Conference Abstracts Book
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1. Medical/Clinical
   a. Oral Presentations

Replacing Intravenous Immunoglobulin (IVIg) with more Efficacious Recombinant(r) Fc Multimers

*One of top two abstracts*

Submission Group
CSTM Abstract Submission

Submission ID
125

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Abstract Body (max. 350 words)

Background: Immune thrombocytopenia (ITP) is an autoimmune disease that is characterized by an insufficient number of platelets in the circulation due to decreased platelet production in the bone marrow and increased peripheral platelet destruction in the spleen and liver. IVIg contains polyclonal IgG molecules that are purified from the plasma of thousands of donors and is recognized as a first-line treatment for ITP and other autoimmune and inflammatory disorders. Despite its unresolved mechanism of action, the Fc portion of IVIg is thought to be critical for its activity. Due to the high demand and ever-growing cost for IVIg, the development of alternative therapies to replace IVIg could provide substantial cost-benefit and prevent a shortage of this blood product. A number of companies have shown that there is great potential for rFc multimers to become a replacement therapy for IVIg. These multimers are more efficacious than IVIg in in vitro and in vivo assays.

Design/Methods: Recombinant IgG1 hexameric proteins (rFc hexamers) were engineered by CSL Behring and used in this work. Using the human and mouse monocyte/macrophage monolayer assay (MMA) with human PBMCs and mouse RAW264.7 macrophages, respectively, the ability of rFc hexamers to inhibit phagocytosis in vitro in comparison to IVIg was tested. For ITP, the passive escalating dose anti-platelet antibody mouse model was used to test the ability of the rFc hexamers to raise platelet counts in vivo in comparison to 2 g/kg IVIg.

Results: The rFc hexamers were exceptional inhibitors of phagocytosis in the MMA, able to inhibit phagocytosis at approximately 375- to 3600-fold lower concentrations than IVIg. The IC50s of the rFc hexamers were approximately 8 ng/ml(human MMA) and 413 ng/ml(mouse MMA) in comparison to the IC50 of IVIg at approximately 3000 ng/ml(human MMA) and 1,500,000 ng/ml(mouse MMA). In
Balb/c or C57BL/6 mice with ITP, the rFc hexamers were able to raise platelet counts to a higher degree than IVIg at 50- to 400-fold lower doses.

**Conclusions:** rFc hexamers are more potent than IVIg and show great potential to replace IVIg in some/all of the conditions where IVIg is currently being used.

**Acknowledgements:** CSL Behring; CBS GFP award
Autologous Blood Collection in Canada

Submission ID

9

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Abstract Body (max. 350 words)

Background: The Choosing Wisely Canada campaign released the 8th CSTM recommendation in June 2015, Don’t routinely order perioperative autologous and directed blood collection. This recommendation and changes in transfusion practice prompted a review of the current state of the Canadian autologous blood collections.

Method: The autologous blood collections data were extracted from ePROGESA at Canadian Blood Services (CBS) and Héma-Québec (HQ) between 2007 and 2016. Health Canada registered hospital based autologous programs were contacted for collection information.

Results: Autologous collections decreased between 2007 and 2015, from 4,419 to 148 collections at Canadian Blood Services and from 1,263 to 28 collections at Héma-Québec. The majority of the requests were for orthopedic patients with the top three indications being total hip replacement, total knee replacement and hysterectomy. Rare blood types represent only a small number of autologous units collected each year (2015-14 units at CBS & HQ). The average hospital discard rate between 2007 and 2015 is 63% (range 52%-80%). Thirty-two hospitals had been issued autologous units in 2015 and 2016 (7% of hospitals/networks in Canada, excluding Quebec). The top hospital users of autologous blood do not correlate with the top RBC users. The autologous units issued to the top five hospital users represent 0.33% to 1.87% of all RBC issued in 2015/2016. The two hospital-based autologous collection sites collected 0 to 1 donation per year for the last few years.

Discussion: There has been a significant decrease in autologous blood use. Published data from Héma-Québec for 1993 and 2000 reported autologous donations representing 0.8% to 2% of total blood collections. In Canada, autologous donations represent approximately 0.03% of all whole blood collections between 2013 and 2015. The estimate manufacturing cost to Canadian Blood Services in 2015 is $75,628 with 80% of units being discarded.

Given advances in surgery and patient blood management, the majority of patients referred to autologous transfusion programs do not require transfusion. There is a need to revise the current autologous donation program with the proposal to restrict the use of autologous collections for patients with a rare blood type, where allogeneic blood may not be available.
 Gamma-irradiation Practices for Red Blood Cell (RBC) Units Prior to Implementation of Proposed National Advisory Committee (NAC) Recommendations

Submission ID

42

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Abstract Body (max. 350 words)

Background: Gamma-irradiation of RBC units prevents the proliferation of residual lymphocytes reducing the risk for transfusion-associated graft-versus-host disease in immunocompromised recipients. However, irradiation is associated with increased hemolysis and extracellular potassium accumulation, particularly in older units. The proposed NAC recommendations suggest limiting irradiation to units that are 28 days old or younger. Prior to adapting local policy to reflect these new recommendations, a retrospective review of irradiation activity was performed to determine if a gap exists between current practices and proposed changes.

Methods: A retrospective review at an academic hospital in Toronto, Canada was conducted on all RBC units that received gamma-irradiation between January 1, 2016 and December 31, 2016. Irradiation of RBC units with 25 Gy was performed onsite using Gammacell 1000 Elite (Best Theratronics). Characteristics of interest include age of the unit at irradiation, date of transfusion, and indication for irradiation. The NAC draft recommendations (dated September 26, 2016) were used for comparison in the analysis.

Results: In total, 791 RBC units were irradiated for 204 unique patients. The median age of the unit at irradiation was 20 days (interquartile range, 14 to 27). Six-hundred and thirty six units (80%) were irradiated at 28 days or younger. Most units (92%) were transfused on the day of irradiation with the longest interval being 7 days. The clinical indication for irradiation complied with local policies in 79% of the units. However, when NAC recommendations are applied, only 14% of the units required irradiation.

Conclusion: A review of current practices reveal that most RBC units are irradiated within 28 days of age, but may not clinically require irradiation as proposed in the new NAC guidelines. Given the potential harm that can be associated with irradiation of old units, as well as unnecessary transfusion of irradiated units, implementation of these recommendations is likely forthcoming Canada-wide. With such a large gap existing between current and proposed irradiation indications, significant education will be required in both prescribers and laboratory personnel.
Improving AB plasma utilization in a large tertiary care facility

Submission ID

100

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Abstract Body (max. 350 words)

Background: AB plasma is the universal donor plasma yet is only 4% of the donor population. The use of AB plasma for emergency release in massive transfusion protocols (MTP) contributes to potential shortages of this rare blood component.

Ensuring that there are 2 units of AB thawed plasma available at all times is an essential practice in MTP. Once an MTP is initialized, 2 AB thawed plasma are immediately issued with 4 group O red cells. Additional AB plasma units are thawed and issued until the patient’s blood group is determined or the MTP is discontinued. Once the patient’s blood group is known, blood group compatible plasma is thawed and issued. To avoid wastage of AB thawed plasma not transfused as part of MTP, the plasma is issued to patients of any blood group requiring plasma prior to outdating (<5 days thawed). We reviewed the AB plasma utilization to identify areas of possible improvement in our MTP in order to conserve this limited product for AB patients that require it.

Method: A review of all AB plasma transfusions in 2016 was performed using the laboratory information system (LIS).

Results: Of 174 patients that received AB plasma, 51 (29%) patients did not have a blood group on record at the time the plasma was issued. From these patients reviewed only one (1/51) was found to be AB. A total of 416 AB thawed plasma were transfused; 127 (30%) units were transfused to patients with unknown blood groups at the time of the MTP. Only one unit was transfused to an AB patient. Of the remaining 289 units, 46 (16%) were transfused to patients known to be group AB and 243 (84%) were transfused to non-AB patients that would have been able to receive group specific plasma.

Conclusion: Shortages of AB plasma is an ongoing concern. The practice of having AB thawed plasma is an essential life-saving practice in the initial stages of an MTP. Our review of AB plasma utilization shows that a large portion of the AB plasma thawed was transfused to patients with known blood group to avoid outdating. Receiving a patient specimen for ABO grouping as soon as possible and establishing a blood group would help conserve AB plasma.
Interference of Anti-CD38 in Multiple Myeloma Patients

Submission ID

75

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Abstract (max. 350 words)

Darzalex (Daratumumab), the first therapeutic CD38 monoclonal antibody to treat multiple myeloma, was approved by Health Canada in June 2016. The CD38 transmembrane protein is highly expressed in malignant myeloma cells. This human CD38-directed (IgG1) monoclonal antibody reacts with glycoprotein found on the surface of many types of cells including red blood cells. It binds to CD38 expressed on RBCs and may result in positive indirect antiglobulin tests (IAT) performed to identify clinically significant alloantibodies. DARA-mediated positive IAT may persist for up to 6 months after the last DARA infusion. It may variably affect autocontrol, direct antiglobulin test (DAT) and eluate results.

From June 2016 to January 2017, 17 patients under Daratumumab treatment were tested using routine methods in our Immunohematology Reference Laboratory. 27 serological investigations were performed in total (1 to 5 studies per patient). In addition to ABO and Rh typing, DAT, IAT in Gel LISS and Papain and auto controls were tested. DTT treated cells, trypsin treated cells, phenotyped cord cells or cells expressing a low level of CD38 were also tested when relevant. Eluate were prepared and tested when criteria were met. (Positive autocontrol n: 2, positive DAT n: 10, transfusion >3 months n: 13). Phenotype (n: 4) and/or genotype (n: 14) were also performed.

No interference was noted in ABO and Rh typing. DARA-mediated positive IAT was found in 13 of 17 patients and panreactivity was observed. Anti-K (n: 4) and anti-Lea (n: 1) were identified using complementary method and panreactivity was observed in the eluate (n: 10).

Anti-CD38 interferes with serological tests. It is possible to mitigate this interference by using complementary methods such as DTT treated cells. However, some clinically significant antigens that are sensitive to DTT, namely the Kell antigen should be considered. Our tests allowed identifying anti-K for 4 patients out of 17 using trypsin treated cells or cord cells. Moreover, genotyping was performed whenever phenotyping could not be established. These results emphasize the importance for the blood bank to refer these cases for investigation to the reference laboratory as well as to point out if anti-CD38 therapy is being initiated.
Providing Kell negative red cells to female patients in Canada: The time has come

Submission ID
17

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Abstract Body (max. 350 words)

Background: Anti Kell (K) antibodies are common in pregnancy and can cause severe fetal anemia, even at low titre, necessitating frequent fetal ultrasound monitoring. Kell allo-immunisation can occur either from pregnancy or transfusion. Ensuring pre-menopausal female patients receive only Kell negative red cell transfusions could decrease allo-immunisation rates in prenatal patients. Prospectively transfusing females with Kell negative red cells may be feasible as increasing Kell phenotyped donor inventory is available.

Methods: Transfusion services in 6 cities from four different provinces participated in a 3 month audit. No change in inventory ordering practices occurred prior to the study. Eligible patients included those who were female and less than 45 years old. Prior to issue of red cells the blood bank inventory was assessed for availability of units that were compatible, ABO and Rh specific and Kell negative. If not available, group O Rh compatible, Kell negative units were identified. The number of patients who could be successfully treated with Kell negative red blood cells was determined.

Results: 1950 donor units were transfused. In 1822 cases ABO Rh matched, Kell negative units were available for transfusion. In 179 cases group O substitution was required to provide Kell negative units. In three transfusion services the fill rate was less than 100% (96%; 71 %; and 89%). These three transfusion services have a substantial pediatric/neonatal transfusion practice as a common feature.
**Discussion:** Routine donor phenotyping has contributed to an inventory of donor red cell units known to be Kell negative. This inventory can be successfully allocated to female patients of child bearing potential without a significant shift in blood inventory ordering by hospitals. In Europe, routinely providing Kell negative red cell units to female patients has led to a substantial reduction in anti Kell alloimmunisation and an attendant reduction in complex prenatal monitoring. This successful audit of Kell negative red cell unit availability indicates that routinely providing Kell negative units to female patients in Canada can be accomplished with current phenotyped red cell inventory in most cases.
Residual Risk of Bacterial Contamination of Platelets: Six Years of Experience With Sterility Testing at Canadian Blood Services

Submission ID
35

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Abstract Body (max. 350 words)

Background: Canadian Blood Services screens platelet concentrates for bacterial contamination with the BacT/ALERT system within 24-30h post-phlebotomy. Quality Control (QC) sterility testing of 1% outdated platelets (or minimum 10 units) is performed on a monthly basis. Data of routine screening, QC testing, and septic reactions obtained from 2010 to 2016 are presented herein.

Design and Methods: All platelet products are leukocyte-reduced and screened for bacterial contamination using aerobic BacT/ALERT culture bottles. QC sterility testing is performed in 6-7 day-old platelets using aerobic and anaerobic BacT/ALERT bottles. From 2010 to 2016, 601,988 buffy coat (BC) pools and 186,737 apheresis units were screened during routine testing. In the same period, 8,535 BC and 8,498 apheresis platelets were screened during QC testing. Positive results were classified as: true positives if the same bacterium was isolated in initial and confirmatory cultures; false positive machine failures if no bacteria were isolated in initial cultures; false positive contamination during sampling if bacteria were present in the initial culture but not in confirmatory testing; and, indeterminate if no platelets were available to confirm initial results. False negatives were those units captured during QC that were missed in early screening. Reports of septic reactions were documented by Regulatory Affairs.

Results: Routine screening revealed similar true positive and contamination false positive rates between BC and apheresis platelets (p>0.05). In contrast, machine failures and indeterminates were higher in apheresis than BC units (p<0.0001). During QC testing, true positives, contamination false positives, and indeterminates were similar between both platelet types (p>0.05). QC machine failures were higher in apheresis than BC platelets (p=0.0004). Seventy-five bacteria were isolated during early screening including Gram-positive and Gram-negative organisms while all 15 QC isolates were Gram-positives. Six septic reactions were reported implicating coagulase negative staphylococci (3) and Staphylococcus aureus (3).

