Michigan Association of Blood Banks presents

Summer 2013

In A Different Vein

Michigan Association of Blood Banks, c/o Linda Cardine or Terry Downs
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PRESIDENT'S MESSAGE

By Barbara A. O'Malley, M.D.

Dear MABB Members,

How time flies when you're busy. The MABB Executive Committee is busily preparing this year's Annual Meeting, once again to be held at VistaTech on the Schoolcraft College Campus. We had a great meeting last year with some really glowing evaluations. This year's brochure should have reached you recently, and we hope to host another successful meeting.

Inside This Issue

Our message to our members this year is "let's grow the organization". If every one of us just asks the technologists we work with daily to join MABB, we can get the younger techs involved. They just want to be invited. Like potential blood donors, who do not give because no one ever asked them, I'm finding the new technologists are interested in becoming involved, but they just needed the nudge of encouragement. So let's spread the advantages of becoming an MABB member: networking with others of our profession, gaining CE credits locally and at a reasonable cost and the opportunity of learning the cutting edge technology and research in a friendly, inviting learning environment.

SAVE THE DATE!

59th MABB Annual Meeting: September 18 - 19, 2013

Hope to see you soon in Livonia and bring a friend!

- Barbara

MICHIGAN ASSOCIATION OF BLOOD BANKS

Annual Meeting Minutes: September 12, 2012

By Frances Scher
Secretary, Michigan Association of Blood Banks

Sue Adams Called Meeting to order 11:50am
Education Committee – Jan Deters
-Fall RAP Nov. 2011 West Branch

- presented different challenges between small and large hospitals
- attendees were appreciative of the CE hours and the networking available

-Spring RAP June 2012 Grand Rapids

- Gel and Solid phase
- brought case studies
- good discussion

-Nov 2012 Fall RAP Gaylord

- topic to be announced

-Looking for Committee members

- Handle all CE throughout the state (except annual meeting)
- Good opportunity to share information, enhance careers and network
- Normally hold a wet workshop (Need increase participation to continue this.)
- If interested see Jan or another board member

Membership Committee
-Position of chair is available
-If a member of the committee can be an ambassador to coworkers

Publications - Jim Fiedor
-No articles submitted to publications
-Putting pictures of meeting and slide presentations on the website
-Articles needed
-Lab issues, case studies, interesting articles, crossword, and others

Archives – Jim Fiedor
-Centralizing MABB historical materials
-Scanning 5 bins of historical records (about 20% done)
-Once computerized will determine what to keep and archive
-Might put on website
-Creating Master Document List

By Laws/Policy Committee – Terry Downs
-Need to be revised.
-Will be working on it this year/will vote on next year
-If interested in helping, let Terry know

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Secretary – Frances Scher
-All board meeting minutes approved
-Copies of the minutes from last year's annual meeting were passed out to members during lunch.
    -Members were given the opportunity to make any corrections if necessary.

Financial Report – Linda Cardine
-Non-profit organization that is dedicated to professional education
-Inflow - $24,447.84 and Outflow - $26,078 with overall loss - $1630.16
-Eliminating expenses by now engaging a volunteer office manager, Linda Cardine
-$38,236 – checking account
-$23,805.33 – Dreyfus account balance
-Encouraged everyone to join and be a member to keep MABB viable

Founder's Award
Karen Gizzi
-Takes care of vendors for the past 8 years as the vendor coordinator for the annual meeting
-Karen accepted the award and thanked the membership

Sheikh Saeed Memorial Scholarship
-No applicants
-Scholarship to annual meeting
-Provided by Henry Ford Health System
-Honors a past president of the MABB
-Apply on the website

President remarks – Sue Adams
-Large amount of budget was going to office support
    -Linda is doing a great job taking on this now volunteer position and will continue for the next year.
-Encourage everyone to get involved
    -Can improve a career and networking
    -Want younger techs and generalists to get involved
        -Only requirement is to love blood banking
        -Talk to board members for more information

Kay Bettie Award
Cynthia Flickinger
-MI Blood supported this lecture

President Award given to Sue Adams by Terry Downs
-accepted position for the second time
-good leader/good person to work with
-made good decisions to balance the budget

Voted on board members for next year:

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President Elect Judy Easter
President Barbara O'Malley
Past President Sue Adams

Members at Large:
Dr. Barry Siegfried (1 year term)
Dr. Peter Millward (2 year term)
Karen Gizzi (2 year term)
Secretary – announced second day of meeting, Sueann Dorr (2 year term)

The members approved the slate of officers

Sue Adams performed the installation of officers

Adjourned at 12:20 by Sue Adams

-Respectfully submitted by Frances Scher

Highlights of the 2012 Meeting

By Barbara O'Malley, MD

The meeting began with morning remarks began with Sue Adams, who introduced Dr. Laura Cooling of University of MI. Laura introduced Ms. Cindy Flickinger from the American Red Cross Rare Donor Program, centered in Philadelphia, PA. Dr. Cooling remarked of how proud Kay Beattie would be of the work being done by the Rare donor program. Ms. Flickinger revealed data about the growth of the rare donor program and the difficulty of providing blood for the highly immunized sickle cell populations over several regions. Units have been provided, not only nationwide, but also internationally. Places as far away as Trinidad, India and the Philippines. She also revealed many of the databases for which blood is provided. High incidence antigens constitute one database; while another is multifactorial and provides phenotype matched units, particularly for sickle cell patients. When requested from Penn-Jersey for a rare donor type, a notice goes forth to all members of the rare donor program to search their inventory. Blood may be present in liquid state or frozen.

Ms. Flickinger presented the obituary of Kay Beattie which was originally featured in Immunohematology, the Journal of the American Red Cross. This is the same journal Ms. Flickinger is currently Chief Editor.

The meeting progressed with Clinical Case Studies presented by Dr. Laura Cooling. Dr. Cooling's case was of life-threatening hemolysis due to cold antibody, unresponsive to all medical therapy. The apheresis instrument could not be used for removal of the antibody because the patient's blood would coagulate tubing in the instrument. Manual apheresis with blood reconstituted to 50% hematocrit was performed over 14 hours. The result of these heroic measures was survival of the patient. The etiology of the patient's hemophagocytic syndrome was never elucidated. The patient recovered because of the extraordinary treatments used in this case.

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Following the Clinical Case Studies, the MABB Annual Meeting was called to order by Susan Adams, current President. Jan Deters presented the Education Committee Report: RAP sessions were held, the first in West Branch, MI and the second was hosted by MI Blood in Grand Rapids, MI. The third will be held in December in Gaylord, MI.

Jim Fiedor, our Publications and Archives Chair reported that no articles were submitted to "In a Different Vein". He appealed to the audience for articles, puzzles and news to be submitted to him to get the publication going again. The archives, historical material from previous meetings, in being converted to electronic format and he is also working on a master index of all materials.

Terry Downs, Past President, reported for the Bylaws Committee, which she will now chair and appealed to the audience for involvement on this committee to review and revise the Bylaws for presentation at the next annual meeting.

Linda Cardine, Treasurer and volunteer MABB Office Administrator, reported the financial status of the organization. Linda's past year of volunteering has saved the organization a great deal of funds and also has resulted in improvement in all organizational facets.

The secretarial report by Frances Scher, the minutes of last year's annual meeting, was printed and distributed at lunch for approval. A plaque was presented to Cindy Flickinger, the recipient of the Kay Beattie Award. An engraved crystal vase with a dozen roses was given to Karen Gizzi, who was surprised to receive the Founder's Award. Sue Adams received the President's Award, a beautiful engraved crystal vase with a dozen roses from Terry Downs, past President. Sue Adams officiated the swearing in of the new officers. Judy Easter accepted the nomination for President Elect and Dr. Barbara O'Malley accepted the Presidency. The offer of the position of Secretary was given to SueAnn Dorr of Karmanos Cancer Center, who accepted following the meeting. Ending with an appeal by Sue Adams to bring new members into the organization, the meeting was adjourned.

