ICTMG guidelines <sup>4</sup> ; <sup>‡</sup> AABB guidelines <sup>5</sup>		

The strong recommendation for transfusing hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia and a platelet count less than or equal to  $10 \times 10^9$  cells per litre is based on three randomized controlled trials (RCTs). The two largest and most recent RCTs<sup>6,7</sup> examined bleeding outcomes in hospitalized patients with chemotherapy-induced hypoproliferative thrombocytopenia, comparing patients treated with prophylactic platelet transfusions versus no platelet transfusions. Both studies concluded that prophylactic platelet transfusions significantly reduced risk of clinically significant (grade 2 or greater) bleeding. Based on subgroup analyses, some populations (e.g. allogeneic stem cell transplant recipients) were identified as being at higher risk for bleeding than others (e.g. autologous stem cell transplant recipients). Further exploratory analyses and meta-analysis of these trials are in progress.

**Platelet thresholds:** For inpatients without bleeding and no additional risk factors for bleeding, transfusion of

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platelets is not indicated unless the platelet count is less than or equal to  $10 \times 10^9$  cells per litre. Two large RCTs and one prospective controlled cohort study demonstrated that lowering the prophylactic platelet transfusion threshold from  $20 \times 10^9$  cells per litre to  $10 \times 10^9$  cells per litre would decrease platelet utilization by more than 20% without increasing major bleeding.<sup>8,9</sup> Smaller studies have suggested that a transfusion threshold of  $5 \times 10^9$  cells per litre may also be safe, but this has not been demonstrated in adequately powered RCTs. The evidence to support specific thresholds for platelet transfusions in patients with risk factors for bleeding is limited. For patients at increased risk of bleeding due to fever, antibiotics, anticoagulant use or other factors, higher thresholds (e.g.  $15 \times 10^9$  cells per litre) for prophylactic platelet transfusions have been used but evidence supporting this practice is lacking.

**Platelet dose:** In Canada, the standard adult dose of platelets is derived from pooling four whole blood donations (pooled platelets) or from one plateletpheresis donation (apheresis platelets). The adult dose of platelets distributed by Canadian Blood Services has a volume of approximately 242 to 342 ml and a platelet content of approximately  $298$  to  $370 \times 10^9$  (Table 1). In children, a dose of 10 ml of a platelet unit per kilogram is reasonable. Higher doses of platelets have been used historically, but there is no evidence that higher doses are more effective in preventing or treating bleeding. For prophylactic platelet transfusions, higher doses of platelets increase post-transfusion platelet counts and prolong the time until the next transfusion, but recent studies including a large RCT<sup>10</sup> suggest that higher doses of platelets do not reduce bleeding and increase total platelet utilization in patients requiring repeated platelet transfusions. For prophylactic platelet transfusions, a lower dose of platelets (equivalent to half of a standard platelet unit either pooled or apheresis) has been shown to be as clinically effective as one standard dose at preventing bleeding.<sup>10</sup> Furthermore, although more frequent platelet transfusions are required, the lower dose reduces total platelet utilization. Since Canadian Blood Services provides platelets in single standard units, giving a lower dose would require a sterile technique for splitting the standard unit. For this reason, lower dose platelet transfusions are not routinely used, but, in times of platelet shortages, this can be a useful strategy to manage inventory challenges.

**Table 3:** Summary of clinical practice recommendations for platelet use in adult inpatients\*

Clinical setting	Platelet count ( $\times 10^9/l$ )	Recommendation and dose
Diagnosis/Indication		
Non-immune thrombocytopenia	Less than 10	One dose
Procedures not associated with significant blood loss, including percutaneous procedures other than epidural anesthesia or lumbar puncture	Less than 20	One dose
Therapeutic anticoagulation that cannot be stopped	Less than 30	One dose, and consult <b>thrombosis specialist</b>
- Epidural anesthesia or lumbar puncture - Procedures with expected blood loss greater than 500 ml - Major non-neuraxial surgery - Significant bleeding	Less than 50	One dose immediately before procedure and check platelet count before starting procedure
- Neuraxial surgery - Head trauma or central nervous system (CNS) hemorrhage- Life-threatening hemorrhage	Less than 100	One dose and check platelet count