Conclusion: PC screening for bacterial contamination at Canadian Blood Services has reduced septic transfusion reactions. However, detection of false negative screen cultures and septic transfusion events reveals a residual safety risk that merits further intervention.

Acknowledgements: Dr. Qi-Long Yi for statistical analyses and Ms. Heather Howell for providing data on septic transfusion events.
b. Poster Presentations


Submission ID

136

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Abstract Body (max. 350 words)

Background: Albumin use in Canada has increased by approximately 20% since the delisting of starches by CBS in 2012. Using a previously developed model, we sought to demonstrate that patient level demographics and albumin utilization could be extracted and meaningfully summarized using administrative data.

Methods: Three Ontario hospitals collected information on all inpatient albumin transfusions from April 2011 to November 2014. Hamilton Health Sciences Centre used their existing transfusion (TRUST) database. The London Health Sciences Centre abstracted data from existing lab and administrative databases. The Ottawa Hospital used their data warehouse, which routinely integrates laboratory and administrative medical information. Albumin utilization was summarized for each site using ICD10 codes, specific procedure codes and location of transfusion, and compared across the 3 centres.

Results: The proportion of inpatients transfused albumin varied from 2.8% to 6.5% across the 3 centres, and increased in all centres from 2011-14. The 2 most common diagnostic groups receiving albumin were Diseases of Circulatory System and the Digestive System, which represented more than 40% of all albumin transfused.

Patients undergoing CABG surgery received 3-14.3% of the albumin transfused at the 3 hospitals. The percentage of patients undergoing CABG receiving albumin varied from 12.9% to 64.2%; the proportion of patients transfused increased at all sites.
Patients undergoing thoracic surgery procedures accounted for 20-28.2% of the albumin transfused at the 3 hospitals; the percentage of patients receiving albumin varied from 15.3 to 44%.

Patients in the ICU accounted for 37-67% of the albumin transfused at the 3 hospitals; the percentage of patients receiving albumin varied from 10 to 24.1%.

Inpatients receiving dialysis received 15-20.8% of the albumin transfused at the 3 hospitals; the percentage of patients receiving albumin varied from 21.2% to 63.7%.

**Conclusions:** Through administrative data records, we were able to examine changes in albumin utilization over time at 3 Ontario hospitals. Overall, the data showed substantial variation in usage, particularly the proportion of patients transfused, and an overall increase in utilization during the study period. The variation in albumin utilization observed in these administrative data suggests there could be substantial improvement in the utilization of albumin.
An Approach to Ensuring Quality in Cell-Free Fetal DNA (cffDNA) Testing.

Submission ID
13

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Abstract Body (max. 350 words)

Background: Canadian Blood Services (CBS) perinatal laboratories in western Canada submit maternal blood samples for cffDNA analysis to the International Blood Group Reference Laboratory (IBGRL) in Bristol, U.K. for mothers with critical titres of Rh antibodies (>=16) and for anti-K. To ensure the accuracy of a laboratory assay, results should be correlated with clinical outcome. Neonatal phenotype (NP) is important in ensuring that the cffDNA assay is performing as expected. In September 2014, IBGRL notified CBS that 3 samples submitted internationally had been mistyped as K negative due to suboptimal performance of an assay control. One of the patients was Canadian.

Method: NP is difficult to obtain as delivery occurs in disparate hospitals weeks following prenatal testing. A 2014 survey asking physicians to provide NP was not successful. After the 2014 incident indicated above, a more directed approach to obtaining the NP was considered warranted. A Maternal Consent for Release of Neonatal Test Results to CBS was implemented on 2015-06-30. Hospitals and physicians were informed that samples would be processed but not shipped for testing until the signed consent was received. This consent allowed CBS to contact the hospital of delivery to obtain NP results or to request that a sample be submitted to CBS for neonatal phenotyping. An information sheet was developed to assist hospitals in meeting this requirement.

Results: From 2013 tomid-2015, NPs were available for 2 of 33 (6.1%) of patients. Between 2015-06-30 and 2016-12-16, 27 signed consents were received at CBS, 18 mothers delivered, and neonatal phenotype was provided for 14 of 18 (77.8%) patients. 4 phenotypes were not performed due to IUT, serological findings or laboratory error. Of NPs received, 13 of 14 correlated with the PFP indicating the reliability of the cffDNA assay. One K positive neonate had been mistyped as K negative as described above.

Conclusions: Correlation of test results with clinical outcome is essential to ensuring the quality of laboratory testing. Reporting of NP improved significantly following implementation of a formal maternal consent process.

Mistyping of samples led to an extensive root cause analysis by IBGRL and assay improvements to prevent future incidents.
An audit of transfusion management of obstetric patients with massive hemorrhage

Submission ID

123

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Abstract Body (max. 350 words)

Introduction: Postpartum hemorrhage (PPH) is the leading cause of maternal mortality worldwide. Massive hemorrhage protocols (MHP) have been shown to resolve bleeding at an earlier stage, result in fewer blood products used, and reduce development of DIC. This quality assurance exercise was designed to assess practice in our obstetrical MHPs to identify areas of future improvement in MHP management.

Methods: A retrospective analysis of our MHP database and healthcare records of consecutive obstetrical MHP initiations between July 2012 and September 2016 was performed. Blood component usage, wastage, and laboratory data during, 24 hours pre and post MHP were all compared. Statistical analysis was performed using a Students t-test and the Pearson Chi-square test.

Results: 97 Patients were included. The mean duration of MHP was 3.4 hours. The median unit usage of red cells was 10 (IQR 5, 14.5), plasma 4 (IQR 2,7), platelets 1 (IQR 0,2), cryoprecipitate 2 (0,10), and fibrinogen concentrate 2g (IQR 0,10). Two patients received recombinant VIIa. 26% of patients received fewer than 6 units of RBC, and 4% received 0 units of RBC. 23% received unmatched components. 51% received ≥ 10 red cell units, these patients had higher initial PTTs (59 vs 41, p = 0.013) and lower initial fibrinogens (1.6 vs. 2.4, p = 0.03). Patients with initial fibrinogen ≤ 2.0 were more likely to receive fibrinogen replacement prior to or in the first pack (61% vs 30%, p = 0.009). Of patients with an initial fibrinogen 2.0 not receiving fibrinogen replacement prior to or with their first pack, a trend to higher red cell and plasma use was seen, (red cells 16.1 vs 12.7, p = 0.27, plasma 9.0 vs 6.3, p = 0.19). Blood product wastage occurred in 24% of MHP (7% RBC wastage, 16% plasma wastage, and 2% cryoprecipitate wastage).

Conclusion: This review has demonstrated multiple areas for improvement in the transfusion management of hemorrhage in obstetrical patients. These include (1) reducing MHP use in patients who are not severely bleeding, (2) earlier fibrinogen replacement for patients with an initial fibrinogen ≤ 2.0 and (3) reducing blood product wastage.
Anti-Jra causing hemolytic disease of the fetus/newborn with suppression of erythropoiesis

Submission ID

111

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: Anti-Jra is a clinically significant red cell antibody to the high incidence Jra+ antigen. It has been reported to cause hemolytic disease of the fetus/newborn (HDFN). Anti-Jra+ mediated HDFN typically causes hemolysis with a positive DAT; however, anti-Jra- causing fetal anemia with a negative DAT, potentially caused by antigen modulation, has been recently described. We report an additional case of anti-Jra- mediated HDFN with a negative DAT and evidence of erythroid suppression.

Case: A 37-year-old patient (G4 T1 A1 L1) with a history of anti-Jra+ presented at 27 weeks gestation with severe anemia of her fetus, suspected based on elevated middle cerebral artery Doppler ultrasound. Fetal blood sampling confirmed anemia at 58 g/L with normal platelet and leucocyte counts for age. Normal RBC morphology was observed with decreased nucleated RBCs. Four intrauterine transfusions (IUT) were performed at 2 week intervals using deglycerolized Jra- negative, O-negative, Kell-negative donor units and the baby was delivered via C-section at 35 weeks. Initial bilirubin level was 59 umol/L increasing to 109 umol/L within 24 hours. The baby was treated with phototherapy during hospitalization. Postnatal transfusion was not required.

Investigation and Results: Maternal anti-Jra+ titer was 8 at initial prenatal testing and throughout pregnancy. All other clinically significant antibodies were excluded with differential alloabsorptions (CBS) and testing using Jra- negative rare RBCs. Testing the pre-IUT fetal blood sample showed a negative DAT by gel (Biorad (BCWH), and tube testing and an eluate was non-reactive with all cells tested (CBS). Phenotyping of fetal red cells showed a negative Jra+ phenotype with seven separate, anti-Jra- antisera (CBS). Paternal Jra+ typing was positive. Fetal genotyping predicted a Jra+-positive phenotype (New York Blood Center). MMA testing of maternal plasma with Jra+-positive red cells and donor monocytes was positive.

Conclusion: The very low hemoglobin in utero coupled with low numbers of nucleated red cells suggests erythroid suppression by the anti-Jra+. The negative DAT and apparent negative Jra+ phenotype with a Jra+-positive genotype suggests a mechanism of antigenic modulation with downregulation of Jra+ expression on fetal red cells.
Anti-Sc2 of the Scianna Blood Group System can cause hemolytic transfusion reactions: Serendipity and Monocyte Monolayer Assay confirm clinical significance

Submission ID
124

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Abstract Body (max. 350 words)

Case Report: A sample was referred to the reference laboratory from an adult hospital for investigation of an acute hemolytic transfusion reaction. A thalassemic patient, after 75mL of plasma-reduced red cells, had a fever of 39.4oC, elevated unconjugated bilirubin and LDH. The unit was issued by electronic crossmatch but was found to be 3+ incompatible on re-crossmatch by Gel-IAT.

In 2007, while receiving transfusion in a pediatric hospital, the patient developed back pain, vomiting, dark urine, fever of 39oC, and elevated unconjugated bilirubin. A unit crossmatched by immediate spin was found to be 1+ incompatible by Gel-IAT on re-crossmatch with both pre and post-transfusion samples. Post-transfusion urine was positive for hemoglobin. Investigation at the reference laboratory failed to identify the antibody, so the patient was switched to Gel-IAT crossmatch for further transfusions. In 2009, one unit was 3+ incompatible by Gel-IAT and was not transfused. The reference laboratory identified anti-Sc2 (2+ by Gel-IAT with two in-house Sc2 positive cells). Red cells from the segment of the incompatible unit typed Sc2 positive with two in-house antisera. This was not the same donor as the 2007 donor, who later returned to donate in 2012 and was phenotyped as Sc:1,2.

In 2010, the patient was transferred to the adult hospital, who did not consider the anti-Sc2 to be clinically significant. The unit transfused was selected from the hospitals general inventory. Review of donor records by the reference laboratory discovered that this unit was donated by the same donor as the 2007 unit.

In 2016, we tested patients serum and two Sc2 positive donors by the Monocyte Monolayer Assay (MMA), which was highly positive.

Conclusion: Anti-Sc2 was not known to cause hemolytic transfusion reaction, and was not included in the investigation of the first reaction. After the patient was discovered to have anti-Sc2, it could not
be determined in retrospect if this was the basis for the hemolytic transfusion reaction. However, given the similarity in the clinicolaboratory outcome when re-exposed to the same donor, and the highly positive MMA results, we conclude that anti-Sc2 likely accounted for the acute hemolytic transfusion reactions in both instances.
Assessing the Usefulness of Direct Antiglobulin Test (DAT) in all Neonates in the Neonatal Intensive Care Unit (NICU).

**Submission ID**

77

**Authors/Co-Authors & Affiliations**

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**Abstract Body (max. 350 words)**

**Background:** The Direct Antiglobulin Test (DAT) is used to predict hemolysis in the neonate, as hyperbilirubinemia secondary to hemolysis may result in considerable neurological morbidity. Hyperbilirubinemia may still occur with a negative DAT result, however, thus suggesting that routine use of the DAT may not be predictive of the need for phototherapy or red blood cell (RBC) transfusion. The overall objective is to assess the correlation of the DAT in neonatal intensive care unit (NICU) with the level of bilirubin and the need for phototherapy and/or RBC transfusion.

**Study Design and Methods:** We retrospectively reviewed the charts and hospital information system of 272 neonates admitted to the NICU at Mount Sinai Hospital (MSH) in Toronto from April 1, 2013 to March 31, 2014 who had a DAT. We defined significant hyperbilirubinemia as an increased bilirubin level requiring phototherapy and/or the need for RBC transfusion.

**Results:** Of the 272 neonates, 22 had a positive DAT, of whom 45% required phototherapy and none required RBC transfusion. Of the 250 neonates who had a negative DAT, 30% required phototherapy and 8% required RBC transfusion. The table describes the mean bilirubin levels, the mean hemoglobin levels, the mean neonatal weight and gestational age at delivery of the groups.

<table>
<thead>
<tr>
<th>DAT</th>
<th>N=272</th>
<th>Mean Bilirubin+SD</th>
<th>Mean Indirect Bilirubin+SD</th>
<th>PT (yes) N (%)</th>
<th>RBCs (yes) N</th>
<th>Mean Hemoglobin+SD G/L</th>
<th>Mean neonatal wt +SD (kg)</th>
<th>Mean GA (range) (wks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POS N=22</td>
<td>213.14+75.55</td>
<td>207.57+75.49</td>
<td>10 (45%)</td>
<td>0</td>
<td>172+33.32</td>
<td>3.17+0.63</td>
<td>37.6 (31.3-41.5)</td>
<td></td>
</tr>
<tr>
<td>NEG N=250</td>
<td>177.68+83.83</td>
<td>182.01+66.76</td>
<td>76 (30%)</td>
<td>20 (8%)</td>
<td>178+29.94</td>
<td>2.48+1.05</td>
<td>33.2 (26-41.2)</td>
<td></td>
</tr>
</tbody>
</table>

DAT, direct antiglobulin test, GA, gestational age, PT, phototherapy, SD, standard deviation, wks, weeks

**Conclusions:** These preliminary results demonstrate that hyperbilirubinemia requiring phototherapy and/or RBC transfusion still occur despite a negative DAT result. The usefulness of the DAT in
determining the need for phototherapy and exchange transfusion in addition to the level of bilirubin needs to be further examined.