Following a lovely lunch put on by the Schoolcraft Culinary Arts School, the afternoon session progressed with Dr. Laura Cooling announcing Dr. Tamar Abdelhak of Henry Ford Hospital System. Dr. Abdelhak is the head of Critical Care Neurology service and the director of the Neurology Fellowship Program. He gave a most interesting talk about reversal of anticoagulation and anti-platelet therapy. He reviewed the coagulation system and included the sites of action of the various drugs used clinically today. The lecture rang true with many in the audience who had seen patients with bleeding complications secondary to coumadin, heparin, LMWH, aspirin, plavix and the newer direct thrombin inhibitors.

The afternoon moderator was Judy Easter, who introduced Dr. J. Lynne Williams, Director of the School of Health Sciences at Oakland University. Dr. Williams gave us the historical chronical of the profession of medical technology. It was a long journey until the profession was recognized as such. She stressed the components of a profession, including an examination which must be passed for certification, regulation by a board composed of those in the profession, and maintenance of certification. She also discussed the struggle for state licensure. It is astounding that barbers, hair stylers, manicurists and massage therapists are licensed by the state and recognized as professionals, but we as med techs have not attained licensure. The ASCP has recently come out in favor of licensure and CAP has announced that they will not oppose licensure.

The afternoon session continued with Dr. Larry Lum of the Karmanos Cancer Center, who fascinated us with the concept of "armed T-cells" and patient anti-tumor vaccination. Dr. Lum's research is showing increased survival rates among patients with triple negative breast cancer, multiple myeloma and ovarian

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cancer. Truly, this is cutting edge science leading to personalized medicine and therapies.

Dr. Charles Schiffer, also of the Karmanos Cancer Center, closed the first day's sessions with an interesting lecture on the treatment of thrombocytopenic patients. He reviewed megakaryopoiesis and the story of thrombopoietin (TPO), the hoped-for growth factor to stimulate platelet production in the thrombocytopenic setting, but which ended with patients forming antibodies to TPO. He emphasized alloimmunization to platelets and explained how to start with random donor transfusions, hoping that one of the platelet units in the pool would survive and give the recipient an incremental rise in platelets. Failing RDPs, patients would need HLA matched or crossmatched platelets. Dr. Schiffer recounted a time when platelets were stored at 40F and the resultant increase in transfusion reactions seen when they were converted to a room temperature product. He also enlightened us about his research years ago, freezing autologous platelets in DMSO and returning them to recipients of bone marrow transplants post-myeloablative chemotherapy. Dr. Schiffer also referred to randomized controlled studies which yet must be done to determine safe platelet counts for invasive procedures, such as central line placement, thoracentesis, paracentesis, lumbar puncture, etc. The existent guidelines in the literature are based on very weak evidence or the guidelines simply don't exist.

2011 ANNUAL MEETING SCRAPBOOK

SAVE THE DATE!

59th MABB Annual Meeting: September 18-19 2013

L to R: Sue Adams, Terry Downs, Barbara O'Malley, Allyson Henstock, Linda Cardine, Suzanne Butch

Registration Table

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L - R: Terry Downs, Susan Adams, Allyson Henstock

Allyson Henstock presents Terry Downs with the President's Award

Terry Downs presents the Founders Award to Vija Miske

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THANK YOU, VENDORS!

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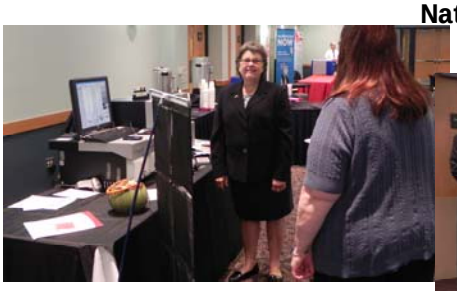

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ABO-incompatible Solid Organ Transplants

By A. Bradley Eisenbrey, MD, PhD

Antibody to blood group A and B substances remains one of the most significant barriers to transplantation of deceased donor and living donor solid organs. Pre-formed antibody to other histocompatibility antigens, such as the HLA antigens, can result in immediate or accelerated graft rejection, but the hyperacute vascular rejection of an ABO-incompatible transplant remains impressive, feared and respected. There are circumstances in which an ABO-incompatible transplant is considered, particularly in situations in which a recipient is unlikely to otherwise obtain a transplant.