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Clinical setting		
Diagnosis/Indication	Platelet count (x10 <sup>9</sup> /l)	Recommendation and dose
Platelet dysfunction <b>and</b> significant bleeding (e.g. ASA, P2Y12 therapy)	Any	One dose
Treatment of intracranial hemorrhage in patients on ASA and P2Y12 therapy	Any	Platelet transfusion may cause harm in patients with spontaneous intracranial hemorrhage on dual antiplatelet therapy. <sup>11</sup>
Prophylactic invasive procedure for patients on dual anti-platelet therapy (e.g. ASA and P2Y12 inhibitors)	Any	Platelet transfusions may be effective but must be tailored to the individual based on the specific level of platelet inhibition and should be done in consultation with transfusion medicine experts. <sup>12</sup>
Platelet dysfunction and significant bleeding associated with cardiopulmonary bypass	Any	Standard platelet transfusion may be associated with increased adverse events and may not be beneficial. <sup>13</sup>
Immune thrombocytopenia (ITP)	Case specific	One dose, for life-threatening bleeding only and <b>consult a hematologist</b>
<p>*Clinical Practice Recommendations were compiled from a review of evidence-based guidelines, Choosing Wisely® and Choosing Wisely Canada lists, the current literature, selected hospital transfusion guidelines, and expert opinion. Because a formal literature search was not part of the preparation of these recommendations, they are presented as recommendations rather than guidelines. <b>These recommendations are modified from the Ontario Quality Improvement Plan Toolkit and were produced with support from ORBCoN.</b><sup>14</sup></p> <p><b>Additional notes:</b></p> <ul style="list-style-type: none"> <li>• In general, one dose raises the platelet count by approximately 15–25 x 10<sup>9</sup> per litre.</li> <li>• One dose = one buffy coat pooled platelets unit or one apheresis platelets unit.</li> </ul>		

## PLATELET ADMINISTRATION

Platelets have A and B antigens on their cell surface but do not express the Rh antigens. Ideally, ABO-identical platelet transfusions should be transfused, but non-identical ABO transfusions can be given if ABO-matched platelets are not available. Some evidence suggests that ABO-mismatched platelets are a risk factor for poor platelet count increments.<sup>15</sup>

Hemolysis due to anti-A and anti-B antibodies in the plasma of mismatched ABO platelet transfusions has been reported. Plasma reduction of platelet units can be considered to remove these antibodies, but is often unnecessary. Some transfusion services routinely determine anti-A/anti-B titres of group O platelets (supernatant) and avoid use of group O platelets units in non-group O patients when the titres exceed a pre-determined threshold.

Additionally, some studies have suggested that increased morbidity and mortality may be associated with mismatched platelet transfusions. A secondary analysis of the Platelet Dose (PLADO) trial showed that although apheresis source, ABO-identical and fresher platelets had modestly-increased post-transfusion platelet increments compared with whole blood, non-identical and/or older platelets, there was no measurable impact on prevention of clinical bleeding.<sup>10, 16</sup>

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While platelets do not express Rh antigens, platelet products may contain small amounts of red blood cells. As a result, transfusing platelets from Rh positive donors to Rh negative recipients can result in the recipient producing antibodies targeting the Rh D antigen, which may interfere with future transfusions or complicate pregnancies. Therefore, administration of anti-D immune globulin (WinRho) may be considered for all Rh negative female children and women of child-bearing age within 72 hours of platelet transfusion from an Rh positive donor.<sup>4, 17</sup> Evidence suggests a low rate of alloimmunization amongst those receiving Rh D antigen incompatible platelet transfusions without anti-D immune globulin in the general population.<sup>18</sup> Clinical factors such as recent chemotherapy or immunosuppression can reduce the rate of alloimmunization and might affect the decision to give anti-D immune globulin. Apheresis platelet units manufactured with current protocols have minimal contamination with red blood cells<sup>19</sup> and therefore the rate of alloimmunization after Rh-incompatible apheresis platelet transfusions is extremely low.<sup>20, 21</sup>

### ADVERSE REACTIONS

Platelet transfusions are associated with both infectious and non-infectious adverse effects. See Chapter 10 of this [Guide](#) and the [Adverse Reactions Reporting](#) information made available by Canadian Blood Services.

