Platelet Refractoriness: Platelet Cross-Matching Requests

Platelet Transfusion Guidelines:
Platelet products are generally in short supply in the UCSF hospital blood bank and at Blood Centers of the Pacific (BCP), the blood supplier for UCSF. To help guide providers in more appropriate use of these valuable resources, the hospital Transfusion Committee, clinical services commonly using platelets, and the Transfusion Service have set some useful guidelines for platelet transfusion. These guidelines can be found on the transfusion service website in the UCSF online Lab Manual:
http://pathology.ucsf.edu/labmanual/mftlng-mtzn/test/info/4bb.html#Platelets

Evaluation of a Patient with Platelet Refractoriness:
Crossmatched platelets are frequently requested for patients who seem to be refractory to platelet transfusion. It is important to note that it is much more common to have a non-immune cause for an inadequate post-transfusion increment, as opposed to an immune cause. Common scenarios that may suggest a patient is allo-immunized while in fact they are not include:

1. The post-count was drawn many hours after the platelet transfusion. Patient may have had an appropriate platelet increment in the immediate post-transfusion period and subsequently the count decreased gradually over time.

2. The pre-count was drawn many hours before the platelet transfusion. Patient may have had a much lower immediate pre-transfusion platelet count in vivo, and therefore the increment observed would have been appropriate for that pre-count, while it appeared inadequate based on the platelet count done much earlier.

3. The platelet dose given was not large enough to increase the count sufficiently. An example would be:
   a. Number of platelets in the unit was on the lower acceptable range (~3.0 x 10^11 per unit), and the patients had a high BSA (body surface area).

4. The patient is consuming platelets (but is NOT allo-immunized):
   a. Fever
   b. Sepsis
   c. Mucositis
   d. Occult or obvious bleeding
   e. DIC
   f. Splenomegaly (sequestration of platelets)
   g. GvHD
   h. Hematopoietic Stem Cell Transplantation
   i. Hepatic veno-occlusive disease (VOD)
In order to determine whether or not your patient may be allo-immunized to platelet products it is necessary to perform multiple 10 min-1 hour post transfusion counts (blood sample drawn between 10 min-1 hour after end of platelet transfusion).

Corrected Count Increment (CCI) Calculation:
When a request for cross-matched platelets is received by the blood bank, the lab medicine resident uses the 10 min-1 hour post count values to calculate multiple corrected count increments (CCIs) to help decide whether or not a patient would benefit from cross matched platelets.

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CCI = \frac{[post \ count-pre \ count] \times BSA \ (m2) \times 10^{11}}{\# \ of \ platelets \ transfused}
\]

Blood bank uses the exact number of platelets in the specific unit transfused to the patient for accurate CCI calculation, but when this number is not available the minimum acceptable number of platelets in each apheresis unit (3.0 x 10^{11}) may be used instead. If the CCI is < 7.5 on at least two occasions, platelet crossmatching may be indicated.

An online tool is also available at:
http://hccapps.musc.edu/hemonc/cci.htm
This tool uses 3.0 x 10^{11} as the estimated number of platelets transfused per each apheresis unit. (Note: make sure you check the “Pheresis” box instead of “Random donor”)

**Example:**
Pre-transfusion platelet count: 3,000/μL
1 hour post-transfusion platelet count= 21,000/μL
BSA=1.85 m²
1 apheresis unit was transfused ~3.0 x 10^{11} platelets

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CCI = \frac{[21-3] \times 1.85 \times 10^{11}}{3 \times 10^{11}} = 11.1
\]

How is a Platelet Crossmatch Test Performed?
Your patient’s plasma is tested against a panel of platelets from the most recent platelet donors at BCP (usually those units that were donated the day before and/or on the same day as cross-match testing). The test method currently used is a solid phase red cell adherence assay (Capture-P, Immucor). More information on this test
How are the Results of Platelet Crossmatches Reported?
The first time the Blood Bank Resident is consulted to evaluate a new patient suspected of being platelet refractory, they will enter a consult note in APeX, including a brief assessment of patient and results of the initial cross-match or HLA testing. The results are reported as the number of units that are reactive out of the total tested.

- Units that are REACTIVE against patient plasma are INCOMPATIBLE.
- Units that did NOT show reactivity are considered COMPATIBLE.