World-wide, the most common situation leading to consideration of an ABO-incompatible transplant is in living donor organ transplants (kidney, liver lobe, lung lobe) in which the intended HLA-compatible donor is ABO-incompatible with the intended recipient. These transplants are much more common in countries, like Japan, where deceased donor transplants are not as well accepted. Complex, multi-way transplant chains can allow an incompatible pair to find acceptable donor and recipient matches and these combinations can be further facilitated by crossing the ABO barrier.

In Europe, anti-A, anti-B and anti-A,B titres are reduced using immunosorbent columns that have A or B substances attached to a Sepharose® matrix (Glycosorb®, Glycorex Transplantation, Sweden). When combined with anti-CD20 antibody (rituximab), apheresis (plasma exchange) and infusion of intravenous immunoglobulin (IVIg), antibody titres can be reduced to less than 1:8 and maintained until accommodation. ABO-incompatible transplants have been successful with patient and graft survival rates similar to ABO-compatible rates. In Japan it is standard practice to include splenectomy in the preparative regimen to reduce the risk of re-forming isoagglutinin titres to the pre-transplant levels (use of the immunosorbent column has not been reported in the Japanese literature).

ABO-incompatible solid organ transplants are much less common in the United States. The immunosorbent column is not approved for use in the US so there is reliance on apheresis, IVIg, rituximab and anti-rejection immunosuppression to keep antibody titres less than 1:16. This protocol avoids the surgical and long-term immunologic consequences of splenectomy. Intentional ABO-incompatible transplants of heart, liver and kidney have been reported and successful in the US.

One group of ABO-incompatible transplants that is becoming more common in the US is the use of A2 (non-A1) kidneys for transplant to group O and B recipients. The original literature only provided evidence of the efficacy of these transplants in patients with low titres of anti-A (less than or equal to 1:8). As more sensitive, solid-phase or gel-based assays have been adopted for determination of anti-A titre, each program must define their own cutoff for acceptable anti-A titre, usually less than 1:16.

The bottom line for the Transfusion Medicine and Blood Banking community is that a standardized method of determination of anti-A titre needs to be adopted and available in the blood bank supporting each solid organ transplant program and the cutoffs that are acceptable to the transplant surgeon and team needs to be established. Proficiency testing is available through the College of American Pathologists for labs that wish to provide anti-A or anti-B titre testing (Survey J).

MATCHING PUZZLE

Match terms in the right column to the findings in the left column. Use each answer only once to give the most accurate associations.

1. _____ mixed field agglutination	**A.** multiple myeloma
2. _____ positive DAT	**B.** anti-M
3. _____ positive antibody screen	**C.** autoantibody with Rh specificity
4. _____ rouleaux	**D.** *in vivo* antigen-antibody reactions
5. _____ antibody demonstrates dosage	**E.** *in vitro* antigen-antibody reactions
6. _____ cold autoimmune hemolytic anemia	**F.** transfused RBCs
7. _____ warm autoimmune hemolytic anemia	**G.** possible autoanti-I

Answers available on last page of newsletter!

Lab On Alert: WBIT

"The Emergency Room physician is on line one, and he's ranting over a negative tox screen. He wants to know how his patient, who is obviously intoxicated and belligerent, could possibly test negative."

"The ER charge nurse is on line two, and she's complaining that the Blood Bank will not issue blood for the patient with the 8 g/dl hemoglobin. She says that the wristband number was the only thing wrong on the tube she sent to Blood Bank and they want her to redraw the patient."

Do these scenarios sound familiar? Has anyone thought about WBIT ? Does anyone other than the lab staff know what WBIT is? For the laboratory, it is the most dangerous, most surreptitious preanalytical error. It creeps into the laboratory looking like any other specimen. It has a computer-generated label on it. It has two sets of initials of the persons *identifying* the patient.

So what is WBIT and why are the blood bankers and the Transfusion Medicine docs such sticklers, such difficult people who prevent the rest of us from making simple corrections to blood labels? We know our patients. We can identify which tubes we drew and when we drew them, in the middle of all the chaos when the Level I trauma arrived. Right?

Dead wrong! WBIT stands for *Wrong Blood in Tube* and it has the potential to kill someone. The blood bank is sometimes fortunate enough to have a historical blood grouping on a patient previously treated in our facility. We have averted 22 potential disasters, this year to date, by finding discrepancies between the blood grouping of today and that on record. How many occurrences are really happening? Is this just the tip of the iceberg?

