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. Platelets circulate individually in the bloodstream 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 10⁹ 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 10⁹ per litre. The risk of bleeding complications from surgery or other injury increases with platelet counts below 30–50 x 10⁹ 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 and lists guidelines for administering platelet transfusions.

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.

Table 1: Platelet component characteristics at Canadian Blood Services*

<table>
<thead>
<tr>
<th>Platelet component</th>
<th>Volume (ml) Mean ± 1 SD</th>
<th>Platelet count (x10⁹) Mean ± 1 SD</th>
<th>Residual leukocytes (x10⁶) Mean ± 1 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled platelets LR CPD</td>
<td>342 ± 15 (n=583)</td>
<td>298 ± 68 (n=583)</td>
<td>0.09 ± 0.54 (n=550)</td>
</tr>
<tr>
<td>Apheresis platelets</td>
<td>242 ± 8 (n=519)</td>
<td>370 ± 48 (n=519)</td>
<td>0.067 ± 0.208 (n=510)</td>
</tr>
</tbody>
</table>

* Table reproduced from Canadian Blood Services Circular of Information. 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% labelled volume in all units tested; Platelet count: >240 x 10⁹/unit in ≥75% of units tested; Residual leukocytes: <5 x 10⁶ in all units tested.

- **Apheresis platelets**: Platelet count: ≥240 x 10⁹/unit in ≥75% of units tested; Residual leukocytes: <5 x 10⁶ in all units tested.
Both 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. Apheresis platelets offer the advantage of providing matched platelet products for specific indications. Apheresis platelets also decrease exposure to blood donors and, as a result, may be associated with lower rates of some adverse reactions. However, with a limited supply of apheresis platelets available, the only absolute indication for apheresis platelets is the provision of matched platelets for patients with (1) documented antibodies targeting human leukocyte antigen (anti-HLA) or human platelet antigen (anti-HPA) and (2) alloimmune platelet refractoriness, or in the setting of post-transfusion purpura or neonatal alloimmune thrombocytopenia.

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

Figure 1: Buffy coat platelet production at 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 $15-30 \times 10^9$ per litre; 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.
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 guideline on platelet transfusion make a number of recommendations for the use of platelet transfusions to prevent bleeding (Table 2).

<table>
<thead>
<tr>
<th>Recommendation for platelet transfusions</th>
<th>Quality of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
</table>
| Hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia<sup>11</sup>  
- Transfuse with a platelet count of ≤10 x 10<sup>9</sup> cells/l  
- Single standard apheresis or equivalent | Moderate | Strong |
| Patients having elective central venous catheter placement with platelet count <20 x 10<sup>9</sup> cells/l<sup>‡</sup> | Very low | Weak |
| Patients having elective diagnostic lumbar puncture with platelet count <50 x 10<sup>9</sup> cells/l<sup>‡</sup> | Very low | Weak |
| Patients having major elective non-neuroaxial surgery with a platelet count <50 x 10<sup>9</sup> cells/l<sup‡</sup> | Very low | Weak |
| Consider platelet transfusion for patients undergoing cardiopulmonary bypass who exhibit periop 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>1</sup>ICMTG guidelines<sup>3</sup>; <sup>2</sup>AABB guidelines<sup>4</sup>

The strong recommendation for transfusing hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia and a platelet count less than or equal to 10 x 10<sup>9</sup> cells per litre is based on three randomized controlled trials (RCTs). The two largest and most recent RCTs<sup>5, 6</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 platelets is not indicated unless the platelet count is less than or equal to 10 x 10<sup>9</sup> cells per litre. Two large RCTs and one prospective controlled cohort study demonstrated that lowering the prophylactic platelet transfusion threshold from 20 x 10<sup>9</sup> cells per litre to 10 x 10<sup>9</sup> cells per litre would decrease platelet utilization by more than...
Chapter 18: Platelet Transfusion, Alloimmunization and Management of Platelet Refractoriness

20% without increasing major bleeding. 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 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. 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*