Acknowledgements: Shelley Solomon, Marietta Biscocho
Blood Donation and Testosterone Replacement Therapy

Submission ID

32

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Abstract Body (max. 350 words)

Background: Polycythemia is the most common adverse effect of testosterone replacement therapy (TRT) and may predispose patients to adverse vascular events. Current Canadian guidelines recommend regular laboratory monitoring and discontinuing TRT or reducing the dose if the hematocrit exceeds 54% (hemoglobin 180 g/L). This threshold has been interpreted by some physicians and patients to indicate the need for phlebotomy or blood donation while on TRT.

Study Design and Methods: We reviewed all male blood donors in Southwestern Ontario at Canadian Blood Services from December 2013 to March 2016 who self-identified or were found on donor screening to be on TRT. Hemoglobin concentration was measured at the time of donation or clinic visit and with each subsequent appointment in repeat donors.

Results: We identified 39 donors on TRT who presented for blood donation over a two year period. The mean hemoglobin level at all clinic visits was 173 g/L (range, 134-205 g/L; n=108). Hemoglobin concentrations of 180 g/L or more (calculated hematocrit, 54%) were measured at 25% of appointments. Of the 27 repeat donors, 12 (44%) had persistently elevated hemoglobin levels (180 g/L) at subsequent donations.

Conclusion: Hemoglobin concentrations were elevated in donors on TRT, and significant numbers had hemoglobin levels above those recommended by current guidelines. These data also suggest that repeat blood donation was insufficient to maintain a hematocrit below 54%. Our findings raise concerns about the persistent risk of vascular events in these donors, particularly when coupled with the misperception by patients and health care providers that donation has reduced or eliminated the risks of TRT-induced polycythemia.
Blood Donor Notification Centre (BDNC) - A Medical application for the retention of Blood Donors registry and Reminder system.

Submission ID

135

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: The theme for 2011 Blood Donor day by W.H.O was More blood, More life where it was emphasized that more people should get awareness regarding donating blood as they are carrying a precious gift which is beneficial to mankind. In Pakistan reportedly there are 170 public and 450 private blood banks in the country but still a lack of blood Donors Pool. Retention of Blood Donor is the most important part of any Blood Donation centre so that we all the time maintain an active Blood Donor registry.

Problem Statement: How to maximize Blood Donation Campaign while Donors engage and provide them timely reminders for upcoming Blood donation per their eligibility.

Method: Blood Donor notification Centre -BDNC is a Medical Application and is specially design to campaign and store the data related to Blood Donor registration and retention. The BDNC is unique because it manages the patient data and is a customizable application and allow users to perform multiple task with ease.

This unique system has multiple filter options and once you register a Blood Donor it keeps all the relevant information with a registration number. This system is designed to develop reminders calls, text messages, Life calls & recorded call. It gives you the freedom to plan your campaign and with multiple options to retain or get connected with your Blood Donor.

Result.

At present AMTF helping Blood Disorder Program in Karachi, Pakistan with this software is able to manage more than 2900 Blood Donors and various campaign are designed with this application in multiple ways and we are able to retain the Blood Donor through this notification system.

Conclusion: A constant communication/reminder has proven to be very effective and is required between a health care professional and Blood Donor. We believe that Blood Donor Notification Centre (BDNC) is probably one solution which can retain a Blood Donor intact for a longer period of time through this IT Application.
Cell-based therapy using umbilical cord blood for novel indications in regenerative therapy and immune modulation: an updated systematic scoping review of the literature.

 Submission ID

 130

 Authors/Co-Authors & Affiliations

 Mina Rizk, BSc (1), Joseph Aziz, BSc (1), Risa Short, BSc (2), David Allan, MD (1,3,4)

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 (2) Library Services
 (3) Department of Medicine, The Ottawa Hospital
 (4) University of Ottawa Centre for Transfusion Research

 Abstract Body (max. 350 words)

 Background: Cell-based therapy using umbilical cord blood is used increasingly for novel applications. Moreover, new cellular products are increasingly described using cord blood cells as a starting material. To balance heightened public expectations, evidence-based assessment of emerging applications of cord blood-derived therapies is needed to avoid inappropriate use of unproven cord blood-derived therapies.

 Methods and Results: We updated a systematic search of the literature that we previously published and identified 58 studies (926 patients) for analysis. 17 studies (447 patients) included control groups for comparison. The most commonly reported novel indication for therapy was neurological diseases (25 studies, 476 patients). Cerebral palsy was the disease most frequently studied amongst this subgroup (12 studies, 276 patients). Other indications included diabetes mellitus (9 studies, 149 patients), cardiac and vascular diseases (8 studies, 116 patients) and hepatic diseases (4 studies, 106 patients). Most studies administered total nucleated cells, mononuclear cells or CD34-selected cells (30 studies, 526 patients), administered intravenously (17 studies, 294 patients) or intrathecally (5 studies, 79 patients), or a combination of both (2 studies, 115 patients). 21 studies administered cord blood-derived mesenchymal stromal cells, delivered intravenously (10 studies, 156 patients), intrathecally (5 studies, 52 patients) or otherwise. The majority of reports (46 studies, 719 patients) described a cellular product obtained from an allogeneic source. 11 studies (187 patients) used an autologous cord blood product. We identified 3 indications where multiple prospective controlled studies have been published (4/4 reported clinical benefit in cerebral palsy, 1/3 studies reported benefit for cirrhosis, and 1/3 studies reported biochemical response in type 1 diabetes).

 Conclusions: Heterogeneity between studies precluded meaningful pooled analysis of results. We anticipate a more clear understanding of the clinical benefit for these indications in the near future once more controlled studies are reported. Patients should continue to be enrolled on registered clinical trials for novel therapies. The appropriateness of cord blood-derived cell-based treatments is
gaining clarity and blood establishments, transplant centres, and regulatory bodies need to prepare for greater clinical demand.
Comparison of ultrasound evaluation and serology in hemolytic disease of fetus and newborn and look back of D-immunization failures in a large tertiary care hospital.

Submission ID

103

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Hemolytic disease of the fetus and newborn (HDFN) needs good prediction for timely intervention.

Study design and methods: 11505 normal and at risk pregnancies were censed in a 17 month period. Serologic investigations and clinical data were extracted. Objectives were: antibody specificity and need for transfusion, cerebral artery Doppler velocity (CADV) and serology(S) predictions for hemolysis, lookback for D immunized patients to explain failures.

Results:

Table 1- Intrauterine transfusions:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-C,D,G,E, Jk^a</td>
<td>1</td>
</tr>
<tr>
<td>Anti-C,D,G,</td>
<td>1</td>
</tr>
<tr>
<td>Anti-C,D,G,Jk^a</td>
<td>2</td>
</tr>
<tr>
<td>Anti-c,K</td>
<td>6</td>
</tr>
<tr>
<td>Anti-D,G,E,Jk^b</td>
<td>6</td>
</tr>
<tr>
<td>Anti-E,M</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2- Comparison CADV / Serology (S) (29 cases)

<table>
<thead>
<tr>
<th>CADV+ / SEROLOGY+ (7)</th>
<th>D,G,E ; D,C,G,Jk^a ; D,C,Jk^a ; D,G,Jk^a ; E ; E,M ; K,c</th>
<th>Severe hemolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CADV + / SEROLOGY- (1)</td>
<td>D,E</td>
<td>No hemolysis</td>
</tr>
<tr>
<td>CADV - / SEROLOGY + (3)</td>
<td>D,C,E ; c ; Lu^a</td>
<td>No hemolysis</td>
</tr>
<tr>
<td>CADV - / SEROLOGY (15)</td>
<td>D,C,G ; D ; c,Lu^a@ ; E^* ; E,c ; E,Jk^b ; M ; E,C,Kp^@ ; E,c ; K</td>
<td>No hemolysis</td>
</tr>
</tbody>
</table>
Good correlations are noted between CAD and S for hemolysis prediction or none. CAD was wrong for one case (D,E) and S falsely predicted hemolytic risk for D,C,E / c / Lu^a with antigen match. 5 cases with no hemolysis (CADV-/serology-) were antigen unmatched.
Lookback were done on 7 D-immunized patients to explain failures of anti-D prophylaxis. 4 were probable underdosing for abortions and prenatal prophylaxis, one related to major 2nd trimester fetomaternal hemorrhage (FMH), two to probable underdosing of large at birth FMH.

**Conclusions:** 1- Serology and CADV complement one another. 2- Serology will need refinement with plasma maternal genotyping. 3- Anti-D prophylaxis still have failures.
Consent to Blood Transfusion: Recalling the Discussion

Submission ID
52

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Abstract Body (max. 350 words)

Purpose: Informed patient consent must be obtained prior to the administration of blood products, including review of the indications, associated risks and benefits to transfusion, and available alternative therapies. The purpose of the current inquiry was to assess the degree to which consent discussions at our institution address these requirements.

Method: Patients at different hospital transfusion locations at a large academic hospital were approached shortly after signing a consent form to transfusion and asked a series of questions regarding the consent discussion. The clinicians who had originally engaged in this discussion were not notified ahead of time that their patients were to be approached. Patients received assistance from family members with answering the survey questions if required.

Results: A total of 51 patients were interviewed, age range 19 to 81 years (median 59), and 27 (53%) women. 36 (71%) were first-time transfusees. Assistance with answering questions was provided due to trouble with recall, language barrier, and physical barrier in 4 (8%), 3 (6%), 2 (4%) cases, respectively. All patients had a signed consent form present on their chart. 45 (88%) remembered signing the consent form and 43 (84%) recalled the consent discussion. 43 (84%) indicated that they received an explanation about what a blood transfusion is, 44 (86%) recalled the reason they were told they required the transfusion, and 43 (84%) could recall what the benefits of having a blood transfusion were. 35 (69%) reported that infectious risks associated with a blood transfusion were explained to them, and 32 (63%) indicated that transfusion risks generally were reviewed. Alternatives to blood transfusion were apparently discussed with only 7 (14%) of patients. 45 (88%) recalled being given the opportunity to ask questions, and 22 (43%) endorsed receiving a patient education pamphlet about blood transfusion.

Conclusions: Although all patients reviewed had informed consent documented, the audit identified a number of apparent gaps in the preceding discussion. While these findings are potentially limited
by recall bias, they suggest a need for greater education of health care workers regarding the necessary elements of the consent discussion, in particular on the available alternatives to transfusion.
Contribution of older donors to the blood supply

Submission ID

46

Authors/Co-Authors & Affiliations

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Sheila F O'Brien, Canadian Blood Services

Abstract Body (max. 350 words)

Background: Until Dec 2004, Canadian Blood Services (CBS) had an upper age limit of 61 for first time allogeneic donors and 70 (71st birthday) for regular repeat donors. Criteria were changed to allow repeat donors to continue donating with no upper age limit (but an annual external medical enquiry), and further liberalized in Sept 2015 to remove the upper age limit for first time whole blood (WB) donors, increase the age limit to 67 for first time apheresis donors, and remove the need for external medical enquiries. We assessed the current contribution of older donors (71 and above) to the (WB) and plasmapheresis (PA) programs.

Methods: Data were extracted from the National Epidemiology Data Base (NEDD) based on age and sex.

Results: In 2005, 925 WB donors aged 71 or older made 2,988 donations (0.35% of WB donations). This increased gradually to 2016, when 4,484 older donors made 12,438 donations (1.5% of WB donations). The biggest annual increase occurred from 2015 to 2016. Compared to all WB donors, older donors were predominantly male (65% vs 51%) and made more yearly donations (3.0 vs 2.3 for males, 2.4 vs 1.8 for females). Two-thirds of older donors were 71 to 73. Older PA donors constituted 0.73% of donors and made 1.6% of all PA donations in 2005, and 3.8% of donors making 7% of PA donations in 2016. Compared to all PA donors, there was heavier over-representation of males (80% vs 70%), and a higher frequency of yearly donations (20.5 vs 11.7 for males, 14 vs 6.7 for females).

Conclusion: More than a decade after changing criteria for older donors, their contribution of the blood supply is still increasing. The majority of older donors are in their early 70s, with few remaining in the donor pool past age 75. For WB donors, increased participation in 2016 compared to 2015 may reflect both overall aging of the donor cohort or removal of the cumbersome medical enquiry process. For plasma donors, little recruitment of new donors may have contributed to the high representation of older donors.
COST-EFFECTIVENESS OF IG ISOLO® MANUFACTURING PROCESS FOR IVIG IN THE CANADIAN PUBLIC HEALTH SYSTEM

Submission ID
67

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Abstract Body (max. 350 words)

Background: The risk of hemolytic events (HEs) with IVIG therapy appears to be linked to anti-A and anti-B (isoagglutinins). Patient risk factors include non-O blood group, high dose and underlying inflammation. Isoagglutinin reduction by immunoaffinity chromatography (Ig IsoLo®; IAC) for IVIG and SCIG products was implemented for Privigen® and Hizentra® for the Canadian market from October 2015 onwards. IAC reduces anti-A and anti-B levels by 87-90% (median), which is expected to produce a meaningful risk reduction for HE, based on a mathematical model.

Objectives: To compare the cost-effectiveness of high-dose IVIG (>\(=\) 1g/kg) treatment using an IVIG (Privigen®) manufactured with and without the Ig IsoLo® isoagglutinin reduction step in Canadian high risk patients.