How do we prevent WBIT ? The only way to prevent wrong blood in tube is to identify the patient's specimens **at the bedside from the wristband directly.** The unique identifier imprinted on the wristband is supposed to be found only on the wristband, not on the chart, not in the nurse's pocket, not

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written on the resident's scrubs. It was designed to be a *force function* obligating the phlebotomist or nurse to look at the patient's wristband and copy the alphanumeric identifier directly to the labeled blood tube. In turn, at the time of transfusion, the donor blood product carries on its label the unique identifier to match again with the recipient's wristband.

We ask, please do not take shortcuts. The minute required for two people to correctly identify the patient prior to transfusion is the most important minute in the course of the patient's visit. Appropriate therapy depends on accurate diagnosis which depends on getting the *Right Blood in Tube*. May all your WBITs become RBITs.

ABO and Platelet Selection: Beyond Standard 5.14

By Laura Cooling MD, MS

This article is a summary of a lecture given at the 2011 Spring Meeting, Illinois Association of Blood Banks, Chicago, IL

Platelets and ABO

The relative importance of ABO-compatibility and platelet transfusion has been a matter of debate for over 50 years. Like whole blood, platelet transfusion involves transfusion of cellular components that express ABO antigens, accompanied by the passive transfusion of anti-A and/or anti-B in donor plasma. In the literature, therefore, ABO "compatible" platelets may refer to the either 1) compatibility between donor platelets and recipient plasma, 2) compatibility between donor plasma and recipient red cells or 3) transfusion of type-specific or ABO-identical platelets, in which both platelets and plasma are compatible with the recipient. Although transfusion of ABO-identical platelets is always preferred, it is frequently necessary to transfuse non-identical platelet concentrates due to limited platelet inventories or special patient needs (ex. HLA-selected). This review will briefly summarize the impact of ABO on platelet transfusion therapy.

ABO Antigen on Platelets

Like red cells, ABO antigens are also expressed on platelets. H and LeY (an H-active antigen) are strongly expressed on CD34 stem cells and early hematopoietic precursors.[1-3] The ABO gene is expressed later in hematopoiesis at the CFU-Meg/E stage, a committed biphenotypic progenitor that will give rise to both erythroid and megakaryocytes. Unlike red cells, there is signifant disparity in ABO expression among individual megakaryocytes, with some clones strongly positive for H and A/B antigens and other clones virtually negative for both antigens.[1,4]

ABO antigens are found on a wide range of platelet glycoproteins (GPIIb/IIIa, GPIb/IX, GPIa/IIa, GPIc, GPIV, GPV, CD31 [PECAM], CD109) and glycolipids.[1,5,6] GPIIb/IIIa is a major determinant of ABO expression on platelets.[5] GPIIb/IIIa numbers nearly 250,000 molecules per platelet and displays 10-16 potential ABO sites per molecule. ABO expression can increase 50% during platelet storage due to residual synthesis of GPIIb/IIIa synthesis, as well as translocation of platelet alpha granules, which contain GPIIb/IIIa and other proteins.[7,8] ABO-active glycolipids are predominantly type 2 chain, simple glycosphingolipids and number < 5000 molecules/platelet.[1] Platelets can also adsorb type 1 chain ABH antigen from plasma although the contribution of soluble ABH antigen on overall platelet antigenicity is nominal.[5]

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ABO Compatibility and Platelet Transfusion Response

Several studies over the last 5 decades have shown major ABO-incompatibility can lead to decreases in the post-transfusion response. The earliest studies examining the effect of ABO and platelet transfusion were performed by Richard Aster in 1965.[9] Using radiolabeled platelets, Aster et al followed the 1 hour post-transfusion recovery following transfusion reported a mean 60-90% decrease in the one-hour post-transfusion increments following transfusion of group A and AB platelets to group O recipients. This was substantiated in an elegant study by Jimenez et al,[10] who compared the post-transfusion recovery in split apheresis products from the same donor. The authors found similar platelet recoveries when both recipients were ABO compatible with the donor (R=0.8); however, transfusion to an ABO incompatible recipient was accompanied by marked, significant decreases in post-transfusion recovery at 1 (<0.001), 4 (<0.004) and 24 hours (<0.04). ABO-incompatibility can independently lead to positive platelet crossmatches and is associated with a 40-60% decrease in CCI in some studies.[11,12] Improved platelet recovery with ABO-identical and ABO-compatible platelets was also observed in large clinical trails, including the TRAP trial.[13,14]