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Platelet count ((x10^9/l))</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-immune thrombocytopenia</td>
<td>Less than 10</td>
<td>1 dose</td>
</tr>
<tr>
<td>Procedures not associated with significant blood loss, including percutaneous procedures other than epidural anesthesia or lumbar puncture</td>
<td>Less than 20</td>
<td>1 dose</td>
</tr>
<tr>
<td>Therapeutic anticoagulation that cannot be stopped</td>
<td>Less than 30</td>
<td>1 dose, and consult thrombosis specialist</td>
</tr>
<tr>
<td></td>
<td>- Epidural anesthesia or lumbar puncture</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Procedures with expected blood loss greater than 500ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Major non-neuraxial surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Significant bleeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Neuraxial surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Head trauma or CNS hemorrhage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Life-threatening hemorrhage</td>
<td></td>
</tr>
<tr>
<td>Platelet dysfunction and significant bleeding (e.g., ASA, clopidogrel therapy, post cardiopulmonary bypass)</td>
<td>Any</td>
<td>1 dose</td>
</tr>
<tr>
<td>Immune thrombocytopenia (ITP)</td>
<td>Case specific</td>
<td>1 dose, for life-threatening bleeding only and consult a hematologist</td>
</tr>
</tbody>
</table>

Published: Monday, August 1, 2016

**Important disclaimer:** This material is an educational tool providing guidelines for the care of patients. These recommendations should thus not be applied rigidly, since they could result in some patients receiving unnecessary transfusions or experiencing adverse effects from under-transfusion. The guidelines are mainly for adult patients and may not necessarily apply to the treatment of children. The recommendations do not replace the need in some cases to consult an expert in Transfusion Medicine to provide optimal patient care.
Clinical setting

<table>
<thead>
<tr>
<th>Diagnosis/Indication</th>
<th>Platelet count (x10^9/l)</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>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. These recommendations are part of the Ontario Quality Improvement Plan Toolkit and were produced with support from ORBCoN.</em> Additional notes: • Transfusion of platelets is indicated for prophylaxis against bleeding or for management of acute bleeding in patients with thrombocytopenia or platelet dysfunction. • In general, one dose raises the platelet count by approximately 15–25 x 10^9/l. • One dose = one buffy coat pool or one apheresis unit.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 transusions 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.

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.6, 11

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.3, 12 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.13 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 and therefore the rate of alloimmunization after Rh-incompatible apheresis platelet transfusions is extremely low.15, 16

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.

Published: Monday, August 1, 2016

Important disclaimer: This material is an educational tool providing guidelines for the care of patients. These recommendations should thus not be applied rigidly, since they could result in some patients receiving unnecessary transfusions or experiencing adverse effects from under-transfusion. The guidelines are mainly for adult patients and may not necessarily apply to the treatment of children. The recommendations do not replace the need in some cases to consult an expert in Transfusion Medicine to provide optimal patient care.
Chapter 18: Platelet Transfusion, Alloimmunization and Management of Platelet Refractoriness

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. The rate of bacterial contamination of platelet units is estimated at 1:1,000 - 1:3,000; the rate of bacterial sepsis from platelet transfusions is estimated at 1:100,000 and the rate of death from bacterial sepsis is estimated at 1:500,000. The source of the bacteria may be bacteremia in the donor or more commonly, bacterial contamination during collection. All platelet units issued in Canada are examined for bacteria by removing a small sample which is cultured for a minimum of 24 hours after collection. Units that are positive for bacterial growth are recalled, or, in the event that the unit has been transfused into a patient, the physician is notified.

According to the 2016 Canadian Blood Services Surveillance Report, 113,133 platelet products (21,266 apheresis and 91,867 pooled products) were tested in 2016, of which 24 apheresis and 74 pooled products had initial positive results for bacterial growth in the culture bottle. Of these, one apheresis and 15 pooled product cultures were confirmed as true bacterial contaminations and four apheresis and seven pooled products could not be confirmed as they were issued and/or transfused. This represents 27 products in total (2.39 per 10,000) with suspected or confirmed bacterial contamination based on current testing. Similarly, as part of its adverse transfusion reactions reporting, the Public Health Agency of Canada has reported a rate of 0.4 bacterial infection per 100,000 units transfused. This low rate makes bacterial infection the least common type of transfusion-related adverse reaction reported.