Methods: A Markov model simulated the lifetime risk of HEs and quality-adjusted life years (QALYs) associated with Ig IsoLo® and conventional high-dose IVIG. The model cohort of 34,486 patients was based on Canadian patients with indications for high-dose IVIG in 2015, including Kawasaki disease, renal transplant and myasthenia gravis. Prevalence, indication-specific hemolysis rates and associated costs, impact on quality of life, resource utilization and patient profiles were obtained through a literature search, as well as Statistics Canada and ORBCON, and were validated by a clinical expert. Direct medical costs were based on Ontario unit costs. A lifetime time horizon was employed, with costs and benefits discounted at 5% per annum.

Results: The base-case results indicate that the Ig IsoLo® process could reduce lifetime risk of HE from 2.5% to below 0.2% in high risk patients. Direct medical cost savings are $1,152 per avoided HE. At the level of the entire cohort, cost-savings of $945,861 and a gain of 102 QALYs are predicted.

Conclusions: The reduction of anti-A and anti-B in IVIG manufactured by the Ig IsoLo® process is expected to reduce the risk of hemolysis in high risk Canadian patients, resulting in meaningful health benefits and reduced costs. Limitations of the model include reliance on spontaneous HE reports.
Cryopreservation of adult unrelated donor products in hematopoietic cell transplantation: the OneMatch experience and systematic review of the literature.

Submission ID

129

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(1) Ottawa Hospital Research Institute
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(3) Library Services and (4) Department of Medicine, The Ottawa Hospital and University of Ottawa
(5) University of Ottawa Centre for Transfusion Research.

Abstract Body (max. 350 words)

Background: The frequency of cryopreserving peripheral blood progenitor cells and/or marrow products from unrelated donors is not known and the underlying reasons are poorly documented. Greater understanding is needed to develop policies on cryopreservation that optimize the balance between patient interests and donor safety.

Methods: We performed a retrospective review of cryopreservation requests between January 1, 2014 to May 31, 2016 at the OneMatch Stem Cell & Marrow Network and performed a systematic review of the literature.

Results: Our analysis revealed an overall incidence of approximately 4% (30 cryopreserved products / 719 collections facilitated by OneMatch). We identified patient-related reasons including need for prolonged anti-microbrial treatment (6 patients), too deconditioned to proceed with transplant (5 patients), and/or relapsed disease (3 patients) as the most commonly identified rationale for requesting cryopreservation. Donor-related issues leading to cryopreservation requests were less common (5 cases), mainly due to lack of donor availability after rescheduling. Cryopreservation of a product that was never infused occurred infrequently (2 cases, 7%). In our systematic review of the literature, 993 cases were identified in 32 published reports and both patient-related and donor-related reasons were cited. Quantitative insight regarding incidence or relative frequency of causes was not possible due to lack of reporting. The impact of cryopreservation on hematopoietic engraftment appears negligible when compared to controls in a subset of studies but a lack of
systematic reporting of mean values for rates of engraftment and yields of viable total cells and CD34+ cells precluded pooled meta-analysis.

**Discussion:** Most of the recent experience relates to PBSC with few studies of marrow cryopreservation. Some of the published reports only described cryopreservation of products from related donors. Policies that balance patient needs with donor safety should guide decision-making with unrelated donors. The lack of clear guidelines may underscore practice variations among transplant centres and by different international registries.

**Conclusions:** Future studies are needed to clarify the impact of cryopreservation on engraftment and other transplant outcomes using standard outcomes measures. The international community should develop working guidelines to provide an ethical framework that could ensure appropriate consideration of cryopreservation requests concerning unrelated adult donors.
Determining The Factors For Reassessment After Transfusion: A Canadian Survey

Submission ID

81

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Abstract Body (max. 350 words)

Background: Recent recommendations indicate one red blood cell (RBC) unit should be transfused at a time with reassessment after each transfusion to determine the need for more. However, the practices of Canadian transfusion medicine (TM) experts and what constitutes a reassessment are unknown. Therefore, we conducted a survey of TM experts across Canada to gather information on their practices and criteria for reassessment.

Methods: TM experts were identified and contact information obtained from the Canadian National Advisory Committee (NAC) and from contacting least one TM expert per province. Each respondent was assigned a unique study ID after consenting to the survey, allowing for anonymity on analysis. The survey contained demographics, general practice questions, and questions regarding transfusion in: 1) a stable anemic inpatient, 2) a stable anemic inpatient to be discharged, and 3) an asymptomatic post-operative inpatient.

Results: We identified 67 Canadian TM experts: 48 (71.6%) provided a response and most had a primary place of practice in a laboratory setting (38/48; 79.2%). For a stable, non-bleeding, anemic inpatient, 87.5% of respondents recommended transfusing one RBC unit, then reassessing. Recommendations were more variable in outpatient settings, with 31.2% generally recommending transfusing two RBC units then reassessing. Recommendations for reassessment were mainly functional status/symptoms and vitals within a short time period (1-2 hours), a repeat hemoglobin >18 hours later dependent on the clinical scenario, and a search for an underlying cause of anemia in outpatient settings. Lab practitioners emphasized volume status, cardiac examination, and transfusion at lower hemoglobin thresholds. With an asymptomatic patient to be discharged, fewer respondents chose to transfuse (38.1%) compared to an inpatient potentially symptomatic due to anemia (72.1%). None of the respondents suggested transfusion in an asymptomatic post-operative patient who had a hemoglobin trending down.

Conclusion: TM experts generally recommend transfusing one unit at a time in stable inpatients. Assessment for transfusion should focus on patient symptoms, pertinent physical exam, hemoglobin levels, and an underlying cause. “Top-up” transfusions were not recommended. These recommendations may help guide clinicians, but further research is needed to generate higher quality evidence around the clinical benefits and cost effectiveness of these practices.
**Donor Reactions at Canadian Blood Services between 2013 and 2016**

**Submission ID**

10

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**Abstract Body (max. 350 words)**

**Background:** The Donor Reaction and Incident Manual (DRIM) at Canadian Blood Services provides a guideline for assessment and management of reactions related to the donation process. In 2013, the DRIM was updated to align with international definitions, terms and descriptions. The objective of this study is to evaluate the donor reaction data since the implementation of the standardized definitions.

**Method:** The data was extracted from the data warehouse for the 2013 to 2016 time period.

**Results:** Between 2013 and 2016, 3,611,158 donations were collected and 24,966 donor reactions were reported. The reaction rate in new donors (124 per 10,000) is higher than in repeat donors (49 per 10,000). There is a higher rate of reactions in the 17-25 year old donors (99 per 10,000) compared to older donors (51 per 10,000). More reactions are reported in female donors in all age groups (72 per 10,000) compared to male donors (48 per 10,000). Whole blood moderate vasovagal reactions (15 per 10,000) and severe vasovagal reactions (3 per 10,000) rates are captured for all donors versus mild vasovagal reactions which do not always require an incident report. Nerve irritation both immediate and prolonged, is reported in 1.7 per 10,000 donations. The most common apheresis incident was the inability to return red cells (80 per 10,000). Moderate and severe citrate reactions occurred infrequently (1.4 per 10,000), as did vasovagal reactions (0.8 per 10,000) in apheresis donors. Donor injuries were most frequently associated with falls from vasovagal reactions in first time donors (3.1 per 10,000) and in female donors (1.5 per 10,000) of whole blood. The majority of the injuries occurred after leaving the donation chair but before leaving the clinic.

**Discussion:** Canadian Blood Services has a much lower overall rate of donor reactions (69 per 10,000) as compared to the AABB 2014 Report (223 per 10,000). This is likely related to the reporting requirements at Canadian Blood Services; only moderate and severe in-clinic reactions are routinely reported.

This evaluation is important for donor safety, obtaining donor consent and assessing the need for mitigation steps in selective donors (i.e. muscle tension, hydration).
Effect of donor age and whether donors related or unrelated on time to allogeneic hematopoietic stem cell transplantation

Submission ID
132

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Abstract Body (max. 350 words)

Background: Advances in allogeneic hematopoietic stem cell transplantation (allo-HCT) have reduced transplant-related toxicity, allowing older patients to be considered for allo-HCT. Older transplant recipients have older sibling donors who may have co-morbidities that preclude or prolong the workup before donation, delaying the time to transplant. Although unrelated donors are often younger, it can take more time to identify and activate an unrelated donor. In this study, we addressed whether time from diagnosis to transplant in patients with acute leukemia was affected by donor age and whether the donor was related vs unrelated.

Design and Methods: A retrospective review was conducted at our centre of transplant-eligible AML or ALL patients who underwent allo-HCT between October 2009 and December 2014. Recipient and donor demographics were collected, and time intervals between diagnosis and transplant were compared between recipients of MUD versus MRD donors. Cox proportional hazards model was used to determine factors that affected time to transplant.

Results: A total of 100 acute leukemia patients were included. Median recipient age at diagnosis was not statistically different between MRD and MUD allo-HCT (47 and 52 years, respectively, p=0.13). Median age of MUDs were significantly lower, however, than MRDs (29 and 49 years, respectively, p<0.001). While the age of recipient was not associated with time to transplant, younger donor age was associated with reduced time to transplant (HR 0.98 for each additional year, 0.96 – 1.00, p=0.05). Recipients of MUD, when compared to MRD, had a significant increase in time to transplant, adjusting for age of donor and age of recipient (HR 0.437, 0.247 to 0.772, p=0.01).
Discussion / Conclusions. Our study demonstrated that younger donors were associated with reduced time to transplant and MUD were associated with longer time to transplant compared with MRD. Further studies are needed to understand if the added “time to transplant” for MUD contributes to increased rates of relapse or adverse outcomes for recipients. Continued efforts to shorten the time to transplant with MUD is needed and requires concerted coordination with international registries.
Emergency transfusion of one uncrossmatched group O Rh positive red cell unit to a patient with anti-D antibody identified once type and screen were completed. A case report.

Submission ID

62

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Introduction: Patient blood management programs aim to transfuse group O Rh negative red cells (RCS) only to Rh negative recipients. At the Ottawa Hospital, the CODE BLEED policy for trauma patients specifies that if uncrossmatched RC units are required for patients with unknown blood group, only female patients less than 45 years of age receive group O Rh negative RC units. All other patients receive group O Rh positive RC units. We report a patient who was transfused one unit of uncrossmatched group O Rh positive RC and in whom anti-D antibody was identified once the type and screen were completed.

Case Report: The patient was an 87-year-old female trauma patient with pelvic fracture. The patient was initially transported to a community hospital; 2 hours later she was transferred to the Ottawa Hospital (TOH) Civic Campus Trauma Centre (day 0). On arrival the patient was unstable and a CODE BLEED was initiated. One unit of uncrossmatched group O Rh positive RC was transfused. Half an hour after transfusion the patient complained of nausea and back pain. One hour after transfusion, the transfusion medicine (TM) laboratory reported the patient was group B Rh negative with positive antibody screen; subsequently anti-D and anti-E alloantibodies were identified. The clinical team was notified, and no further group O Rh positive RCS were transfused. Following transfusion of the incompatible RC unit the hemoglobin stayed the same, 90 g/L pre and post transfusion and the post transfusion DAT anti-IgG was only weakly positive. Surgical open reduction and internal fixation were performed on day +6. The patient was discharged to rehabilitation on day +32. In retrospect, the community hospital TM lab results of group B negative with a positive antibody screen were available approximately at time of transfer to TOH, but there was no forward feeding of this information.

Conclusion: Transfusion of uncrossmatched RCS has a low but definite risk for incompatible transfusion. Elderly Rh negative females whose childbearing years pre-date the universal introduction of RhIg might have increased incidence of anti-D antibody. Forward feeding of TM laboratory results is important for trauma transfusion protocols.
Evaluation of post-operative transfusion procedures in post-cystectomy patients at The Ottawa Hospital (TOH).

Submission ID
15

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Abstract Body (max. 350 words)

Background: Allogenic blood product transfusions have allowed patients to survive significant blood loss that may occur during surgery. However, blood product transfusions can lead to various infectious and non-infectious complications. To minimize the rate of unnecessary transfusions, both clinical and laboratory findings should direct decisions to transfuse. Pre-transfusion clinical assessment enables physicians to determine risk for complications such as transfusion associated circulatory overload (TACO), and take appropriate preventative measures. Cystectomy surgery historically leads to extensive blood loss, and therefore has a high risk for transfusion both pre and post-operatively. Consequently, our objective was to assess this cystectomy patient population for frequency and quality of recorded pre-transfusion assessments.

Methods: We conducted a retrospective cohort study of 178 patients who underwent cystectomy surgery at The Ottawa Hospital (TOH) over the past 8 years (March, 2008 – May, 2016) using the patients' electronic medical records. A complete peri-transfusion assessment was defined as documented transfusion start/end times, pre-transfusion labs, clinical history and physical exam, and vital signs prior to transfusion. TACO risk factors were defined using accepted criteria to include acute MI, LV dysfunction, renal dysfunction, diuretic held, and age above 70.

Results: After reviewing 178 cystectomy patients, 80 post-operative transfusions were found to be documented. Of these, only 16.3% had a full proper clinical assessment encompassing pre-transfusion labs, histories and physical exams, vitals, and start/end times. In addition, 80% of all post-operative transfusion episodes occurred in the presence of noted TACO risk factors. Despite the presence of TACO risk factors, post-transfusion fluid balance was only monitored in 52.6% of these cases. Of all the transfusions reviewed, only 2.5% resulted in a transfusion-related complication.

Conclusions: Although few transfusions resulted in transfusion-related complications, the lack of proper pre-transfusion clinical assessment is alarming. Patients with TACO risk factors are particularly prone to complications, and despite knowledge of risk factors being present, were found to be inadequately monitored post-transfusion.

Given these results, changes to existing policies and protocols at TOH regarding appropriate transfusion indications may be necessary. Additionally, programs for continuing transfusion-related
medical education of healthcare professionals should be considered.