While each unit of platelets has the same risk of transmitting viral infections as a unit of red blood cells, bacterial infections are a particular concern with platelets because they are stored at room temperature. For the period January 2010 to December 2016, the rate of bacterial contamination of Canadian Blood Services' platelet units was estimated at 1:10,000; the rate of bacterial sepsis from platelet transfusions was estimated at 1:100,000 and the rate of death from bacterial sepsis was estimated at 1:500,000.<sup>22</sup> The source of the bacteria may be skin flora bacteria from the donor acquired during blood collection or less commonly, bacteremia in the donor. A new bacterial screening algorithm implemented in 2017 is improving bacterial detection, allowing the platelet shelf-life to be extended from five to seven days. The new algorithm is anticipated to increase the rate of bacteria detected as more contaminated units will be captured during platelet screening, and to reduce bacterial sepsis rates as fewer units will escape detection (for more information, see the [2017 Surveillance Report](#)). All platelet units issued in Canada are currently examined for bacteria by removing a small sample at  $\geq 36$  hours post-collection and inoculating this sample in culture bottles for monitoring bacterial growth. Platelet units that are positive for bacterial growth are recalled and discarded, or, in the event that the unit has been transfused into a patient, the physician is notified.

Platelet transfusions sometimes have the unique complication of alloimmune refractoriness. In this condition, routine platelet transfusions do not increase the recipient's platelet count because they are immediately destroyed by the recipient's immune system. This occurs in patients who have anti-HLA antibodies or who develop anti-platelet antibodies after a blood transfusion or a pregnancy. The risk of alloimmune refractoriness is significantly reduced (to approximately 4% of recipients) by universal leukoreduction of all blood components.<sup>3</sup> The risks of alloimmunization and platelet refractoriness are similar with platelets derived from whole blood versus apheresis since both products are leukoreduced. Adequate increments in the post-transfusion platelet counts in these patients can only be achieved by the transfusion of specially selected HLA- or HPA-negative apheresis platelet units (see below, platelet refractoriness).

Recent evidence suggests that apheresis platelets may be associated with a higher rate of adverse reactions than pooled platelets.<sup>23</sup> Although transfusions with apheresis platelets may reduce exposure to different donors, apheresis platelets from an HLA-matched donor or a blood relative may increase the risk of transfusion-associated graft-versus-host disease (TA-GvHD). To prevent this rare complication, all HLA-matched blood products should be irradiated to destroy residual lymphocytes. Finally, apheresis platelets may provide a higher "dose" of HLA and HPA to recipients compared to a lower dose of a given HLA or HPA type in a pool of four donors in a buffy coat unit. It is possible that transfusion of apheresis units can result in a higher rate of

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alloimmunization in chronically transfused recipients, although conclusive data is lacking.

**Table 4:** Adverse reactions from platelet transfusions\*<sup>24-28</sup>

Event	Approximate frequency	Symptoms and signs	Notes
Mild allergic reaction	1 in 100	Urticaria, pruritis and/or erythema	Transfusion can be restarted after assessment and necessary intervention
Febrile non-hemolytic transfusion reactions (FNHTR)	1 in 200	Fever, chills and/or rigor	Diagnosis of exclusion. A patient with fever should be evaluated for other more serious transfusion reactions.
Transfusion associated circulatory overload (TACO)	1 in 700	Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.	Due to excessive volume or excessively rapid transfusion rates. May be difficult to distinguish from TRALI
Septic reaction	1 in 100,000	Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and disseminated intravascular coagulation and/or renal failure.	Approximate frequency per platelet concentrate based on Canadian Blood Services data*: - bacterial sepsis 1 in 125,000. - death from bacterial sepsis 1 in 909,091 As reported by other international blood agencies: - estimated risk of bacterial sepsis 1 in 100,000 - estimated risk of death from bacterial sepsis 1 in 1,000,000 For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference. <sup>24</sup>
Transfusion related acute lung injury (TRALI)	1 in 1,200-5,000	New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.	Occurs during or within 6 hours of transfusion. May be difficult to distinguish from TACO.
Post transfusion purpura (PTP)	Rare	Abrupt onset of severe thrombocytopenia 1 - 24 days post transfusion.	Most cases of PTP occur in recipients who are HPA-1b homozygous receiving HPA-1a positive blood components.
Transfusion-related alloimmune thrombocytopenia	Rare	Abrupt onset of potentially severe thrombocytopenia within hours of transfusion.	Passive transfer of platelet antibodies leading to thrombocytopenia.