Platelet transfusions sometimes have the unique complication of alloimmune refractoriness. In this condition, routine platelet transfusions do not increase the recipient’s platelet count. This occurs in patients who have anti-HLA antibodies or who develop anti-platelet antibodies after a blood transfusion or a pregnancy. These antibodies can cause the immediate destruction of transfused platelets from random donor units. Adequate increments in the post-transfusion platelet count can then only be achieved by the transfusion of matched (HLA or platelet antigen) apheresis platelet units. The risk of alloimmune refractoriness is significantly reduced (to approximately 4% of recipients) by universal leukoreduction of all blood components. The risks of alloimmunization and platelet refractoriness are similar with platelets derived from whole blood versus apheresis since both products are leukoreduced.

While transfusions with apheresis platelets 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 white blood cells.

<table>
<thead>
<tr>
<th>Event</th>
<th>Approximate frequency</th>
<th>Symptoms and signs</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild allergy</td>
<td>1 in 100</td>
<td>Urticaria, pruritis and/or erythema</td>
<td>Transfusion can be restarted after assessment and necessary intervention</td>
</tr>
<tr>
<td>Febrile non-hemolytic transfusion reactions (FNHTR)</td>
<td>1 in 200</td>
<td>Fever, chills and/or rigor</td>
<td>Diagnosis of exclusion. A patient with fever should be evaluated for other more serious transfusion reactions.</td>
</tr>
<tr>
<td>Transfusion associated circulatory overload (TACO)</td>
<td>1 in 700</td>
<td>Dyspnea, orthopnea, cyanosis, tachycardia, raised venous pressure and/or hypertension.</td>
<td>Due to excessive volume or excessively rapid transfusion rates. May be difficult to distinguish from TRALI</td>
</tr>
</tbody>
</table>

Table 4: Adverse reactions from platelet transfusions*


Published: Monday, August 1, 2016

Important disclaimer: This material is an educational tool providing guidelines for the care of patients. These recommendations should thus not be applied rigidly, since they could result in some patients receiving unnecessary transfusions or experiencing adverse effects from under-transfusion. The guidelines are mainly for adult patients and may not necessarily apply to the treatment of children. The recommendations do not replace the need in some cases to consult an expert in Transfusion Medicine to provide optimal patient care.
## Event

<table>
<thead>
<tr>
<th>Event</th>
<th>Approximate frequency</th>
<th>Symptoms and signs</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic reaction</td>
<td>1 in 100,000</td>
<td>Fever, chills, rigors, nausea, vomiting, diarrhea, abdominal and muscle pain, hypotension, hemoglobinemia, and disseminated intravascular coagulation and/or renal failure.</td>
<td>Approximate frequency per platelet concentrate based on Canadian Blood Services data*:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- bacterial sepsis 1 in 125,000.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- death from bacterial sepsis 1 in 909,091</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>As reported by other international blood agencies:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- estimated risk of bacterial sepsis 1 in 100,000.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- estimated risk of death from bacterial sepsis 1 in 1,000,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>For evaluation and treatment of a reaction due to suspected bacterial contamination, refer to reference 19.</td>
</tr>
<tr>
<td>Transfusion related acute lung injury (TRALI)</td>
<td>1 in 1,200-5,000</td>
<td>New onset of hypoxemia, new bilateral lung infiltrates on chest X-ray and no evidence of circulatory overload.</td>
<td>Occurs during or within 6 hours of transfusion. May be difficult to distinguish from TACO.</td>
</tr>
<tr>
<td>Post transfusion purpura (PTP)</td>
<td>Rare</td>
<td>Abrupt onset of severe thrombocytopenia 1 – 24 days post transfusion.</td>
<td>Most cases of PTP occur in recipients who are HPA-1b homozygous receiving HPA-1a positive blood components.</td>
</tr>
<tr>
<td>Transfusion-related alloimmune thrombocytopenia</td>
<td>Rare</td>
<td>Abrupt onset of potentially severe thrombocytopenia within hours of transfusion.</td>
<td>Passive transfer of platelet antibodies leading to thrombocytopenia.</td>
</tr>
<tr>
<td>Immediate hemolytic transfusion reactions (HTR)</td>
<td>Rare</td>
<td>Fever, chills, hemoglobinuria, dyspnea, shock, disseminated intravascular coagulation, chest pain and/or back pain.</td>
<td>May be associated with ABO plasma incompatibility.</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>Rare</td>
<td>Hypotension, upper and/or lower respiratory obstruction, anxiety, nausea and vomiting.</td>
<td>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.</td>
</tr>
<tr>
<td>Graft-versus-host disease (GVHD)</td>
<td>Rare</td>
<td>Pancytopenia, rash, liver dysfunction, diarrhea.</td>
<td>Irradiated cellular blood components eliminate this risk.</td>
</tr>
</tbody>
</table>

*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 19.