Acknowledgements: Dr. Elianna Saidenberg, Dr. Rodney Breau, Irwin Schweitzer
Evidence of the covert risk: Propionibacterium acnes associated with a septic transfusion reaction involving red blood cell concentrates

Submission ID
34

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Abstract Body (max. 350 words)

Background/Case report: At Canadian Blood Services, Quality Control (QC) sterility testing is performed every month for 1% (or a minimum 10 units) of outdated blood products. Propionibacterium acnes is the most routinely isolated anaerobic bacterium during QC testing of red blood cells (RBCs). Remarkably not many cases of transfusion reactions (TR) associated with P. acnes have been reported. This case report investigated a recent TR involving a patient suffering from acute leukemia who was transfused with a 40-day old RBC unit. The patient subsequently presented symptoms of a febrile non hemolytic reaction, which was successfully treated with analgesics and antibiotics. Preliminary blood cultures recovered P. acnes from both the RBC unit and the patient. The focus of this report is to determine whether the isolates of P. acnes from the blood product and the patient are clonally related, thereby providing conclusive evidence of the contribution of P. acnes to the TR.

Design and methods: The identity of the P. acnes isolates was determined using Gram staining and biochemical profiling with the Analytical profile index (API). The isolates were further characterized by the PCR amplification of the recA gene, and genotyping was performed by repetitive extragenic palindromic (REP) - PCR fingerprinting using primers against the BOX element.

Results: Gram positive, short rod morphologies consistent with P. acnes were observed for the patient and RBC isolates. API testing confirmed that both isolates were P. acnes strains with identical biochemical profiles. Sequencing of the amplified recA gene demonstrated that both isolates belong to the same phylotype. REP-PCR fingerprinting yielded banding patterns that were identical.

Conclusion: The biochemical profiles taken together with the genetic characterization and fingerprinting confirm that the strain isolated from the patient originated from the transfused RBC unit, thus linking the transfusion of the P. acnes contaminated RBC unit to the TR. The results reiterate the need for a heightened awareness of the safety risk posed by blood products contaminated with anaerobic bacteria and the need for more robust hemovigilance measures.

Acknowledgements: The hospital staff for investigating this case. Funding provided by Canadian Blood Services and Health Canada.
Factors Influencing Long-Term Hematopoietic Function Following Autologous Stem Cell Transplantation

Submission ID

101

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Abstract Body (max. 350 words)

Background: The American Society of Bone Marrow Transplantation (ASBMT) recommends a stem cell infusion target of 3-5 x10^6 cells/kg for autologous hematopoietic stem cell transplant (auto-HCT). However, the number of CD34+ cells to reinfuse to ensure long-term graft function has not been established. Plerixafor increases CD34+ cell collection even in patients who are predicted poor mobilizers (PPM). This study sought to determine the minimum CD34+ cells/kg required for adequate long-term hematopoiesis, identify factors associated with poor long-term hematopoiesis, and determine if plerixafor mobilization improved long-term peripheral blood counts.

Methods: A retrospective chart review was conducted on auto-HCT patients between January 2004 and September 2013. Poor long-term hematopoiesis was defined as an ANC <1 x10^9/L, hemoglobin <100 g/L, or platelets <100 x10^9/L. Patients were stratified into groups based on the infused CD34+ concentration (in cells/kg), and proportions of patients with poor long-term hematopoiesis at 1-5 years post auto-HSCT were compared. Long-term outcomes (platelet and packed red blood cell transfusions, and post auto-HCT infection rates) were compared between plerixafor-mobilized patients and PPM (patients with pre-collection CD34+ <2 x 10^6 cells/kg).

Results: 210 multiple myeloma and 350 lymphoma patients were included. There was a trend towards lower CD34+ infusions and poorer hematopoietic function (see table 1). Based on a univariate analysis, advanced age (OR 1.189, p=0.05), multiple prior collections (OR 2.978, p=0.035), and pre-treatment with more than two chemotherapy lines (OR 2.571, p=0.02) increased the risk of
poor hematopoiesis. Plerixafor-mobilized patients (n=25), compared to PPM (n=197), had a significantly higher median CD34+ cell collection (4.048 x10^9/L and 2.996 x10^9/L cells/kg, respectively, p=0.005), but there was no significant difference in overall cytopenias, transfusion requirements, or infection rates.

**Conclusion:** We support the ASBMT-proposed transfusion target of 3-5 x 10^6 cells/kg given that 5 years post auto-HCT there was no statistical or clinically significant difference in hematopoietic function with higher CD34+ infusion targets. While plerixafor mobilization significantly increased overall CD34+ cell collection when compared with PPM, long-term hematopoietic function and clinical outcomes were similar. This supports limiting plerixafor to patients who are PPM, not universal plerixafor mobilization, thereby facilitating adequate stem cell collection and early engraftment.
False negative septic transfusion case caused by a platelet pool showing visible clotting due to contamination with *Staphylococcus aureus*

**Submission ID**

25

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**Abstract Body (max. 350 words)**

**Background/Case Study:** A 73 year-old female patient with acute myeloid leukemia was transfused with a 4-day-old buffy coat platelet pool through a central venous catheter. The platelet transfusion was interrupted after noticing a large fibrous clot obstructing the infusion pump flow. Shortly afterwards, transfusion of a 34-day old red blood cell (RBC) unit was begun but halted when the patient developed septic symptoms. While the RBC unit tested negative for bacterial contamination, the hospital isolated *Staphylococcus aureus* from the patient blood, central venous catheter, and platelet pool. The patient received post-transfusion antibiotic treatment and had her original central line removed and replaced. The platelet pool had yielded negative results during routine screening for bacterial contamination using the BacT/ALERT culture system. Further investigation was carried out at Canadian Blood Services with results presented in this report.

**Design and Methods:** The remaining platelet pool and associated RBC and plasma units were tested for bacterial contamination utilizing the BacT/ALERT system. The identity and relatedness of the *S. aureus* isolates were confirmed using microbiological methods and genome sequencing, respectively. Production of *S. aureus* superantigens was evaluated by Western blotting. *S. aureus* biofilm formation and slime production were determined using several microbiological and immunological methods. The platelet fibrous clot was examined by scanning electron microscopy.

**Results:** The platelet pool, catheter, and patient samples were found to be contaminated with a *S. aureus* strain that exhibited the same phenotypic and genome sequencing profiles. The isolated *S. aureus* forms biofilms and produces the superantigen enterotoxin-like U, which was detected in a sample of the transfused platelets.

Scanning electron microscopy of the clotted platelet sample showed *S. aureus* biofilms with fibrous materials and platelet debris.
Conclusions: Our investigation revealed a septic transfusion reaction case involving a platelet pool with BacT/ALERT screen negative results. This report highlights the importance of visual inspection of blood components prior to transfusion as an essential safety practice to prevent transfusing bacterially-contaminated units.

Acknowledgements: netCAD for PC supply. Hospital staff for investigation of this case. Dr. D. Mack for providing antibodies for biofilm assays. Canadian Blood Services and Health Canada for funding.
Harnessing immune tolerance of non-inherited maternal HLA antigens in the CBS Cord Blood Bank

Submission ID

114

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Abstract Body (max. 350 words)

Background: The genes encoding Human Leukocyte Antigens (HLA), the immunological determinant of hematopoietic stem cell (HSC) donor compatibility have diversified significantly within individual ethnic groups. As such, individuals are most likely to find a suitable HSC allograft from someone of common ancestry. Since its inception, the Canadian Blood Services (CBS) Cord Blood Bank has strived to create an ethnically diverse cord blood repository to reflect an equally diverse population. Less stringent HLA-matching requirements with cord blood allow for greater HLA coverage using fewer donors compared to other HSC sources, however, the bank will still need to be particularly large. Emerging literature suggests additional plasticity in cord blood mediated immune reconstitution, specifically, an intrinsic permissiveness of donor T cells towards the non-inherited maternal antigens (NIMA) of the donors mother. Leveraging the NIMA effect would significantly decrease the total number of CBUs needed to provide similar HLA-haplotype matching for the Canadian population, reducing costs and expanding the capacity for better HLA-matching. Using matching simulations, this study will assess the likelihood that a Canadian bone marrow transplant (BMT) patient could find a suitable allograft within the cord blood bank, and further, if NIMA substitution at 1, 2, 3, or 4 HLA loci will improve matching probabilities.

Methods: We have obtained registry info for 2000 cord blood units, including 4 loci HLA typing for the cord donor and mother, as well as self-reported ethnicity data. A custom algorithm will generate hypothetical virtual cord phenotypes by substituting 1-4 HLA loci to create between 130,000,160,000 unique cord phenotypes. All cord phenotypes (real and virtual) will be subsequently matched using HLA data and self-reported ethnicity from Canadian patients undergoing a donor search with the Onematch Network at CBS. Match results will be grouped by ethnicity to determine the extent to which NIMA matching can improve donor options within specific groups.

Results: The algorithm to generate virtual cord phenotypes has been written and tested. Matching simulations are ongoing.
Conclusions: Simulations will assess how well our donor and recipient pool overlaps, and if NIMA substitution at 1 or more loci can improve match outcomes in particular ethnic groups.
Implementation of Plasma Transfusion Policy

Submission ID

16

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Abstract Body (max. 350 words)

Background: Both whole blood derived and apheresis plasma are expensive products and may cause transfusion reactions and harm to the recipients. Published reports revealed that plasma transfusion may be over utilized and measures have been taken to reduce unjustifiable transfusions. In our provincial reference hospital, a plasma transfusion policy that is meeting the national and international guidelines had been developed and implemented by May 1st-2014 aiming to minimize unjustifiable plasma transfusions.

Study design: Data of all transfused plasma units was collected retrospectively for the period of October 1st-2011 through November 30th-2016. The collected data included the type of plasma products, indications for plasma transfusion, and the location where transfusion occurred. Data was analyzed and compared for the 2 ½ years before and after the implementation of our policy.

As it is not implicated by the policy, we excluded all plasma units transfused as part of massive transfusion protocols or therapeutic apheresis procedures, for intra-operative patients or during surgical procedures and plasma units transfused to patients in recovery rooms post-operative. The calculation of the cost of plasma products was estimated based on Canadian Blood Services prices for apheresis plasma and whole blood derived plasma for the corresponding years.

Results: The total units of plasma transfused for the study period was 3545. Two plasma products were used; apheresis plasma (AP), 500 ml, and whole blood derived plasma (FP CPD), 300 ml. The total number of AP units used was 3085 (87%), whereas the total number of FP CPD units was 460 (13%).

Comparing transfusion of the two plasma products in the study periods, before and after the implementation of the policy, the transfusion of AP units was reduced from 1886 to 1199, with a drop of 36.4%, whereas the transfusion of FP CPD units was reduced from 322 to 138, with a drop of 57.1%. The reduction in plasma transfusions, for both AP and FP CPD, saved approximately 234,045 Canadian dollars.

Conclusion: The implementation of a policy to guide plasma transfusion practice is found to be cost effective, safe and practical.
Learn Transfusion Seminar Series - A Vital Component of Transfusion Medicine Education in Canada

Submission ID

54

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Abstract Body (max. 350 words)

Clinicians are entrusted with ensuring best practice in transfusion medicine (TM). However, TM education in Canadian medical schools is variable and limited. As a result, most graduating physicians have limited competency in TM best practices. There are few TM specialists in Canada, with most in large academic centres. Yet appropriate and current transfusion-related knowledge is vital for everyone that is involved in treating patients that may require transfusion.

The Learn Transfusion seminar series is presented by Canadian Blood Services (CBS). It is hosted weekly as a component of the AFC Diploma Programs in Transfusion Medicine. Although the seminar series was conceived to support the TM specialty training program, everyone in the TM community is encouraged to attend. The series provides a forum for sharing current TM knowledge, particularly for those with limited access to local experts.

Methods: Seminars were broadcasted via Webinar (GoToWebinar, Citrix Online) with accompanying conference call, from the CBS Toronto centre. Post-seminar feedback was elicited with a weekly survey (Survey Monkey). Survey data, collected the week following each seminar between September 8, 2015 and June 28, 2016 were collated and summarized.

Results: There were 46.3 participants/sites per seminar (range 27 – 81, n = 27); 6 were trainees in the AFC Diploma Program. 922 surveys were analyzed. Response rate was 74.3% (59.1 – 100%/week). Seminar participation and survey response rate was increased as compared to the year prior (35.4 participants/week; response rate 69.5%). Overall, 96% of participants were from Canada, and 67% from Ontario. Most participants were primarily affiliated with a hospital (48%) or the CBS (37%). Approximately half of attendees identified as laboratory staff or nursing, while the other half were physicians. Laboratory-related topics were the best attended. Attendees rated overall presentation effectiveness and “relevance to practice excellent or good 99.0% and 95.0% of the time, respectively.

Conclusion: The learn transfusion seminar series is an effective tool for dissemination of current TM knowledge and best practices; not only for TM specialty trainees, but also for the broader TM audience. It is an important mechanism for delivery of current TM education to a broad and geographically diverse population.
Making TACO In a Downtown Hospital: Where and With What?

Submission ID
70

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Abstract Body (max. 350 words)

Background: Transfusion is one of the most frequently performed procedures in healthcare, and transfusion-associated circulatory overload (TACO) is a common adverse event, while also disproportionately accounting for transfusion-related fatalities. In order to study preventative strategies, the context of TACO may help to identify in whom and where an intervention is best to deploy. The purpose of this study is to determine in which care settings TACO is reported, and what the antecedent transfusion order consisted of.

Design and Methods: Consecutive transfusion reaction investigations in a hemovigilance database were retrospectively reviewed. Events occurred within an academic institution (866 beds) consisting of three facilities performing transfusions (60-70,000 components annually). Possible to definite TACO cases were assessed.