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Event	Approximate frequency	Symptoms and signs	Notes
Immediate hemolytic transfusion reactions (HTR)	Rare	Fever, chills, hemoglobinuria, dyspnea, shock, disseminated intravascular coagulation, chest pain and/or back pain.	May be associated with ABO plasma incompatibility.
Anaphylaxis	Rare	Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea and vomiting.	Resuscitation according to institutional guidelines. IgA-deficient patients who have formed anti-IgA antibodies may experience anaphylactic reactions. However, in most cases of anaphylactic reactions, no specific antibodies are found in the patient.
Graft-versus-host disease (GVHD)	Rare	Pancytopenia, rash, liver dysfunction, diarrhea.	Irradiated cellular blood components eliminate this risk.
Isolated hypotensive reaction	Unknown	Hypotension, occasionally accompanied by urticaria, dyspnea and nausea.	Diagnosis of exclusion. May occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitor.
Infectious disease	See Surveillance Report for residual risk of tested viruses	Variable according to infectious disease.	Blood components have been described to transmit viruses other than HIV, HBV, HCV, HTLV I/II and WNV as well as parasites and prions.

\* Table adapted from Canadian Blood Services 2017 Circular of Information.<sup>2</sup>

## MANAGEMENT OF SPECIAL SITUATIONS

### Platelet Refractoriness

Platelet refractoriness is a major complication in the management of hypoproliferative thrombocytopenic patients. Platelet refractoriness may be due to immune or non-immune causes. The causes of non-immune refractoriness include fever, infection, drugs, splenomegaly and disseminated intravascular coagulation. Obtaining detailed patient history and physical exam findings helps to elucidate cause and determine goals and urgency of treatment.

In patients with poor responses to platelet transfusions, measuring the post-transfusion platelet count approximately one hour after the platelet transfusion can help distinguish between immune and non-immune causes. Studies have used various calculations<sup>29</sup> to define platelet refractoriness:

Platelet Increment (PI) = $P_2 - P_1$ , where $P_1$ is the pre-transfusion platelet count and $P_2$ is the post-transfusion platelet count.
Corrected Count Increment (CCI) = $[(PI \times BSA)/n] \times 100$ , where BSA represents the body surface area in meters <sup>2</sup> and n is the number of platelets transfused.
The percentage platelet recovery (PPR) = $[(PI \times \text{body weight (kg)} \times 0.075 \text{ (l/kg)})/n] \times 100$ . Body weight (kg) x 0.075 (l/kg) is an estimate of blood volume.

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In patients with poor response to platelet transfusion, the platelet response measured between 10 and 60 minutes after completion of a platelet transfusion on two separate occasions may be used to determine if alloimmunization is the likely cause of the refractoriness. A CCI below  $7.5 \times 10^9$  cells per litre at one hour post-transfusion or a PPR at one hour post-transfusion under 30% are suggestive of alloimmune refractoriness. A good increment at one hour with a fall below  $7.5 \times 10^9$  cells per litre at 24 hours suggests non-immune platelet destruction.

Since the platelet count of whole blood-derived platelet units is not routinely measured, **a PI below  $5-10 \times 10^9$  cells one hour post-transfusion** can be used instead of the CCI or PPR.

