

Answers to Questions for CASE REPORT - Acute Hemolysis secondary to ABO incompatible platelet transfusion (Vol. 5 Issue 1 February 2010)

1. What are the most common laboratory indications of hemolysis?

Hemoglobin ↓: Hemoglobin levels will decrease due to destruction of red cells in the circulation. The decrease will be relative to the number of red cells destroyed. The hemoglobin is released into the plasma resulting in a pink to red colouration of the plasma (hemoglobinemia). Free hemoglobin is excreted through the kidneys which causes pink or red colour in the urine (hemoglobinuria).¹

Direct Antiglobulin Test +: The direct antiglobulin test detects antibody and / or complement coating the red cells *in vivo*. As hemolysis can be the result of antibody binding to an antigen on the red cell (as in this case), the direct antiglobulin test is often positive in this situation. Activation of complement (C3a and C5a specifically) causes an increase in vascular permeability, dilation of blood vessels, release of serotonin and histamine which results in the signs of a hemolytic reaction – fever, chills and hypotension.¹

Serum Bilirubin ↑: Total serum bilirubin increases within 4-6 hours of a hemolytic reaction occurring as a result of free hemoglobin released from the destroyed red cells metabolizing. The bilirubin level should return to normal levels within about 24 hours if bilirubin excretion is normal.^{1,2}

Haptoglobin ↓: Haptoglobin is a protein that binds to free hemoglobin released from destroyed red cells. Hemolysis of red cells results in a decrease in haptoglobin levels, usually reaching the lowest levels at 1-2 days post event. As haptoglobin levels and measurement varies, comparison with pre-transfusion levels is recommended. This is often the most diagnostic value in the investigation of slow or subtle red cell hemolysis.^{1,2}

Lactic dehydrogenase (LDH) ↑: LDH levels will rise as a result of hemolysis. Red cells contain large amounts of LDH and, when they hemolyse, the LDH is released into the plasma.^{3,4}

Microspherocytes +: Following a hemolytic reaction, microspherocytes are found on the peripheral blood smear, appearing as small cells lacking the central pallor of normal biconcave red cells.⁴

2. Is a high titre in the donor plasma always related to a hemolytic reaction in the recipient if there is ABO incompatibility?

In most cases reported in the literature, the titre of the ABO antibody involved in this type of hemolytic reaction is over 64, however, there have been some case reports of acute hemolysis where the titre has been below this level.⁴

In addition to the amount of antibody present, hemolytic processes can be related to the antibody subtype present. Some subtypes of antibody are more efficient at clearing incompatible red cells than other subtypes. IgG subclass 1 is more efficient than IgG subclass 3 therefore it takes a smaller amount of IgG1 antibody to cause destruction of incompatible red cells.⁵ Since titres are not routinely performed on the plasma of donors, there are no statistics on how often a unit with a high titre isoagglutinin is infused uneventfully.

3. Name one alternative strategy to reduce the incidence of this type of reaction that was not mentioned in this case report?

This type of reaction occurs most commonly when a Group A recipient receives Group O platelets. Stocking predominantly group A platelets in inventory can lower the risk of having to issue a group O unit to a group A recipient. However, although the blood suppliers (Canadian Blood Services and Héma-Québec) are attempting to increase the per cent of group A Apheresis and Buffy coat platelets available to hospitals, it is not always practical or possible to stock only nongroup O platelets.

Another consideration is to limit the volume of incompatible plasma transfused.



This can be done by (as mentioned in the case report) reducing the plasma in the component through centrifugation or by having a policy limiting the volume of the group incompatible plasma issued to a single patient in a given time period (e.g. 300-500 mL per day).

It is important to note that reducing the volume of incompatible plasma through centrifugation should be performed carefully in order to reduce the platelet loss or damage. Key issues to consider are⁵:

- If the centrifugal force is too high, platelet loss / damage may be large. Expected loss appears to be in the range of up to 20% if spun at 2000g x 10 minutes. At higher g force, platelet loss can be as high as 55%.
- Once the platelets have been centrifuged, it is important to allow the platelet bag to rest at room temperature prior to resuspension. The platelets should remain at room temperature, without agitation for 20 to 30 minutes.
- If the platelet bag is entered during the procedure of plasma reduction, the expiry of the product will be reduced to 4 hours (at room temperature).
- Plasma reduction should occur as close to the actual time of infusion as possible.

4. This type of hemolytic reaction seems to be happening more frequently according to published and anecdotal reports, what is the reason for the increase?

Between 2006 and 2008, Canadian Blood Services implemented a new production method (Buffy Coat production method) that allowed platelets to be processed from whole blood donations within 24 hours of donation. The Buffy Coat method has the benefits of providing an already pooled component for hospitals as well as facilitates bacterial testing of components.

Buffy coat platelet pools are prepared by concentrating the buffy coats from four whole blood donations and resuspending them into the plasma of only one of these donors (male). Because the plasma is from only one donor, if that donor happens to have a high titre or 'dangerously hemolytic' ABO antibody, the risk of a hemolytic reaction occurring is more likely than in the past, when the platelet pools were prepared from separate plasma rich platelets (PRP) containing plasma from all of the donors. (even if one donor had a high titre, it would be diluted by the other three or four donor's plasma). It is important to note that apheresis platelets also pose a similar risk as the plasma in the component is from one donor.⁷

The incidence of group O donors with high-titred ABO antibodies has been estimated to be approximately 3% to 5% of donations although some have reported that the plasma from up to 40% of group O donors may have the potential to cause a hemolytic reaction if transfused to a group A or B recipient.^{4,8}

References for Answers to Questions:

1. Quinley E. Immunohematology – Principles and Practice. JB Lippincott Co, Philadelphia; 1993: p 236-237.
2. Transfusion reactions: - emedicine Emergency Medicine. <http://emedicine.medscape.com/article/780074>.
3. Pierce RN, Reich LM, Mayer K. Hemolysis following platelet transfusions from ABO-incompatible donors. Transfusion 1985; 25: 60-62.
4. Larsson LG, Welsh VJ, Ladd DJ. Acute intravascular hemolysis secondary to out-of-group platelet transfusion. Transfusion 2000; 40: 902-906.
5. Brecher ME Ed. Technical Manual 15th ed. AABB Press, Bethesda. 2005: p258, 817.
6. Laura Cooling MD. AABB News September/October 2005 Q&A: p 38-39.
7. Canadian Blood Services Customer Letter # 2005-03. Buffy Coat Production Method. 2005-05-26.
8. MacLennan S. High Titre Anti-A/B Testing of Donors within the National Blood Service (NBS) Version 11: 2002-05-09.