Results: Over the 7.5 year review period (10/05/2009 – 21/11/2016), there were 2381 consultations for suspected transfusion reactions. TACO comprised 241 (10.1%) of these cases. TACO patients were significantly older (median [interquartile range], in years) than non-TACO patients (63 [51-73] vs 57 [45-68], p<0.05) but sex distribution (males/total) was similar (119/241 vs 1198/2372 respectively, p=0.7). Medical inpatients (MIP) dominated in TACO and were disproportionately represented compared with non-TACO cases (MIP/total:110/240 [46%] vs 828/2375 [35%] respectively, p<0.05). Location rank-order in TACO was MIP > critical care (38 or 16%) = surgical inpatients (38 or 16%) > outpatients (36 or 15%) >ER (12 or 5%) >OR (4 or 2%) > hemodialysis (1) = interventional radiology (1). Of the products transfused before TACO occurred, RBC were involved in 185 orders (77%), 77 of which were single unit exposures (42% of RBC orders, or 32% of TACO cases overall). Multiples of a given component (eg. 2u RBC) marked 106 events (44%), while multiple component types (eg. RBC and platelets) marked TACO in 65 cases (27%). Overlap cases (multiples of a product and multiple component types) occurred in 40 cases (17%).

Conclusions: Strategies to prevent TACO may be best focused on MIP, and on orders incorporating RBC. Although orders involving more than one dose of a product or more than one component type are common in TACO, the single RBC unit order nevertheless accounts for a third of TACO cases.
Mean corpuscular volume and transfusion in cardiac surgery

Submission ID
60

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Abstract Body (max. 350 words)

Background: Mean corpuscular volume (MCV) has recently emerged as a prognostic indicator of adverse outcomes in several clinical settings. However, its role in risk stratifying patients undergoing elective cardiac surgery is unknown. We examined the relationship between MCV and hemoglobin in patients undergoing elective cardiac surgery, and investigated the risks of red blood cell (RBC) transfusion associated with different levels of MCV.

Design and Methods: From January 2010 to January 2014, 16,099 patients underwent cardiac surgery at Cleveland Clinic. 5,510 patients who underwent uncommon, urgent, or emergency operations were excluded, leaving a study cohort of 10,589 patients. Normal MCV is defined as values from 80 fL to 100 fL; microcytosis as MCV below 80 fL, and macrocytosis as MCV greater than 100 fL. Linear regression analysis was performed to examine the relationship between MCV and hemoglobin levels. Multivariable logistic regression analysis was performed to investigate the association between MCV and risks of receiving RBC transfusion adjusting for hemoglobin.

Results: Of the 10,589 patients, 9,992 (94%) presented with normal MCV, 337 (3.2%) with microcytosis, and 260 (2.5%) with macrocytosis. 219 (65%) with microcytosis, 2,364 (24%) with normal MCV, and 131 (50%) with macrocytosis were anemic, with median hemoglobin levels of 12 g/dL, 14 g/dL, and 13 g/dL, respectively. Linear regression analysis using patients with normal MCV as the reference group showed that microcytosis is associated with a 1.78 g/dL decrease in hemoglobin, and macrocytosis is associated with a 0.96 g/dL decrease in hemoglobin. When hemoglobin level is adjusted for, patients with microcytosis had lower risk of receiving RBC transfusion (odds ratio 0.76; 95% confidence interval [CI] 0.59-0.99) and patients with macrocytosis had increased risk of receiving RBC transfusion (1.72; CI 1.29-2.29) compared to patients with normal MCV.

Conclusions: Patients with macrocytosis have higher risks of perioperative RBC transfusion despite having higher median hemoglobin level than patients with microcytosis. Thus, if possible, treatment to normalize MCV and hemoglobin should be undertaken prior to elective cardiac surgery.
Medical Enquiries: To Do or Not To Do? Evaluating the first 1500 Medical Enquiries processed in West Medical Services

Submission ID
29

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: The Medical Enquiry (ME) process is used by Canadian Blood Services to obtain donor health information from community physicians for issues not listed in the Donor Selection Criteria Manual (DSCM). Donors are temporarily deferred until the requested information is provided to CBS medical offices for evaluation. Little is known about the effectiveness of this process with respect to donor retention and subsequent donation.

Recently, CBS consolidated the Medical Offices of three Western Canadian Provinces. As a result the process for ME was restructured, streamlined, and virtualized allowing for data collection which had not previously been possible.

Analysis of the first 1500 MEs completed through this process was performed to determine if the ME process aids in donor retention by counting number of units subsequently donated by this cohort. The secondary objectives were to describe the associated diagnoses and time to file closure to determine if they were correlated with subsequent donor eligibility or donation.

Design and Methods: Data was extracted from an electronic ME datasheet commencing October 1, 2015, in sequential order for 1500 donors. Data included dates, diagnoses, and eligibility assessments. For donors subsequently deemed eligible, the CBS eProgesa system was searched to determine if they returned to donate and number of units collected.

Results: Of the 1500 donors who had MEs initiated, 17% no response, 20% were subsequently deferred, 58% donors were accepted, and 5% donors remain pending. Ultimately 16% of the 1500 donors returned to clinic within 4 months of file closure and donated a total of 241 units.

Cardiac arrhythmia, elevated ferritin/iron and Raynauds disease were the most common reasons for ME initiation. They were also positively correlated with acceptance. There was no correlation between time to closure of donor file and likelihood of donor returning to clinic.

Conclusions: The ME process allowed CBS to save 58% of donors and resulted in an additional 241 donations that otherwise would have been lost if these donors were simply deferred. Three common reasons were identified for ME initiation which were largely associated with donor acceptance and efforts should be made to incorporate these into the DSCM.
Most Common Red Blood Cells Antibodies

Submission ID

93

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Abstract Body (max. 350 words)

Background: Crossmatch-compatible blood is issued to patients requiring red cell transfusions to avoid potential complications relating to red cell antibody incompatibilities. When crossmatch-compatible blood is not available, antigen-negative blood (so-called least incompatible) is issued based on red cell phenotype or genotype. If it is not feasible to determine the red blood cell phenotype or genotype of a patient in need of transfusion, it would be beneficial to know which red cell antibodies are most common among our patient demographic, so that red blood cell units negative for those antigens can be transfused.

Study design: Data on red blood cell antibodies identified in Queen Elizabeth II Health Science Centre, Provincial reference center for red blood cell antibodies tests from February 1, 2010 through December 31, 2016 were collected retrospectively from our laboratory information system and de-identified. The data included: red blood cell antibody identity, date of antibody identification, patient gender, patient age, and patient blood group.

Findings: 3,425 red blood cell antibodies were detected during the study period, including 3,361 (93.1%) allo-antibodies and 64 (6.9%) auto-antibodies. The most frequently detected allo-antibodies are anti-E, 23.6%, anti-K1, 16.6%, anti-D, 12.4% (84% female patients), anti-C, 8.2%, anti-Fya, 6.9%, anti-c, 5.7%, and anti-Jka, 4.8%.

Conclusion: Anti-E, anti-K1, anti-D, anti-C, anti-Fya, anti-c, and anti-Jka are the seven most common antibodies identified in the province. When crossmatch-compatible and least incompatible blood are not available, we will recommend these antibodies be respected. We will request red cells negative for the most common antibodies from Canadian Blood Services for use in emergency situations.
Parent preferences in obstetrical and perinatal care in hemophilia: a survey of hemophilia treatment centre providers

Submission ID
92

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Abstract Body (max. 350 words)

Background: Management of pregnancy and delivery of an infant at risk for hemophilia can be complex. There are a number of areas where important medical decisions must be made, but the evidence guiding these decisions is weak. In areas of medicine where a strong evidence base is lacking, the incorporation of patient and family preferences in decision-making becomes all the more important.

Objective: To determine clinicians (clinic directors and nurse coordinators) perceptions of parental resource needs and preferences for involvement in obstetrical and neonatal management decisions involving a carrier mother and an infant at risk for moderate or severe hemophilia.
**Methods:** Clinicians working at hemophilia treatment centers in Canada were emailed invitations to participate in an online survey. Respondents provided demographic information and answered questions about their perception of parental desire for additional resources and for involvement in key decision points. Open-ended questions permitted respondents to provide additional decision points and comments.

**Results:** Electronic invitations were delivered to 105 clinicians, and 42 (40%) answered all questions regarding parental involvement in decision points. A large proportion of responders agreed or strongly agreed that parents want to be involved in the following: planned mode of delivery (42/42; 100%); prenatal diagnosis (40/42; 95.2%); regional anesthesia (40/42; 95.2%); location of birth (38/42; 90.5%); and infant circumcision (32/42; 76.2%). Disagreement or uncertainty existed regarding parental desire for involvement concerning the use of factor concentrate (FC) prophylactically (22/42; 52.4%) and the choice of FC (14/42; 33.3%). Excluding use of FC prophylactically, the majority of respondents perceived that parents wanted more resources on all decision points. Intracranial monitoring was mentioned as an additional decision point by two clinicians. Survey respondents emphasized the importance of this study, and parents need for information.

**Conclusion:** Clinicians in this study perceived that parents want to be involved in key decision points, and want additional resources to inform decisions during the pregnancy management of a carrier mother and an infant at risk for or affected by hemophilia. Future research should explore parents’ experiences and perceptions of involvement in decision making throughout pre- and post-natal management of an infant affected by hemophilia.
Performing a Massive Online Needs Assessment for Developing a Learner-Centered Online Curriculum for the Management of Bleeding Through the Use of Social Media: A SoMe-KTE3 Project

Submission ID
89

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Abstract Body (max. 350 words)

Background: The internet has become a primary method for how clinicians learn new scientific findings and maintain competency. Methods associated with the Free Open Access Medical Education (FOAM) movement, such as using social media, blogs, podcasts, and other online resources, aim to promote best practices and engage in knowledge translation. However, most materials do not address knowledge gaps and lack structure. The management of bleeding (and thrombosis), often involving transfusion medicine concepts, was chosen as an area well-suited to development of a learner-centered curriculum. We thus performed a Massive Online Needs Assessment (MONA) to determine perceived and unperceived needs.

Methods: A multidisciplinary group developed a survey to identify both perceived and unperceived knowledge gaps. The survey requested demographic information, inquired about topics of interest (perceived needs), and contained 5 case scenarios containing 3 questions each (to determine unperceived needs). This was launched via Google Forms; and was disseminated using the FOAM website CanadiEM.org, Twitter, and Facebook with research ethics board approval. The survey took 30 minutes to complete and was incentivized with a draw for one of four $250 Amazon gift cards. Knowledge gaps were defined a priori as topics where <50% of participants answered correctly.

Results: 866 unique users viewed the survey and 198 complete responses were obtained (22%) over a 2-month period. Most respondents were staff physicians (n=114;57.8%) and medical trainees (n=75;37.9%); in the fields of emergency (n=116;58.6%) and internal medicine (n=38;19.2%). The highest number of responses for perceived needs in acute bleeding and therapy were reversal of anticoagulants (77%) and adjunct treatments for acute bleeding (67%). Appropriateness of transfusion (53%), adverse effects of transfusion (46%), and periprocedural triggers for transfusion (34%) had fewer responses. Knowledge gaps were identified in all transfusion-related topics. Only
21% of responses were correct for appropriate warfarin reversal, 22% for appropriate blood product choice in massive transfusion, and 35% for management during massive transfusion.

**Conclusion:** Our MONA determined both perceived and unperceived learning needs in developing an online curriculum to teach the management of bleeding. This assessment reveals knowledge gaps in transfusion medicine concepts and represents an opportunity to teach them to clinicians.
PERMISSIVE TRANSFUSION OF ABO INCOMPATIBLE RED BLOOD CELLS DURING ALLOGENEIC BONE MARROW STEM CELL TRANSPLANTATION: A Clinical Case Experience

Submission ID
97

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Abstract Body (max. 350 words)

Background and Case: Allogeneic stem cell transplant (allo-HSCT) donor selection is independent of ABO blood group compatibility. In cases of significant incompatible donor product red blood cell (RBC) volume, reduction of either the product RBC burden or recipient isohemagglutinin titer is performed to reduce the risk of recipient acute hemolytic transfusion reaction. Here, we describe the transplant course of a 21-year-old woman with severe aplastic anemia who underwent a 9/10 HLA-matched ABO incompatible (B positive recipient/A positive donor) marrow-source allo-HSCT at our center following plasma exchange for isohemagglutinin reduction.

Methods: Myeloablative conditioning (Flu/Cy/ATG) including total body irradiation was completed by day -3. Plasma exchange on day -2 and -1 successfully reduced the recipient anti-A titer to ≤ 1:4. The fresh donor marrow product was split into aliquots for infusion, and otherwise unmodified. The patient was pre-medicated before product infusion, and clinical symptoms were monitored according to standard protocol. Bloodwork drawn at baseline and after infusion of each aliquot included isohemagglutinin titers, hemolytic parameters and renal function.

Results: The baseline recipient anti-A titer was 1:16, which decreased to 1:4 with plasma exchange. The total volume of the donor product was 1823 mL, with an incompatible RBC volume of 565 mL. The first 129 mL aliquot infused contained 40 mL of RBC, and was well tolerated. Three subsequent aliquots were 500-650 mL each in total volume, including 155-200 mL of RBC. Headache, nausea with vomiting, back pain and visible hemoglobinuria developed with the larger volume infusions. The anti-A titer fell to 1:2 after the first aliquot, but became undetectable only after infusion of the final aliquot. The anti-B titer was undetectable throughout. Cellular engraftment was successful.

Discussion: During infusion of an ABO incompatible bone marrow-source allo-HSCT product, exposure of the recipient to donor RBC is unavoidable. In our patient, pre-medication mitigated adverse reaction symptoms attributable to RBC hemolysis, though larger product volumes significantly increased symptom severity. Surprisingly, the anti-A titer remained detectable until the entire product was infused. Further study of allo-HSCT patients receiving ABO incompatible RBC may help provide valuable information about acute hemolytic transfusion reaction symptoms and effective management strategies.
Platelet Transfusion Thresholds During Anti-thymocyte Globulin Therapy for Aplastic Anemia and Hypoplastic Myelodysplastic Syndrome

Submission ID
43

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Abstract Body (max. 350 words)

Background: Anti-thymocyte globulin (ATG) is an immunosuppressant agent used in patients with aplastic anemia (AA) or hypoplastic myelodysplastic syndrome (H-MDS). Unintended specificity of ATG for platelets can lead to severe drug-induced thrombocytopenia. The British Committee for Standards in Haematology (BCSH) recently published 2016 guidelines recommending a pre-transfusion platelet count of at least 20x10^9/L prior to ATG administration based on expert opinion alone. To determine whether the recommendation is warranted, a review was conducted at a hospital with a large AA/H-MDS population focusing on pre-ATG platelet counts and bleeding outcomes.