Testing for HLA- or platelet-specific antibodies can be done with tests such as the lymphocytotoxic antibody assay and flow cytometry. [Canadian Blood Services' National Platelet Immunology Reference Laboratory](#) provides recipient testing for these antibodies. HLA alloimmunization is more frequent than HPA alloimmunization as the cause of alloimmune refractoriness.

Platelet refractoriness and alloimmunization are not interchangeable. Platelet refractoriness due to alloimmunization is managed differently than non-immune refractoriness (see Figure 3). Once anti-HLA or anti-platelet (anti-HPA) antibodies have been identified, matched or compatible apheresis platelet products may be useful to achieve adequate post-transfusion platelet count increments. HLA and/or HPA selected platelet products can be obtained from typed apheresis platelet donors and may be ordered through Canadian Blood Services using the "[Request for HLA/HPA selected platelets](#)" forms. Selecting and contacting appropriate donors takes time and donors may not be immediately available. As such, there is often a delay of **several days** prior to receipt of the initial HLA/HPA selected platelet product. Timely, scheduled delivery of subsequent selected products cannot be assured because Canadian Blood Services is entirely beholden to the availability of these specially selected donors. Caregivers should anticipate in advance when patients are becoming alloimmunized and/or refractory or when their platelet counts are dropping during therapy, to ensure that these special products are requested as far in advance as possible.

A systematic review on efficacy of HLA-matched platelet transfusions for patients with hypoproliferative thrombocytopenia showed that HLA-matched platelets did not reduce alloimmunization and refractoriness rates beyond that offered by leukoreduction.<sup>30</sup> HLA-matched platelets led to better one-hour post-transfusion count increments and percentage of platelet recovery in refractory patients; however, the effect at 24 hours was inconsistent.<sup>30</sup> In addition, there is no benefit for HLA/HPA selected apheresis platelet products in recipients who do not have demonstrable anti-HLA or anti-HPA antibodies. There is a paucity of rigorous prospective and appropriately powered clinical trials available to support current HLA-matching practices; multi-centre prospective studies comparing approaches designed to detect differences in patient important outcomes and resource implications are needed.<sup>31</sup>

The International Collaboration for Transfusion Medicine Guidelines (ICTMG) made the following recommendations for management of patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions.<sup>4</sup>

- In setting of class I HLA antibodies, should probably receive class I HLA-selected or crossmatch-selected platelet transfusions (weak level of evidence)
- In setting of HPA antibodies, should probably receive HPA-selected or crossmatch-selected platelet transfusions (very weak level of evidence)
- In setting of non-immune causes, should probably not receive HLA-selected or crossmatch-selected platelet transfusions (very weak level of evidence)

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## Chapter 18: Platelet Transfusion, Alloimmunization and Management of Platelet Refractoriness

