

Definitions:

A patient is refractory to platelet transfusions if the patient's circulating platelet levels fail to increase by at least 10,000/microliter after transfusion of an appropriate dose of platelets. There are multiple causes of platelet refractoriness, both immune-mediated and non-immune-mediated.

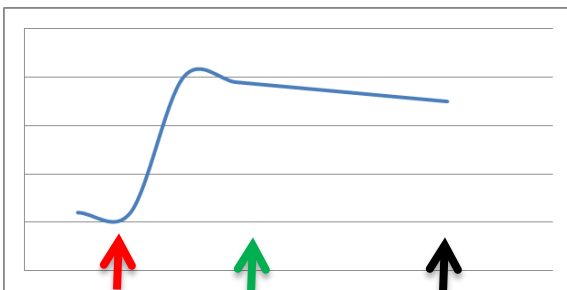
Immune-mediated refractoriness is due to antibodies made by the patient that recognize an epitope on the transfused platelets, most commonly human leukocyte antigen (HLA) class I. Patients produce these antibodies as a result of prior sensitization to specific HLA proteins through prior transfusions, organ transplantation, bone marrow transplantation, or prior pregnancies.

Non-immune-mediated refractoriness is due to a process that significantly decreases the circulation time of transfused platelets. Non-immune causes include splenomegaly, diffuse intravascular coagulopathy (DIC), fever, infection (sepsis), ongoing bleeding, graft-versus host disease, veno-occlusive disease, and some medications.

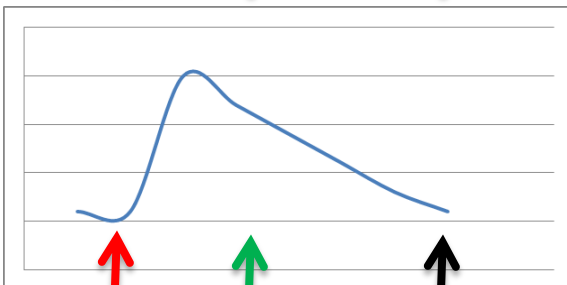
First step – Evaluation of pattern of refractoriness:

At least three 1-hour post-transfusion platelet levels are used to determine both (a) if the patient is platelet refractory and (b) the pattern of refractoriness.

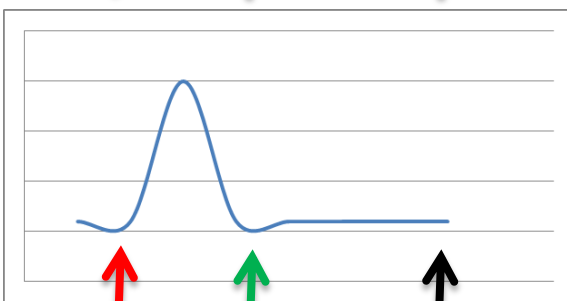
Below are diagrams to illustrate the patterns of platelet refractoriness.



Normal patient showing platelet level graphed against time. The patient shows an increase at the time of transfusion (red arrow) and a minimal decrease over the following hours. Due to this slow decrease, measurement at both 1 hour and 6 hours post-transfusion (green and black arrows) show similar levels.



Patient with non-immune platelet refractoriness (e.g. fever). The patient shows an increase at the time of transfusion (red arrow) and a slow decrease over the following hours. Measurement at 1 hour (green arrow) and 6 hours (black arrow) show markedly different levels.



Patient with either immune-mediated refractoriness or non-immune refractoriness (e.g. splenomegaly). The patient shows an increase at the time of transfusion (red arrow) and a rapid return to pre-transfusion levels. Measurement at 1 hour (green arrow) and 6 hours (black arrow) show low platelet level

The above diagrams show how 1-hour post-transfusion platelet levels are necessary to identify patients who may have immune-mediated refractoriness.

Second step – Cross-match compatibility and HLA-compatibility testing

If there appears to be a component of immune-refractoriness, two pink-topped tubes of the patient's blood are sent to the American Red Cross where the patient's plasma is cross-matched against single-donor (apheresis) platelet units.

This test evaluates if the patient's serum contains antibodies that recognize the platelets in the donor unit. The American Red Cross reports the results of this cross-match evaluation to the blood bank (e.g. patient is compatible with 2 of 9 units tested) and the blood bank resident will contact the care team to apprise them of the results.

If the patient is compatible with the majority (e.g. 9/10) of the cross-match tested units, the patient's refractoriness is not due to an immune cause and pooled platelet units (5-packs) should be used to meet the patient's needs.

If the patient is compatible with a minority (e.g. 2/10) of cross-match tested units, the patient may have a component of immune-mediated refractoriness and the cross-match compatible platelet units will be made available to the care team for transfusion. After transfusion of the cross-matched units, 1-hour post transfusion platelet levels should be drawn to evaluate the patient's response to the cross-matched unit.

If the patient is not compatible with any of the cross-match tested units, the patient may have a component of immune-mediated refractoriness and cross-matched units will not be easily identified. At this point, a red-top tube of the patient's blood should be drawn to evaluate for human leukocyte antigen – percent reactive antibodies (HLA-PRA) and a yellow-top tube should be drawn to determine the patient's HLA genotype. These tests are performed by the Tissue Typing (Histocompatibility) laboratory.

If the patient has a moderate HLA-PRA (e.g. 40 – 80%) and platelet cross-matching is insufficient, then HLA-compatible or HLA-selected platelets will be requested from the American Red Cross. If the patient has a high HLA-PRA (e.g. >80%), then HLA-matched platelets will be requested. HLA-compatible/selected/matched platelets are supplied by the Southern California and Penn-Jersey regions. If platelets are obtained, the blood bank will contact the care team when they have arrived at UMHS and available for transfusion. A 1-hour post-transfusion platelet level should be obtained to evaluate the patient's response.

- **The turn-around time for cross-matched platelets is generally 3 days. This test is not performed on weekends, and thus specimens are only sent to the American Red Cross on Mondays – Thursdays. Specimens received Friday – Sunday will be held by the Blood Bank and sent on the following Monday.**
- **The turn-around time for HLA-PRA is about 5 working days. This test is not performed on weekends. Specimens collected on the weekends will be held by Specimen Processing until the following Monday.**
- **The turn-around time for HLA antigen typing is about 5 working days. This test is not performed on weekends. Specimens collected on the weekends will be held by Specimen Processing until the following Monday.**
- **If the necessary test results have been obtained, the turn-around time for HLA-compatible/selected platelets is 5 – 7 working days. HLA-matched platelets may require more time, especially if the patient has a problematic HLA type.**

Third step – Final evaluation

Once the evaluation is complete, including 1-hour post-transfusion platelet levels after any cross-matched or HLA-matched platelet units transfused, a final report with recommendations for future transfusion usage will be issued.