Methods: A retrospective review at an academic hospital in Toronto, Canada was performed on all AA and H-MDS inpatients receiving at least one dose of ATG between May 2006 and May 2016. Patients were identified from a pharmacy database. A detailed chart review of patients included platelet counts, transfusion history, and documented bleeding.

Results: Overall, 34 courses of ATG (divided over 3-5 days for a total of 141 days) were administered to 18 AA and 13 H-MDS patients. One hundred and thirteen ATG doses (80%) were given with a pre-transfusion platelet count less than 20x10^9/L (median 10x10^9/L, interquartile range 6-17x10^9/L), with no differences between AA and H-MDS patients. Sixty-one platelet transfusions were administered with the majority of transfusions (88%) given for platelet counts less than 10x10^9/L. Of the 53 days with a pre-transfusion platelet count between 10-20x10^9/L, only six platelet transfusions occurred prior to ATG infusion. One bleeding episode (intracranial hemorrhage) was documented in an AA patient two days after discontinuing ATG due to posterior reversible encephalopathy syndrome. The platelet threshold used in this patient was 10x10^9/L with a pre-transfusion platelet count of 4x10^9/L on the day of hemorrhage. In 22 ATG courses (65%), daily prophylactic tranexamic acid was also administered.

Conclusion: Most patients receiving ATG received platelet transfusions at a platelet threshold of 10x10^9/L rather than 20x10^9/L as recommended by BCSH. In the only documented case of bleeding, it is unclear if thrombocytopenia alone was the causative factor. Therefore, the utilization and outcome data from our review does not support adopting the opinion-based BCSH recommendation.
POST-TRANSFUSION PURPURA RELAPSE AFTER TRANSFUSION OF WASHED RED BLOOD CELLS

Submission ID
98

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Abstract Body (max. 350 words)

Background and Case: Post-transfusion purpura (PTP) is a rare transfusion reaction featuring severe thrombocytopenia within three weeks of blood component transfusion. The pathophysiology hinges upon exposure of a human platelet antigen (HPA) alloantibody to its corresponding antigen, and subsequent paradoxical autologous platelet destruction to a critical nadir. The mortality rate in affected individuals is up to 8%, predominantly due to bleeding-related complications. We present a case of a 62-year-old woman with a known history of PTP and confirmed HPA-1a antibody, who developed a PTP relapse following transfusion of a washed RBC unit for critical anemia secondary to advanced-stage esophageal adenocarcinoma.

Methods: A patient chart review was completed for clarification of historical PTP events. Confirmatory HPA antibody testing by ELISA method and HPA genotyping was performed by the Canadian Blood Services (CBS) – Platelet Immunology Laboratory. Washed red blood cells (RBC) were prepared by CBS using the Haemonetics ACP-215 Automated Cell Processor system.

Results: Clinical history included two classic PTP events more than 25 years ago. Genotyping confirmed homozygosity for the HPA 1b/1b allele, and serologic testing identified a persistent high-titer HPA-1a antibody. During hospitalization for anemia due to cancer-associated bleeding, a hemoglobin (Hb) of 50 g/L prompted an urgent request for RBC transfusion. Platelet count was stable at 96 x 10^9/L, without laboratory evidence of coagulopathy. Since HPA-matched donor RBC units were unavailable, washed RBC were requested from CBS. Bloodwork one hour post-transfusion of a single washed RBC unit included Hb 75 g/L, with platelet count 75 x 10^9/L. Unfortunately, the platelet count rapidly fell to a nadir of 12 x 10^9/L by 28 hours post-transfusion. Before IVIg therapy initiation, the patient became acutely hypotensive and exsanguinated.

Discussion: This case demonstrates that PTP relapse may occur despite transfusion of washed RBC. The challenge in identifying effective strategies to prevent relapse and optimize care of affected patients is underscored by the rare incidence of PTP. Further study is necessary in several areas, including: feasibility of maintaining a national stock of frozen HPA homozygous donor RBC; development of a validated HPA antigen deficient washed RBC product; and pre-emptive IVIg therapy before washed blood transfusion.
PREDICTED HEMOLYSIS RISK REDUCTIONS WITH ANTI-A/B IMMUNOAFFINITY CHROMATOGRAPHY IN IVIG

Submission ID

20

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Abstract Body (max. 350 words)

Introduction: Hemolysis can be associated with IVIG products. Risk factors include non-O blood group, relatively high dose and underlying inflammatory state. The latter two are commonly experienced when neurological disorders are treated. The risk of hemolytic events (HEs) with IVIG appears to be linked to anti-A and anti-B isoagglutinins in the product. Proof-of-concept of isoagglutinin reduction by donor screening (excluding ~5 % donors) was published previously. Isoagglutinin reduction by immunoaffinity chromatography (Ig IsoLo; IAC) for IVIG and SCIG products was implemented for Privigen and Hizentra for the Canadian market from October 2015 onwards, as a manufacturing improvement. IAC has the capability to reduce anti-A and anti-B levels by >/= 85% in commercial lots. IAC is expected to produce a meaningful reduction of the hemolytic risk with Privigen.

Methods: Using published titers for seven IVIGs and corresponding HE rates (per 1000 kg IVIG sold) calculated from HEs spontaneously reported to EudraVigilance, we developed a mathematical model to estimate the HE risk of IVIGs. We calculated the HE risk for an IVIG (Privigen, CSL Behring) and evaluated risk reduction with two isoagglutinin reduction measures: anti-A donor screening and anti-A/anti-B specific immunoaffinity chromatography (IAC; Ig IsoLo). Titers in IVIGs from CSL Behring measured by European Pharmacopoeia direct assay were provided by Swissmedic, Bern, Switzerland.

Results: Estimated risk was highest for group AB, followed by A and B; it was low for O. Broken down by blood types, estimated hemolysis risks were: Group AB: 8.45 cases/1000 kg for Privigen versus 0.38 for Privigen with Ig IsoLo; Group A: 3.17 cases/1000 kg for Privigen versus 0.20 for Privigen with Ig IsoLo; Group B: 1.93 cases/1000kg for Privigen versus 0.07 for Privigen with Ig IsoLo. Blood type distribution was based on the US population.

Conclusion: Based on the magnitude of anti-A and anti-B reduction in Privigen (IAC; Ig IsoLo) our model predicts corresponding improvement in hemolysis risk to patients receiving the product. A 620 hospital clinical observational study is ongoing until 2019 to test if the hemolysis risk reduction can be confirmed in clinical practice. Limitations of the model include reliance on spontaneous HE reports.
Proposal for Revision of Canadian Blood Services Donor Eligibility Criteria for Heart Murmur

Submission ID

80

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: Heart murmurs are a product of turbulent blood flow, which may be of no clinical significance (i.e. functional or innocent murmur) or, could reflect underlying cardiovascular pathology (organic murmur). Current Canadian Blood Services (CBS) donor eligibility criteria for heart murmur require donor deferral for murmurs which are not explicitly classified as functional or specifically related to mitral valve prolapse. This criterion results in deferral of a number of donors for whom blood donation may be safe. We summarize a recent review of this issue and present a proposed revision to current donor eligibility criteria.

Design and Methods: Published clinical/scientific literature on the clinical relevance of isolated cardiac murmurs was reviewed. This evidence was assessed in the context of a self-reporting healthy donor presenting to a blood donor clinic. A scan of related regulatory requirements and other blood suppliers practice was also undertaken.

Results: Systolic heart murmurs in particular are very common and data indicate that most incidentally discovered systolic murmurs, without associated clinical signs or symptoms, are a very non-specific proxy, with low predictive value for underlying cardiac disease. Donors presenting with a history of heart murmur will have been advised of this by their physician, who should already have undertaken appropriate medical evaluation of the donor. Following medical assessment, whether or not a specific diagnostic cause of the murmur has been established, if the donor is asymptomatic, and requiring no clinically directed follow-up or treatment, then there is no evident incremental donor health or safety risk precluding blood donation and the donor should be acceptable.

Discussion/Conclusions: In Nov 2016, the CBS-Hema-Quebec Donor Selection Criteria Working Group supported a proposed revision to blood donor eligibility criteria that would accept affected donors if asymptomatic and requiring no clinically-directed follow up; or if symptomatic, temporary deferral while obtaining further information from the donors physician. These changes will be made to the CBS donor eligibility criteria manual.
Reducing Inappropriate Prophylactic Plasma Transfusions in Patients Undergoing Bedside and Image Guided Procedures.

Submission ID

50

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Abstract Body (max. 350 words)

Background: Inappropriate use of prophylactic plasma prior to bedside and image-guided procedures has been noted in several audits (including our own 2014 audit) despite medical evidence that it is ineffective and potentially harmful.

Design and Methods: Despite a prospective review process implemented in 2014, several new interventions were implemented in our multi-hospital transfusion service to further improve appropriateness in 2016 for this patient setting. We shared the 2014 audit data again, developed consensus institutional guidelines for plasma and performed a multipronged educational campaign involving key stakeholders in adult medical, surgical and diagnostic imaging services. This was then followed by implementation of a mandatory plasma request form.

Pre- and post-intervention audits reviewed all plasma requests between April 1 and June 30th in 2014 and 2016 respectively. Requests prior to defined interventional procedures (including paracentesis, thoracentesis, line insertion, lumbar puncture, liver biopsy) were identified and adjudicated as appropriate versus inappropriate based on our new institutional pre-procedure guidelines and plasma thresholds categorized as low (INR>3) versus high risk (INR>1.8).

Results: During our audit periods, a decrease in plasma use was identified and is currently sustained. Excluding intraoperative, pheresis and massive hemorrhage protocol requests, there were a total of 425 and 389 plasma forms in 2014 and 2016 respectively. Pre-procedure requests accounted for 73 (17%) and 68 (18%) respectively. In both, paracentesis accounted for ~60% of requests and ~75% of patients had coagulopathy due to cirrhosis. 27% of 2014 pre-procedure plasma requests had an INR <1.8 versus 6% in 2016 (p=0.4). In the pre-intervention audit 82% (n=60) of plasma requests were inappropriate versus 46% (n=31) in the post-audit (p=0.0006). In 2016, 2/3 of these inappropriate requests were for patients undergoing paracentesis. Requests for plasma for coumadin reversal also notably decreased (14% versus 4%) but in the 2016 cohort 3 patients on coumadin were not identified appropriately on the request form.

Conclusions: Our overall plasma usage and number of inappropriate plasma requests pre-bedside procedure have both demonstrated substantial decreases. However, paracentesis continues to be an
area for improvement and further reductions in plasma utilization can be realized by abolishing the INR cut-off for low risk procedures. Further educational interventions and force functions will be required for further improvement.
Retrospective analysis of antibodies in prenatal screening and relation with hemolytic disease of fetus and newborn in a large tertiary care hospital.

Submission ID

102

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Hemolytic disease of the fetus and newborn (HDFN) needs expertise for monitoring and treatment. A retrospective analysis was done.

Study design and methods: 11505 normal and at risk pregnancies, coming from two major obstetrical sites in an academic tertiary hospital, were censored in a 17 month period (December 2013-May 2015). Serologic investigations and clinical data were extracted. Primary objectives were: time of antibody appearance (order of pregnancies), comparison of our percentages of immunizations for specific antibodies (or group of antibodies) with the literature data, number of exsanguinotransfusions (EST) and/or intrauterinetransfusions (IUT) in total or per patient, link between antibody specificity and transfusions, first antibody detection revealed on 2nd trimester testing.

Results: 104 patients were antibody positive (0,7%). Mean age was 31y (21-42). Patients gravida status: 14(G1), 32(G2), 31(G3), 12(G4), 9(G5), 1(G6), 1(G7), 1(G9), 1(G14), 2(ND). Table 1- describes the specificities.

EST were done on 2 different newborns (anti-D,G,C for both). 13 newborns received a top-up transfusion at birth. 3 babies with anti-D,C,G and 2 others (anti-E,M and anti-D,E) received transfusions inside 1 month post-partum. IUT procedures were required in IUT procedures were required in 6 patients: one procedure in 3 (D,C,G/D,C,G,E, Jka/E, M), two in 1 (D,C,G,Jk^a), six in 2 (D,G,E,Jk^b /c, K).

11 Rh positive pts (out of 77) were analysed at 28 weeks: 6 negatives, 5 positives for the first time during pregnancy (anti-C, E, Jk^a, M(2)).

Table1-

Conclusions: 1- Our panel of antibodies is similar to the literature except for K (lower incidence). In the province of Quebec recommendations of transfusing Rh and Kell completely matched transfusions were not suggested in 2013 for women in child-bearing age. 2- Anti-G is a frequent companion of the cases with severe hemolysis but we are unable to precise its exact involvement. 3-D and combinations are still the major actors of severe hemolysis not excluding E and Kidd possible participation. 4- Third trimester testing still reveals new antibody formation. This practice is a matter of debate.
Rh immune globulin (RhIG) prophylaxis post transfusion of Rh positive red cells in females of child bearing potential

Submission ID

131

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Abstract Body (max. 350 words)

Introduction and Cases: The incidence of HDFN caused by D antigen sensitization has dramatically fallen in Canada over the last 4 decades owing to routine RhIG prophylaxis of Rh negative females. However, anti D remains a rare but important cause for HDFN. In some cases, transfusion of Rh positive red cells for treatment of acute hemorrhage may be the stimulus. We present four Rh negative female patients who were transfused an Rh positive packed red cell(PRBC)unit during obstetrical hemorrhage and their subsequent management/follow up.

Patient A & B were admitted to community hospitals for C-section. However, they became coagulopathic and developed postpartum hemorrhage with Rh positive PRBCs transfused due to error in Aor inventory limitations in B.

Patient C was admitted to a rural hospital with a spontaneous abortion, bleeding and hemodynamic instability. Patient D was also admitted to a rural hospital with intrauterine fetal demise, DIC and shock.