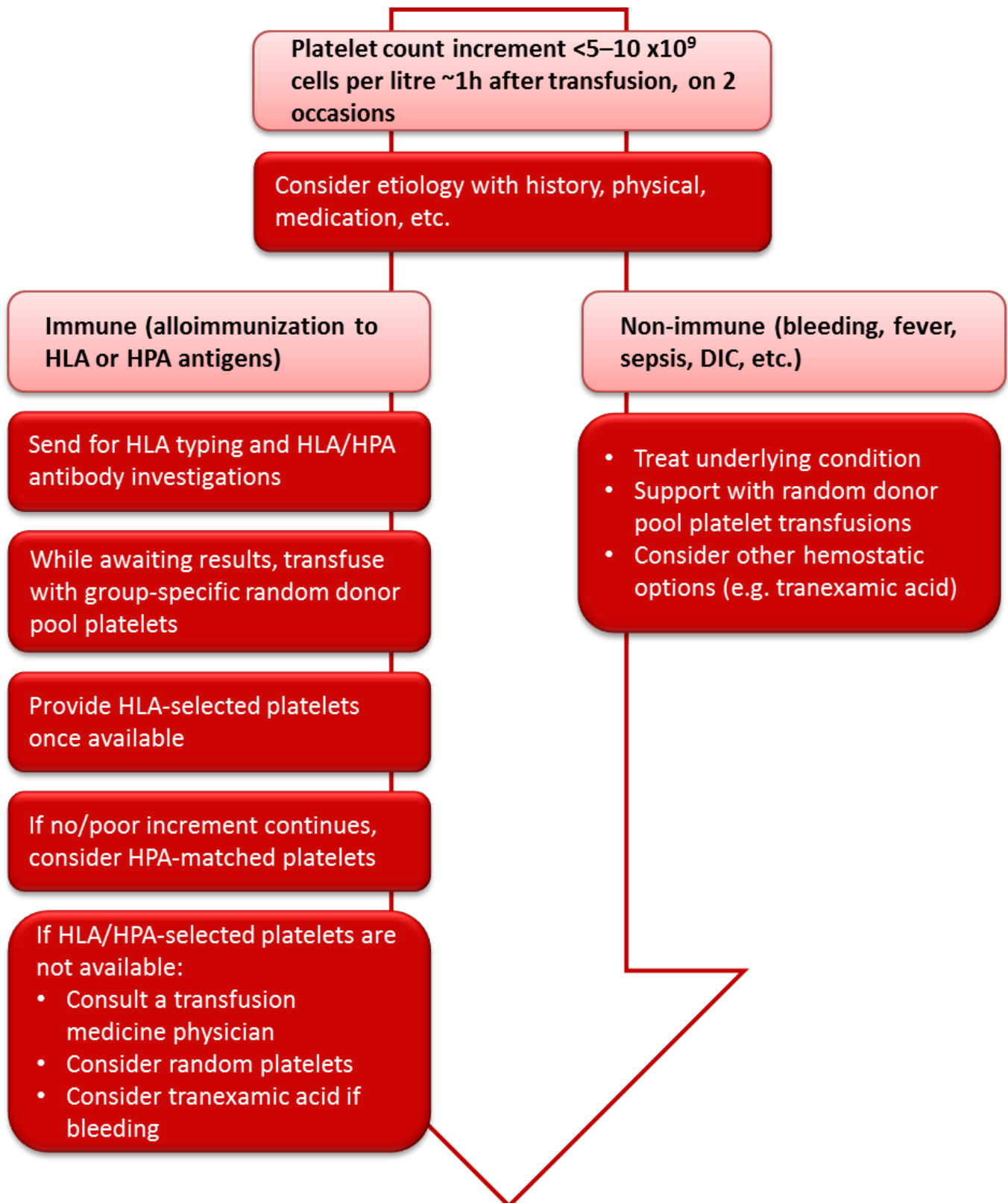
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**Figure 3:** Management of platelet refractoriness. The algorithm includes published ICTMG guidelines.<sup>4</sup>

Note that Canadian Blood Services' National Platelet Immunology Reference Laboratory, in Winnipeg, performs HLA and HPA antibody testing in parallel, and if the recipient has HPA antibodies, donors are selected to be negative for both HLA and HPA antigens where possible. Apart from HLA- or HPA-selected platelets, random donor pools are equivalent or preferable products.

Management of alloimmunized refractory patients who do not respond to matched platelets is problematic. Despite poor platelet count increments and survival, patients may still derive hemostatic benefits from regular platelet transfusions. These patients can be very challenging to treat and a consultation with a transfusion medicine specialist or blood centre physician should be considered.

### Post-Transfusion Purpura

Post-transfusion purpura (PTP) is a rare thrombocytopenic syndrome with an estimated incidence of one or two cases per 100,000 platelet transfusions. PTP can also occur after red blood cell transfusion. PTP is an immune-mediated reaction against human platelet antigens (HPA), most frequently against HPA-1a. PTP presents as profound thrombocytopenia (platelet count below  $10 \times 10^9$  cells per litre), with or without clinically significant bleeding, which occurs five to ten days following exposure to platelets or platelet-containing blood transfusions. Mortality has been estimated to be between five and twenty per cent. Thrombocytopenia can resolve within one or two weeks or may last for months. The majority of PTP episodes occur in women with a history of pregnancy, though cases can occur in men as well.

