The ORBCoN Report
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What's New at ORBCoN?

Education has been a big focus for ORBCoN these past few months. In April, we held, in partnership with our CBS colleagues, two Spring Symposiums. Our Videoconference Symposium was hosted out of the Queensway-Carleton Hospital in Ottawa, Ontario and featured presentations that related to transfusion in the female population. That same week, our Spring Symposium held in Toronto, provided a focus on transfusion related data bases with the ultimate goal of one day having the capability to have a better understanding of how blood is being used in Ontario hospitals. This year our Transfusion Committee Forum will be moved to the Winter and in future years will alternate with our Spring Symposium in an attempt to spread out some of the education initiatives being held in Ontario. The Transfusion Committee Forum will be held on February 24th, 2014. Watch for future announcements on our website!

The ORBCoN team is growing with the addition of administrative support and clinical project coordination support for Nursing and Physicians. We hope these changes will help us to continue providing useful and helpful resources for transfusion specialists across the province.

Recently released resources include:

- Bloody Easy Coagulation…Simplified – a new handbook providing valuable information on managing coagulation challenges in patients.
- Tech Assess – interactive case study activity was launched in July as a fun new learning activity addition to the Tech Assess tool.
- Specimen Collection Audit Tool – an addition to our group of audits available for use in Ontario hospitals. This audit helps with monitoring compliance with proper patient identification and labeling at the time of phlebotomy.
- Informed Consent Mobile Application for iPhones and iPads – provides step by step support for physicians obtaining informed consent for transfusion from patients who may require transfusion therapy.

Check out these resources and much more by visiting our website at: www.transfusionontario.org. The Informed Consent App is available for download from the Apple Store.

contact us

transfusionontario@ottawahospital.on.ca
www.transfusionontario.org

Central ORBCoN Office
416.480.6100 ext. 89433

Northern and Eastern ORBCoN Office
613.798.5555 ext. 19741

Southwest ORBCoN Office
905.525.9140 ext. 22915

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Bone Marrow Transplantation (BMT) and the HLA Matching Process

Chris Bredesen, MD, MSc, FRCPC. Head, Malignant Hematology and Stem Cell Transplantation, The Ottawa Hospital

BMT remains the treatment of choice for many patients with hematologic malignancies and other blood disorders. The HLA lab is a critical partner for Hematopoietic Cell Transplant (HCT) programs. Allogeneic HCTs rely on HLA-matching of patient and donor. The degree of matching is one of the main factors that help determine how to carry out the transplant with regards to intensity of chemotherapy with or without total body irradiation (the conditioning regimen) necessary to facilitate engraftment of the donor cells. The degree of HLA-match also correlates with post-transplant complications, in particular graft versus host disease (the new donor immune system cells attacking the recipient), less commonly graft rejection and ultimately, survival.

Sibling typing may be done using "intermediate resolution" techniques but HLA typing of unrelated donors almost universally utilizes "high resolution" techniques that can detect allele differences between patient and potential donors. In general, programs try to match at 8 loci (HLA A, B, C and DR).

As mentioned above, the degree of matching correlates with post-transplant outcomes. For example, for standard risk leukemia patients each HLA mismatch is associated with a decrease of approximately 10% in overall survival. With regards to the likelihood of finding a match, there is a one in four chance that 2 siblings will be an HLA match. As the average family size has decreased over the last several decades and the transplantation of older patients (age>60 years) increases, more transplants are from volunteer unrelated donors than matched siblings. There are over 14 million volunteer donors registered worldwide. A minority of transplants in adults in Canada are from banked cord blood.

The conditioning regimen is given pre-transplant to suppress the host immune system to facilitate the engraftment of the donor hematopoietic stem cells. Post-transplant, other medications are given for various periods of time from a couple of months to up to 12 months, to both facilitate engraftment and to try and prevent graft versus host disease. The specific drugs and duration of post-transplant immune suppression are influenced by the donor type, degree of HLA matching, emergence of graft versus host disease or disease recurrence.

While traditional myeloablative transplant conditioning therapy almost always results in rapid engraftment of the donor stem cells, less intense conditioning regimens may result in slower or delayed donor engraftment. The degree of donor engraftment is called chimerism and can be followed in the lab. For sex mismatch transplants, metaphase cytogenetics or FISH probes can be used to roughly quantify the percent donor cells in the marrow. More sophisticated chimerism testing of specific cell populations (T cells, B cells, myeloid cells) from the recipient's peripheral blood can be carried out looking at genetic differences between patient and donor using Variable Number of Tandem Repeats (VNTR) or Short Term Repeats (STR) methods in the HLA lab. Decreasing donor chimerism may prompt interventions by the transplant team such as rapid taper of immune suppression or infusion of additional donor lymphocytes to tip the balance in favour of the donor graft.

HLA labs and HCT programmes form a critical partnership that begins with the typing of the patient and continues through post-transplant decision making. We value this partnership!

Another critical aspect of the transplant process is supply of appropriate blood product support throughout the patient's course of treatment. HCT Program are significant users of blood components, primarily RBC and platelets. There are also special issues unique to allogeneic (donor) BMT patients. As the patients are very immune suppressed, all blood products must be irradiated to prevent transfusion associated graft versus host disease from occurring due to passenger lymphocytes in the donor RBC or platelet units. The use of CMV negative blood products for CMV negative recipients with CMV negative donors remains an area of debate. Some adult programs continue to provide these recipients with CMV negative blood products while others have accepted that universal leukodepletion at collection provides satisfactory protection against CMV transmission. Perhaps most interesting, is the situation of ABO mismatched allogeneic transplants. In this setting, the recipient will switch to the blood group of the donor. Under usual circumstances this occurs around 2 months post-transplant. Whether the issue is residual recipient ABO antibodies against a new ABO blood group or new host production of ABO antibodies against some lingering RBC, this can lead to a period of hemolysis, dropping hemoglobin and blood bank results indicating more than one blood group, what is often reported as "Blood Group in Transition". Sometimes this can be clinically problematic if the transition from recipient to donor production or immunity is protracted. A close working relationship with the blood bank is critical to HCT patient care. Every HCT doctor knows the phone number of the blood bank at their institution.