ABO can be a cause of platelet transfusion failures, higher alloimmunization rates, and increased transfusion requirements. In a small randomized trial of ABO-identical and ABO-unmatched platelets, the vast majority of patients receiving ABO-unmatched platelets had a decrease in post-transfusion recovery, with 37 percent having clear evidence of ABO-specific refractoriness.[15] In a second study, clinical refractoriness was significantly higher in patients receiving ABO-mismatched platelet transfusions (69 versus 8 percent) and was typically heralded by a sudden acute rise in isoagglutinin titers.[16] In a more recent study, ABO-incompatible platelet transfusions stimulated isohemagglutinin titers in 40-50% of patients after only 1-2 transfusions.[17]

Risk Factors in ABO-Incompatible Transfusions

The impact of ABO major-incompatibility is highly variable and is a function of patient, donor and product factors. Patient factors include patient ABO type and ABO titers. Group O patients are more likely to demonstrate decreases in platelet recovery following an ABO major-incompatible transfusion (ex. Group A platelets), due to higher anti-A in group O individuals. This is *particularly* true in group O women with a history of a non-O pregnancy and high titer, immune anti-A/B. In case reports of documented ABO-specific platelet refractoriness, patients typically had isoagglutinin titers > 1:500-1:1000 IgG and platelet-associated antibody approaching > 30,000 IgG/platelet.[15,16,18]

Donor-specific factors also play a major role. Group A platelets tend to be more antigenic than group B platelets. In solid phase platelet crossmatching, 52% of group A donors, but only 17% of group B donors, were crossmatch-incompatible with group O sera.[11] Likewise, only 20% of group B donors have detectable B-antigen on platelets by flow cytometry.[5] This data is also consistent with in vivo platelet recovery using radiolabeled group B platelets, which had acceptable 1 hour platelet recoveries (58-65%) in 75% of group O recipients.[9]

There are also significant differences between individual group A donors. One major difference is group A subtype.[5,19] The presence of A-antigen on platelets is restricted to group A_1 donors.[5] However, even between group A_1 donors, there is a wide range in the amount and distribution of A-antigen expressed on platelets. Among individual apheresis donors, the percent-positive platelets can range from 6% to 87%.[5] Interestingly, the percent A-positive platelets in any single donor is a stable trait when donors are studied longitudinally over time.[5]

Unlike group A_1 donors, group A_2 donors do not express A antigen on their platelets and can be considered group O compatible.[5] This has been confirmed by clinical studies showing nearly equivalent transfusion-responses between group A_2 and ABO-identical platelets.[20] In contrast, transfusion of group A_1 platelets to group O and B recipients have a nearly 10-fold risk of transfusion failure due to ABO incompatibility.

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There is also an autosomal dominant "high expressor" or HPX phenotype. It has been described in 4-7% of donors in the United States, South America and Japan.[1,5,19.21,22] These donors have unusually high A/B expression on their platelets. Transfusion of ABO-HXP platelets to a group O recipient have resulted in profound transfusion failures, even with HLA-matched platelets.[21] Platelets from ABH-HXP donors should be reserved for ABO-identical recipients only.