Data from the Serious Hazards of Transfusion surveillance program (UK) showed a reduction in incidence of PTP following implementation of universal leukoreduction.<sup>32</sup> Incidence in 1996–1999 was 10.3 cases per year, and this dropped following implementation of leukoreduction in 1999 to 2.3 cases per year between 2000–2005.

PTP occurs most often in patients homozygous for HPA-1b, who lack the common HPA-1a platelet antigen. A sensitizing event such as pregnancy or prior transfusion can cause development of anti-HPA-1a antibodies. Autoantibodies directed at recipient platelet antigens and antibodies against other platelet antigens have also been described.<sup>33-35</sup>

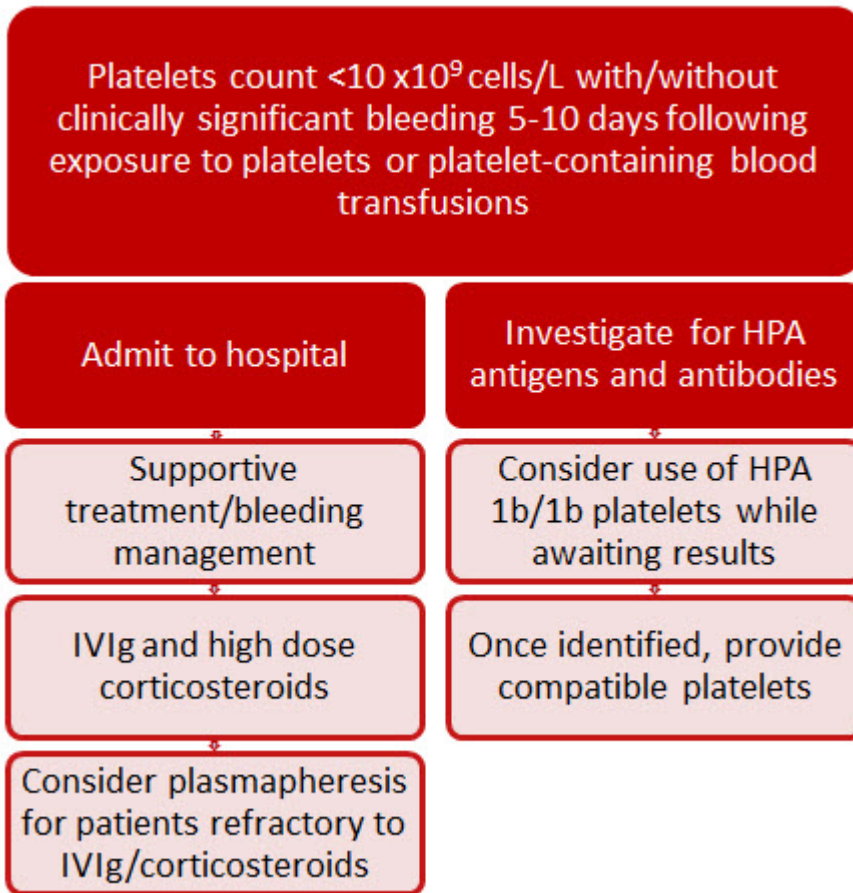
An algorithm for the management of PTP is shown in Figure 4. It is important to rule out other potential causes for severe thrombocytopenia in these patients. Goals of treatment are to mitigate risk of bleeding and often require use of emergent multimodal therapy depending on severity of bleeding. Initiation of treatment should be implemented without waiting for the results of serological investigations.

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**Figure 4:** Management of post-transfusion purpura (PTP) based on accepted current protocols.

## CONTINUING PROFESSIONAL DEVELOPMENT CREDITS

Fellows and health-care professionals who participate in the Canadian Royal College's Maintenance of Certification (MOC) program can claim the reading of the Clinical Guide to Transfusion as a continuing professional development (CPD) activity under [Section 2: Self-learning credit](#). The reading of one chapter is equivalent to **two credits**.

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We're here to answer your questions about the Clinical Guide to Transfusion. We'd also appreciate your ideas on how to improve the Guide. Please contact us through the [Clinical Guide feedback form](#).

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