PLATELET REFRACTORNINESS
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(Updated 4/8/2011)

I. Definition of refractoriness
a. Refractory= failure to achieve an acceptable increment in platelet count following platelet transfusion at least on two occasions. Platelet count must be measured within one hour after transfusion.
b. Rule of thumb: a unit apheresis platelet (or a pool of 6 platelet concentrates) should achieve an increment of 30,000 to 50,000/µL in an average adult.
c. Alternative way to determine whether a patient is refractory is by calculating the corrected count increment or CCI:
   \[ CCI = \frac{\text{Platelet count}_{\text{post}} - \text{Platelet count}_{\text{pre}} \times \text{BSA} (\text{m}^2)}{\text{Number of platelets transfused} \times 10^{11}} \]
   o CCI of 5,500 – 7,000 or above is considered an adequate response
   • Example: A patient with BSA of 1.7m² who received a unit of apheresis platelet containing 3x10¹¹ platelets. His count rose from 10,000 to 30,000/µL post transfusion.

   \[ CCI = \frac{(30,000-10,000) \times 1.7}{3} = 11,333 \]

II. Etiology
a. Nonimmune (more common) factors:
   i. Fever,
   ii. Splenomegaly
   iii. DIC, Bleeding,
   iv. Drugs (amphoterin B)
b. Immune-mediated: platelet destruction mediated by antibodies
   i. HLA antibodies (platelets express HLA-A and HLA-B antigens)
   ii. Platelet-specific antibodies – less common
c. Differentiate non-immune vs. immune refractoriness: Obtain post-transfusion platelet count 10 min to one hour post transfusion:
   i. Non-immune refractoriness typically still show some response at this time
   ii. Immune mediated refractoriness: the destruction of platelets is immediate, poor increment even right after transfusion

III. Prevention
a. Use leukoreduced products to minimize HLA alloimmunization
b. Risk of alloimmunized reduced from 30-40% to 10-15% according to the TRAP study

IV. Management and Platelet Transfusion Support
a. Correct non-immune causes (if possible) such as infection, fever, DIC, offending drugs.
b. Consider fresher, ABO identical apheresis products: data have shown that ABO compatible units lead to a 20-25% increased increment in plt count post transfusion compared to ABO incompatible units. Unclear whether this is clinically significant, but does not hurt to try.

c. If one hour count shows poor increment, then try to demonstrate the presence of antibodies (HLA and platelet antigen specific antibodies)
   • PRA (Panel-reactive antibody): result is the percentage of HLA targets to which the patient’s serum reacts with, assayed based on lymphocytotoxicity or is EIA-based
   • ASP (antigen-specificity prediction): flow cytometry based test in which patient serum is reacted with beads coated with specific HLA antigens.

V. Transfusion Support
a. Non-immune mediated refractoriness: Transfuse as indicated, may require more frequent transfusions
b. Immune-mediated refractoriness due to anti-HLA
   i. Use HLA phenotype matched units (See below for match grades)
   ii. Use select HLA antigen negative platelets if antibody specificity is known
   iii. Use crossmatch compatible units
Note: Always get post-transfusion counts, to determine the response to these specially selected products

<table>
<thead>
<tr>
<th>Platelet HLA Match Grades:</th>
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<tbody>
<tr>
<td>A: 4 antigen match</td>
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<tr>
<td>B1X: 3 antigens match. 1 antigen is cross-reactive</td>
</tr>
<tr>
<td>B1U: 3 antigens match. 1 antigen is unknown (possible homozygosy)</td>
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<tr>
<td>B2UX: 1 unknown, 1 cross-reactive</td>
</tr>
<tr>
<td>C: 3 antigen match. 1 mismatch with no crossreactivity.</td>
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<tr>
<td>D: 2 antigen match. 2 mismatch with no crossreactivity.</td>
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VI. Other Measures to consider
a. Raise the hct to 30% if patient also very anemic: platelet will adhere to vessel wall and function better as they are pushed by the RBC’s to the periphery of a vessel space (“rheostatic effect”)

b. Consider local treatment if bleeding is local: sutures, packing, fibrin glue etc.

c. Consider anti-fibrinolytic agents such as Amicar
d. NovoSeven in patient with severe bleeding