Finally, sex and race may contribute to higher ABH levels. Cooling et al noted increased A expression in women, particularly after 50 years of age.[5] Higher platelet A expression among women was also reported by Brazilian investigators. These investigators also noted higher mean A expression on the platelets of donors from European ancestry when compared to Brazilian blacks.[22]

Acute Hemolytic Transfusion Reactions

Currently, the greatest discussion around ABO and platelet transfusion is the risk of acute hemolytic transfusion reactions (HTR) with minor-incompatible or "out-of group" platelets. Although most queried transfusion services provide ABO-identical platelets or plasma-compatible platelets when available,[23] it is estimated that 10-40% of transfusions are plasma-incompatible with the recipient.[1] The most common reasons for transfusing out-of-group platelets are limited inventory of ABO-specific platelets, HLA-matched platelets and to minimize product wastage.[23] Based on the sheer number of out-of-group platelet transfusions transfused each year (200,000-400,000), the number of severe HTRs reported in the literature and blood bank chat rooms suggests that platelet-associated HTR is a relatively rare adverse event.[1]

Product, donor- and patient-specific factors may raise the risk for a HTR following an out-of-group platelet transfusion. Donor-specific factors are donor ABO type, parity and dietary factors. Group O donors, who tend to have higher anti-A and anti-B titers, are implicated in the vast majority (>80%) of platelet-associated HTR.[1,23] A history of an ABO-incompatible pregnancy is also a risk due to the development of high-titer, immune anti-A/anti-B. Finally, there is recent data showing a link between high titer anti-B and the use of probiotic supplements.[24] Probiotics contain a mixture of 3-7 different bacterial strains, including several strains with B-like activity capable of stimulating anti-B titers.

Recipient factors include patient age, ABO and secretor type. Group A and AB recipients tend to be at greater risk for HTR from a group O platelet transfusion due to higher anti-A titers. The Secretor phenotype, on the other hand, could potentially lessen the severity of incidence of HTR due to the presence of soluble ABO substances in blood capable of neutralizing anti-A.[25] The ability of Secretor to neutralize anti-A is also dependent on recipient ABO subtype: group A_2 and A_1B donors have reduced neutralizing capacity when compared to A_1 secretors.[25] Developmental delays in ABO and Secretor expression in neonates and infants, coupled with small total blood volumes, could also increase the risk of HTR in very young transfusion recipients.[1] Finally, other ill-defined patient factors could also play a role. Look-back investigations of two high-titer group O apheresis platelet donors failed to identify any additional HTRs in 70 prior transfusion recipients.[26,27]

The type of platelet concentrate transfused (apheresis, pooled, buffy coat, additive solution) is also a major determinant in out-of-group transfusions. Apheresis platelets, which contain 200-400 mL of plasma from a single donor, carry a significantly higher risk of hemolysis due to a high-titer donor then pooled platelets. This is substantiated by a review of the literature, in which 23/28 (82%) of platelet-associated HTRs were associated with apheresis platelets.[1] This risk is substantially lessened with pooled platelets due to the smaller volume of plasma per donor (50 mL), which is subsequently diluted 4-6 fold in the final product.[28] Likewise, platelets stored in platelet additive solution are substantially less likely to result in HTR due to reduced volume of donor plasma in the product.

Other Risks Associated with Out-of-Group Platelet Transfusion

In addition to HTR, out-of-group or plasma-incompatible transfusions have been associated with platelet transfusion failures and increased morbidity. Plasma-incompatible transfusions are reported to decrease

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post-transfusion recovery almost 20% when compared to ABO-identical transfusions.[12] It is hypothesized that transfusion of incompatible-plasma leads to the formation of immune complexes composed of donor ABO antibodies and soluble ABO substances in blood.[29,30] These immune complexes may then bind to either complement and/or Fc receptors on platelets, leading to accelerated immune clearance.[29] Among refractory patients, forty percent have elevated levels of circulating immune complexes. Among group A patients transfused with ABO mismatched platelets, 80% had evidence of immune complexes containing anti-A IgG of donor origin.[30]

ABO-incompatible platelet concentrates have also been linked to increased toxicity in HPC transplantation. Benjamin et al reported an increase in veno-occlusive disease (VOD), renal failure, pulmonary insufficiency, multiorgan failure with routine transfusion of out-of-group platelets.[31] Organ dysfunction was often preceeded by 1-2 weeks by increasing platelet transfusion requirements. An increase in VOD has also been reported in children undergoing allogeneic HPC transplantation.[32] In the latter study, the risk of VOD with out-of-group platelet transfusion was equivalent to Busulfan.