For example: “Platelet cross-match results show reactivity in 20 out of 30 units tested” means only one third of donors tested were found to be compatible.

Results of all subsequent platelet crossmatch tests will also be entered in APeX as a short result note by the Blood Bank Resident.

Interpretation of the Platelet Crossmatch Results:
- If 100% of the donor platelet units tested are compatible, your patient is NOT ALLOIMMUNIZED and has some other reason for inappropriate response to platelet transfusions (for example, non-immune mediated causes). Crossmatch compatible units are NOT indicated in such cases.

- If 100% of the donor platelet units tested are reactive (incompatible), this most likely suggests a significant degree of alloimmunization to HLA antigens, although in rare instances platelet-specific alloantibodies or autoantibodies (the latter seen in ITP) may be the reason for such significant reactivity. Additionally, false positive reactions due to unknown interference may also be seen. In such instances blood bank will recommend a repeat cross-matching against a new set of platelet donors, and also may consider HLA Class I typing/ anti-HLA Class I antibody testing to ensure the reactivity is from HLA antibodies and also to prepare for potential support with HLA-matched units.

- Most platelet cross-matching results fall somewhere in the middle of these two extremes, suggesting mild, moderate or significant degree of alloimmunization.

- Cross-matched platelets are only helpful for platelet refractoriness due to alloimmunization (either to HLA antigens, or rarely to platelet specific antigens).

- Cross-matched platelets do not prevent transfusion reactions.

- In patients who have a combination of immune and non-immune causes for platelet refractoriness there is no guarantee that the cross-matched platelets will be superior to random donor units.
- Cross-matching is not indicated for patients with platelet-specific autoantibodies (ITP patients) as it is expected these patients destroy both self and non-self platelets equally.

**Ordering Cross-matched Platelets:**
Requesting crossmatched platelets is a different process than RBC crossmatching and it is important to note:

- Unlike RBC cross-matching (done on-site in our blood bank), platelet cross-matching is performed offsite at the BCP Immunohematology reference lab, therefore needs more careful coordination between blood bank and clinical services.

- If you suspect your patient is alloimmunized, perform 10 min-1 hour post-transfusion platelet counts. If your patient still shows inadequate increments, please contact the lab medicine/blood bank resident at 353-1313 (or pager 443-8296) as soon as possible to discuss the case and possible need for platelet cross-matching.

- If the lab medicine/blood bank approves crossmatching, you may proceed to order the ‘Platelet Crossmatch Test’ in APeX.

- Platelet cross-matching can only be sent out Monday-Friday. PLEASE follow the instructions of the Blood Bank Resident on when to order the Platelet Crossmatch test.

- Samples for cross-matching should be received in the blood bank as early as possible in the morning of testing (ideally before 10AM).

- Each platelet cross-matching requires 2 large lavender top tubes.

- Sometimes left-over sample is available for repeat crossmatching. The blood bank resident will instruct you in such cases to use the ‘Add on ONLY to sample in Lab’ frequency when ordering the test in APeX.

**Additional Information:**

- Results of crossmatch testing are available the same afternoon, but actual platelet products may become available slightly later (usually the next day after results are available, but sometimes the night of the crossmatch), given the time required to complete bacterial and infectious marker testing.

- Shelf-life of platelets is significantly shorter than an average RBC unit:
  - Platelet shelf-life is 5 days from day of donation, but at least 2 days of this will be dedicated to infectious disease and bacterial screening.
Therefore by the time a unit is available for transfusion the shelf-life is only **1-3 days**.

- In contrast, RBC shelf-life is 35 or 42 days (depending on anticoagulant used)

**Transfusing Cross-Matched and HLA-Compatible Platelets**

*It is VERY important to continue checking 10 min-1 hour platelet counts after EACH cross-match or HLA-compatible unit.* This is especially useful for patients with a significant degree of allo-reactivity. Patients respond differently to each transfused unit and occasionally, there is discrepancy between *in vitro* cross-matching or HLA antibody compatibility, and *in vivo* responses to various donors. Performing the post count will allow the blood bank and BCP to identify donors that have proven to be most compatible clinically, and therefore provide the best units for the patient. Such donors can often be recruited and are willing to repeatedly donate for the patient (historically compatible).

**Useful review articles on platelet refractoriness:**