---

**Important disclaimer:** This material is an educational tool providing guidelines for the care of patients. These recommendations should thus not be applied rigidly, since they could result in some patients receiving unnecessary transfusions or experiencing adverse effects from under-transfusion. The guidelines are mainly for adult patients and may not necessarily apply to the treatment of children. The recommendations do not replace the need in some cases to consult an expert in Transfusion Medicine to provide optimal patient care.
**CLINICAL GUIDE TO TRANSFUSION**

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

---

### MANAGEMENT OF SPECIAL SITUATIONS

**Platelet Refractoriness**

A major complication in the management of thrombocytopenic patients is platelet refractoriness. 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 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$^2$ and $n$ is the number of platelets transfused.

- The percentage platelet recovery (PPR) = $[(PI \times \text{body weight (kg)} \times 0.075 (l/kg))/n] \times 100$. Body weight (kg) x 0.075 (l/kg) is an estimate of blood volume.

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 evidence of alloimmune refractoriness. 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 Platelet Immunology Services provides access to those tests. HLA alloimmunization is more frequent than HPA alloimmunization as the cause of alloimmune refractoriness.

See Figure 3 for management of platelet refractoriness. Once anti-HLA or anti-platelet (anti-HPA) antibodies have been identified, matched apheresis platelet products may be useful to achieve adequate post-transfusion platelet count increments. Matched platelet products can be obtained from HLA-typed apheresis platelet donors and may be ordered through Canadian Blood Services using the “Request for HLA/HPA selected platelets”.

---


Published: Monday, August 1, 2016

**Important disclaimer:** This material is an educational tool providing guidelines for the care of patients. These recommendations should thus not be applied rigidly, since they could result in some patients receiving unnecessary transfusions or experiencing adverse effects from under-transfusion. The guidelines are mainly for adult patients and may not necessarily apply to the treatment of children. The recommendations do not replace the need in some cases to consult an expert in Transfusion Medicine to provide optimal patient care.
forms. Matching for HLA A and B antigens can result in adequate post-transfusion platelet count increments in up to 70% of immune refractory patients. Failure of HLA-matched apheresis platelets to produce an expected increment in the post-transfusion platelet count may be the result of anti-platelet antibodies. A platelet crossmatch can be used, in conjunction with or as an alternative to HLA matching, for patients with alloimmune refractoriness. While this would be useful for patients with anti-platelet antibodies, a large number of platelets may need to be screened during platelet crossmatch, and false negative results also occur. More information about platelet crossmatch may be obtained from the hospital transfusion service or from Canadian Blood Services Platelet Immunology Services. Management of 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.

ICTMG made the following recommendations for management of patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions.

- 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)
Post-Transfusion Purpura

Post-transfusion purpura (PTP) is a rare thrombocytopenic syndrome with an estimated incidence of one or two
cases per 100,000 transfusions. 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 x10^9 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. 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.

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.
ACKNOWLEDGEMENTS

The authors acknowledge Alan Tinmouth, MD, FRCPC as an author of a previous version of this chapter and Donald Arnold, MD, MSc, FRCPC, and Kathryn Webert, MD, FRCPC, for their review of the current version.

REFERENCES

4. Kaufman RM, Djulbegovic B, Gernsheimer T, Kleinman S, Tinmouth AT, Capocelli KE, Cipolle MD, Cohn CS.

Published: Monday, August 1, 2016

Important disclaimer: This material is an educational tool providing guidelines for the care of patients. These recommendations should thus not be applied rigidly, since they could result in some patients receiving unnecessary transfusions or experiencing adverse effects from under-transfusion. The guidelines are mainly for adult patients and may not necessarily apply to the treatment of children. The recommendations do not replace the need in some cases to consult an expert in Transfusion Medicine to provide optimal patient care.
Chapter 18: Platelet Transfusion, Alloimmunization and Management of Platelet Refractoriness


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