Platelet Transfusion Refractoriness and HLA matching

Christine M Cserti-Gazdewich, MD, FRCPC, FASCP, Transfusion Medicine Specialist & Consultant Hematologist, University Health Network

The platelet transfusion refractory patient can evoke a sense of fear and frustration akin to having no transfusable platelet concentrates (PC) at all. Regionally, and because of its simplicity, platelet transfusion refractoriness (PTR) is defined as the inability to achieve an increment of > 10,000/µL within 15-60min of PC administration. This definition aims to capture those with immune-mediated rapid rejection, as opposed to the illusion of PTR from delayed/next day measurements and/or non-immune stresses promoting faster but nevertheless gradual platelet turnover (eg. for the patient: fevers, drugs, splenomegaly, consumptive endothelial pathologies following high-dose chemotherapy or BMT or DIC; and for the product: long storage, ABO mismatch, and low dose relative to recipient size). Immune hostilities persist despite providing freshest-possible, ABO-identical PC, therein justifying a search for alloantibodies, which may then be circumvented by careful selection of (antigen-target-negative) "matched" single donor apheresis PC. PTR cases may come to the Blood Bank's attention externally (by consult request), internally (by inventory strain), or automatically (by computer alerts) on heavy users (eg. ≥1PC/24h for ≥1-3days). Once suspected, samples are directed to the CBS Platelet Immunobiology Lab to profile the patient's antigenic identity (by DNA typing) and the intolerant antibody repertoire (by serum studies). Most cases (~90%) of alloimmune PTR are due to HLA class I sensitization, as in those chronically transfused and/or multiparous, and are denoted by the "PRA" (% reactive antibody) score, with 0 being negative, and >70-80% predicting rejection of randomly selected PC. Platelets, which express a dizygotic HLA A and B type, can thus be chosen by "theoretical crossmatch," with a donor antigen being either identical (Matched), structurally/serologically related (Acceptably mismatched), or unmatched but invulnerable to the host antibodies (antigen-Negative). This 2-way, 4-antigen "MAN" paradigm discovers compatible donors, and with notice, CBS can gather PCs having higher odds of clinicolaboratory success. If these fail, Human Platelet Antibody (HPA) sensitization can be tested for and similarly managed. Minimizing the need for PCs (if scarce) and bleeding (in general) can also be achieved by use of antifibrinolytic tranexamic acid with local measures for injured tissues.

Case Study: A Community Hospital Experience with a Hematopoietic Stem Cell Patient Visit to their ER Department

Darlene Blouin, MLT Cambridge Memorial Hospital

Setting:
Patient A comes into a community based hospital emergency department with no family members accompanying her. This particular hospital does not routinely stock platelets, but platelets are available at any time through CBS.
Background information:
Patient A is complaining of feeling unwell. ER doctor orders blood work on patient and determines a general diagnosis of "unwell". Patient does not mention any other health history at the time of examination.
Description of event:
Blood work indicates a low platelet count ($<5x10^9$); the rest of the patient's blood work results are unremarkable. One adult dose of platelets is ordered by the ER doctor. The lab places the order with CBS and awaits arrival. While waiting for the shipment, the patient's family arrives and informs the care team that patient A had a stem cell transplant at a large University hospital several months ago, and she requires special blood components. Just before the platelets arrive from CBS the blood bank receives a call from the ER department to advise them that the platelets for Patient A need to be irradiated in light of this new health history information. A second irradiated dose of platelets is ordered and transfused without incident.
Conclusion:
Well informed patients and family members can help in the avoidance of transfusing inappropriate products. This case shows that the family was informed, however many times this is not the case and it's discovered only after the transfusion that a patient should have received irradiated components.
Questions to Ponder:
1. Why do hematopoietic stem cell transplant recipients present a distinct set of challenges for hospital transfusion services?
2. What is the best way to communicate patient special requirements for blood products?

Please refer to our website www.transfusionontario.org August 30, 2013 for a posting of a discussion paper on this case study.

Upcoming Events

EVENT	DATE	LOCATION
U of T Monthly Transfusion Rounds (opening session)	Sept. 19, 2013	Mt. Sinai Hospital Auditorium or videoconference
OSMT Conference 2013 – London Hilton Hotel London, ON	Sept. 20–22, 2013	London Hilton Hotel London, ON
11th Annual Canadian Blood Services International Symposium – Utilization of Blood Products: a Focus on Platelets	Sept. 21, 2013	Bahen Centre for Information Technology University of Toronto
GHEST Annual Transfusion Seminar - Audits and Inventory 101	Sept. 28, 2013	Beacon Inn and Conference Centre Jordan, ON
AABB CTTXPO 2013	Oct. 12 -15, 2013	Denver, Colorado
London Laboratory Services Group – Annual Transfusion Medicine symposium	Nov. 9, 2013	Four Points Sheraton London & Suites London ON

The single biggest problem in communication is the illusion that it has taken place.
- George Bernard Shaw