Strategies for Minimizing Platelet-Associated HTR

In the United States, the transfusion service has borne the primary responsibility for intervention policies aimed at minimizing the risk platelet-associated HTR, as stated in Standard 5.14.4:

> "the transfusion service shall have a policy concerning transfusion of components containing significant amount of incompatible ABO antibodies or unexpected red cell antibodies". [33]

These strategies include policies regulating 1) platelet selection, 2) limitations in the number of out-of-group platelets, 3) plasma reduction and 4) in-house screening of group O platelet apheresis units (Table 1).

There are also strategies at the blood supplier level. In general, our European colleagues have been more proactive in addressing this issue.[1,34] These strategies include recruitment efforts aimed at increasing the percentage of non-O apheresis and group A_2 donors. Group A_2 platelets are particularly advantageous for transplant recipients since they lack A antigen on their membranes (group O compatible) and possess only anti-B in their plasma (group A and O compatible).[5]

Other strategies to reduce the risk of platelet-associated HTR are increased production of pre-pooled platelet concentrates, platelet additive solutions and screening for high-titer ABO antibodies. Both pooled platelet concentrates and platelet additive solutions limit the total volume of donor plasma infused, decreasing the risk of an HTR by a rare high-titer donor. Donor screening for high-titer antibodies is generally limited to group O apheresis platelet units. Units identified as high titer are reserved for group O recipients only.

Two issues face large-scale implementation of donor screening: 1) the absence of a recognized gold-standard testing method and 2) a validated, clinically-significant "critical titer. At present, several methods are currently used for measuring ABO titers (tube, gel, automated solid phase, immediate spin, IAT, hemolysis) with different sensitivities and endpoints.[1,28,35] Even when using a standard "uniform" method, there are issues with intralaboratory variability as highlighted by several recent CAP proficiency surveys.[35]

The second issue facing donor screening is determining an appropriate critical titer that appropriately balances the available platelet inventory for non-O patients and the risk of HTR with out-of-group transfusion. Historical values for "critical values" are unreliable due to variation in testing method, coupled with a general decrease in isoagglutinin titers due to changes in diet.[1,36] Currently, critical titers can vary from 1:16 (hemolysis) to 1:512 (IAT). A critical titer of 1:50 (saline, tube) and 1:128 (AHG) could potentially affect 30-40% of group O units and severely hamper platelet availability to non-O recipients.[28,37] In contrast, the ABO titers of donors actually implicated in HTR are generally higher than 1:128-256 (tube, saline) and >1:512 (AHG).[1] The critical titer set by any testing facility will be dependent on the test method, the distribution of

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ABO titers within the specific donor population and impact on local platelet inventories.

Summary
Like whole blood, ABO compatibility in platelet transfusion includes ABO antigens on platelets and ABO antibodies in plasma. Routine transfusion of ABO major-incompatible platelets can be associated with cumulative adverse effects including decreased post-transfusion recovery, increased platelet utilization, incompatible platelet crossmatches, HLA alloimmunization and ABH-specific refractoriness. Out-of-group platelet transfusion can also be associated with adverse effects including decreasing platelet increments and rarely, severe HTRs. Out-of-group platelet transfusion may have more severe consequences in ABO-mismatched bone marrow transplant patients, who are at increased risk for significant morbidity and mortality due to ABO-incompatibility. ABO-identical platelets should be provided whenever possible, particularly for patients requiring long-term transfusion support.

Table 1: Strategies to Minimize Platelet-Associated HTR

A. Transfusion Service Strategies
   1) ABO-identical platelets
   2) ABO-plasma compatible
   3) Pooled platelet concentrates
   4) Limitation Out-of-Group Platelets
      a. 4 plasma-incompatible platelets/week
      b. 2 plasma-incompatible platelets/72 hours
      c. 1000 mL incompatible plasma/week
      d. 300-500 mL incompatible plasma per day
   5) In-house screening

B. Blood Supplier
   1) Increasing non-O platelet donors
   2) Increased prepooled platelets
   3) Screening A2 donors (Europe)
   4) Platelet additive solutions
   5) Donor/unit screening for “high-titer” ABO antibodies
      a. Group O apheresis units
      b. Reserved for group O recipients

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Matching Puzzle (from page 10) - ANSWERS : 1.F, 2.D, 3.E, 4.A, 5.B, 6.G, 7.C

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