Due to inventory limitations in both patient C and D, only group ORh positive units were available as unmatched support and were transfused prior to subsequent transfer to tertiary care facilities.

Management: All patients were managed similarly. The dose required was calculated using a rule of thumb stating 300 ug of Rhlg would cover 15 mL RBCs and assumed a PRBC unit average volume of 250 mL (280 minus 30 mL additive). Total doses of Rhlg ranging from 5100 to 12000 ug were given intravenously as 600 ug doses every 6 hours until completion. Larger vials (1000ug) were issued when available to facilitate patient care with the same overall dose.

Close follow up of hemoglobin level and subsequent antibody screening were recommended to assess for hemolysis and determine the success in avoiding anti-D sensitization. Antibody screening in patient A and B showed a passive anti-D at initial follow up but was negative for immune anti-D later. Patient C and D antibody confirmatory follow up testing are pending.
**Conclusion:** RhIG prophylaxis using the dosage mentioned above can be a utilized as a method to prevent anti-D alloimmunization if Rh positive PRBC transfusions are necessary as lifesaving measures. However, studies indicate that immunization rate may only be as high as 25% in settings of significant blood loss which may be a confounding factor.
Rituximab as an alternative to intravenous immune globulin for autoimmune diseases

Submission ID

126

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Abstract Body (max. 350 words)

Background: Intravenous immune globulin (IVIG) is a plasma-derived blood product that is used as a treatment for various autoimmune diseases. The anti-CD20 monoclonal antibody rituximab has similar immunomodulatory properties and mechanisms of action. We did a systematic review and meta-analysis to determine the efficacy and safety of rituximab across a broad range of autoimmune diseases with a view to investigate this agent as an alternative to IVIG.

Study design: Systematic review and meta-analysis.

Methods: We identified the most common indications for IVIG (besides immune replacement therapy) from a recent Ontario audit based on total amount of IVIG used. Starting with the highest users, these were: chronic inflammatory demyelinating polyneuropathy (CIDP); immune thrombocytopenia (ITP); myasthenia gravis (MG); multifocal motor neuropathy (MMN); Guillain-Barre syndrome (GBS); systemic lupus erythematosus (SLE); Sjogrens syndrome (SS); and pemphigus vulgaris (PV). Next, we did a systematic review of rituximab for each of these conditions by searching MEDLINE, EMBASE and the Cochrane Library until July 2016. Randomized controlled trials (RCT) and observational studies of 10 adult patients were included. The primary outcome was clinical response at 6 months from RCTs across all conditions. Secondary outcomes were clinical response for each condition and adverse events. Pooled relative risk (RCTs) or pooled proportions (observational studies) were calculated using fixed and random effects models. Risk of bias was assessed for each study using the Cochrane Collaboration tool.

Results: We identified 108 studies for the target conditions (n=3536 patients) including 11 RCTs (n=1044). Most studies were in ITP (n=1543), SLE (n=1192), PV (n=504) and SS (n=200). There were 4 studies in MG (n=66), 2 studies in CIDP (n=31) and none in GBS or MMN. Risk of bias in 9 of 11 RCTs was low. Response to rituximab was 30% higher than controls (RR=1.30, 95% CI 1.01, 1.67) based on pooled results of 11 RCTs in ITP, SLE, PV and SS. Pooled proportions for disease-specific responses
ranged from 48% (95% CI 30% 66%) for CIDP to 94% (95% CI 88% 98%) for PV. Adverse events were mild.

**Conclusion:** Rituximab is an effective immune-modulating treatment and may represent an alternative to IVIG for some conditions.
Abstract Body (max. 350 words)

**Background:** World Health Organization (WHO) assigned voluntary non-remunerated donation as the safest form of Blood donation. Moreover, it emphasized on developing strategies and program to induct regular donors in large quantity to maintain the highest possible quality of blood supply. However, the major bone of contention is the number of drop outs in blood donor pool, hence the blood donor agencies always keeps this thought process moving that how to affiliate a long-term relationship with blood donors. There is continuous search and effort for the development of a successful program which can strengthen the long term relation between the blood donor club and blood donor.

**Methods:** It was therefore mandatory to put forward a novel idea which can bring a drastic change in blood supply campaigns and amalgamate the donors with the recipients through a humanitarian binding force. After an year of project development the concept of SALIFOME Saving A Life In front Of My Eyes was coined by Dr Asim Qidwai which was then forwarded for rigorous pilot study and reviewed by a multidimensional team (MDT) comprising of Hematologist, Thalassemia experts, Blood Bank Experts, Nursing Educationist, Psychologist and Pharmacist.

**Result:** SALIFOME wherever implemented would provide the following benefits to the health care system specifically systems associated with chronic blood disorders including but not limited to: donor immediate satisfaction, lateral communication, long term engagement of donors, learning experience for others, establishment of large blood donors pool, community education, cost effective solution, better utilization of human model.

**Conclusion:** At present almost 2700 Blood Donors are motivated and registered with this concept of SALIFOME.

Our intention with SALIFOME was to start and initiate something which will provide the blood donor one strong motivational and sustain long term relationship among donors and donor club. This concept can be used as reference for other centers dealing with Haemoglobinopathies.
Severe allergic transfusion reactions reported to Canadian Blood Services Eastern Medical Services from 1st January 2014 through 31st December 2016

Submission ID
28

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Abstract Body (max. 350 words)

Background: Severe allergic transfusion reactions are characterized by rash/hives and systemic manifestations including respiratory, cardiovascular or gastrointestinal symptoms. Most of these reactions are unexplainable and could be related to variable interactions of the recipients’ immune system with the transfused blood.

Study design: Retrospective data on recipients and donors associated in severe allergic transfusion reactions were assessed for the period of January 1\textsuperscript{st}, 2014 through December 31\textsuperscript{st}, 2016 from Eastern Medical Services (ON, NS, PEI, NL, NB, MB).

Findings: 34 severe allergic transfusion reactions were reported. 15 (44.11\%) were assigned a final diagnosis of severe allergic reaction after investigation. The majority of these 15 recipients (66.6\%) were female. Two (both female) had previous transfusion reactions of unknown type, three did not receive blood transfusion in the past, eight received blood transfusion but did not experience a reaction and we were unable to determine previous transfusion or reaction history in two cases. Three recipients had documented history of allergy (20\%) whereas 7 (46.7\%) reported no history of allergy and 5 (33.3\%) had no available data.

The 19 associated blood components included 7 (36.8\%) plasma units, 6 (31.6\%) red cells, and 6 (31.6 \%, 5 pooled, 1 apheresis) platelets units.

There were 34 (18 male) associated donors. Six were first time donors. The mean number of donations for these donors was 32.4 (range 1 – 325). Four donors (11.8\%) gave a history of allergy whereas 9 (26.4\%) had no known history of allergy, and no allergy data were available for 21 donors (61.8\%). None of the associated blood donors were found to be involved in other transfusion reactions.

Conclusion: Our retrospective study revealed that severe allergic transfusion reactions were seen more in female patients. About 20\% of recipients had documented history of known allergy. Severe allergic reactions were seen in relation to plasma rich components mainly (plasma and platelets,
63.2%). While most of the associated blood donors had no documented history of known allergy, specific allergy data were not available for over 60% of the donors. None of the donors associated with severe allergic reactions had been involved in other transfusion reactions.
Sickle Trait Testing of Donor Red Cell Units Allocated to Sickle Cell Recipients: Costs and Yields in a Carte-Blanche Approach

Submission ID
55

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Abstract Body (max. 350 words)

Background: Red blood cell transfusion (RBC) strategies in sickle cell disease (SCD) range from simple transfusions (ST) to therapeutic exchanges (TREx). Improved oxygen delivery by RBC is expected by the increments achieved in the quantity and/or quality of circulating hemoglobin (Hb). Diminishing proportions of sickle hemoglobin (HbS), from levels in disease (ie dominant ratios), to levels at or below those in asymptomatic sickle trait individuals (HbS 30%), can be quantified by high performance liquid chromatography (HPLC). A comparison of HbS% calculation-based expectations versus observations may be pursued after ST or TREx. Use of RBC free-of-HbS (trait-negative) simplifies this exercise, but is not medically necessary. Laboratories may nevertheless favour the use of RBC verified as such.

Design and Methods: Our procedures relating to RBC allocated to SCD patients were reviewed. RBC for SCD is match-selected beyond ABO/RHD, (for RHCE and KELL [at a minimum], and for additional antigen systems in the alloimmunized), thereby increasing the odds of African-ancestry donors and HbS trait. RBC undergo SickleDex screening (integrated cost: $10CAD/test), a positive result of which leads to return to general inventory, irrespective of RBC prescription (ST or TREx). Attribute information (SCD recipient, HbS+ RBC) is recorded in the laboratory information system, HCLL.

Results: Over the 7.7 year audit period (12/05/2009 – 21/01/2017), 26,003 RBC were HbS screened, and 56 (2.2/1000, 95% confidence interval [CI] 1.7-2.8/1000) were HbS+. HbS+ RBC were uniformly crossed over to non-SCD patients. In 2016, the ratio of HbS+:HbS- units was 13:4417 (2.9/1000, 95% CI 1.7-5.0), with $44,300 CAD spent in the last calendar year for this testing. For a number-needed-to-test (NNT) of 341, $3408 would be spent to interdict one HbS+ RBC, without including workload to source a replacement RBC, the transfusion of which may also have been delayed as a result of this
activity. The odds of 1 RBC in an order being HbS+ and adversely affecting calculations or clinical outcomes was judged to be too low by all stakeholders to justify the existence of the testing policy.

**Conclusions:** Scrutiny of the RBC HbS trait testing policy demonstrated that it was costly, low-yield, and without identifiable benefits.
Simulating the urgent release of blood-type irrelevant products in a hospital setting

Submission ID

59

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Abstract Body (max. 350 words)

Background: Simulation is effective in many health disciplines as an experiential learning modality for increasing skills, confidence, and teamwork to the level demanded by the workplace. Our group has used simulation to identify issues with standard operating procedures, physical space layout, and skill and knowledge gaps. Many types of processes in the transfusion medicine laboratory are suitable for simulation, particularly because blood bank products have critical consequences for patients, and simulation allows participants to engage in a safe and realistic environment. Simulation is valuable in rare-event scenarios, allowing participants to practise a process they do not see very often. The primary objective of our project is to simulate the urgent release of blood-type irrelevant products that do not require the complete workup that is expected for blood-type relevant products, because a delay has been noticed that is not congruent with expectations if this process was consistently performed efficiently.

Design: For the blood bank products that carry low risk for patient incompatibility such as plasma products, platelets and cryoprecipitate, there are procedures in place to allow quick release of these products rather than waiting until ABO testing is complete. We performed in situ simulations in 4 transfusion medicine laboratories in Edmonton region hospitals with medical laboratory technologists (MLTs). Several scenarios were created relating to issuing blood products before preliminary testing has been completed, and accessory material was created (i.e. simulated blood products). The scenarios were of varying complexity, and we recruited the participation of transfusion medicine pathologists and nurses to act in their normal roles. A simulation facilitator was on-site to record observations during the scenario and perform each pre-brief and de-brief.

Results: The simulations are taking place from January until the end of February 2017.

Discussion/Conclusions: Preliminary results demonstrate that simulation is having a positive impact on MLT confidence with the processes, and is identifying procedural steps that are particularly problematic and contributing to a delay in the release of blood-type irrelevant products. We will be able to use this information to develop specific recommendations for process improvement and
further staff training. Complete conclusions incorporating final results will be presented by conference time.
Summary of Cell-Free Fetal DNA (cffDNA) Testing in Pregnant Women in Western Canada.

Submission ID
12

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Abstract Body (max. 350 words)

Background: Molecular testing of cffDNA is widely used throughout Europe for management of pregnant women with clinically significant alloantibodies and for targeted administration of Rh Immune Globulin (RhIG) to RhD negative women carrying RhD positive fetuses. There has been limited application of this technology in North America, partly due to patent considerations.

Method: Between September 2013 and December 16, 2016, Canadian Blood Services (CBS) regional perinatal testing laboratories in western Canada forwarded maternal blood samples to the International Blood Group Reference Laboratory (IBGRL) in Bristol, U.K., for determination of predicted fetal phenotype (PFP) based on molecular analysis of cffDNA. All samples were processed and sent from the Edmonton laboratory. Women were eligible for the program if they had a clinically significant titre (>/= 16) of anti-D, -C, -c, -E, -D+C, -D+E, -E+c, or if they had anti-Kell regardless of titre. Samples were collected at 13 to 32 weeks gestation for Rh antibodies and at 20 to 32 weeks gestation for anti-K.

Results: During this timeframe, 71 patients were tested (Alberta - 56, British Columbia - 14, Saskatchewan - 1). The following maternal antibodies were present: Anti-D 22, -C 1, -E 14, -c 8, -D+C 4, -D+E 2, -E+c 3, -K 17. PFPs were positive for the antigen in question in 30 patients, negative in 32 patients and inconclusive in 9 patients.

Conclusions: Molecular determination of PFP has several advantages in terms of identifying mothers for whom follow-up can be safely attenuated with attendant cost-savings, and offers a non-invasive approach to obtaining samples for analysis. In this cohort, 32 of 71 (45.1%) fetal samples were negative for the antigen in question and the mothers were eligible for a reduced frequency of monitoring of the pregnancy. In future, this method could be used to target antenatal RhIG prophylaxis to only those Rh negative women carrying an Rh positive fetus. This will reduce the number of women receiving RhIG unnecessarily by 35 to 40% as cited in the literature, and will optimize the use of a valuable blood product and avoid the risk of exposure of pregnant women to an as yet unrecognized pathogen.
**Systematic review of the effectiveness of tranexamic acid at reducing blood loss in women undergoing myomectomy for fibroid removal**

**Submission ID**

58

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**Abstract Body (max. 350 words)**

**Background:** Uterine fibroids (UFs) are benign growths in the uterine muscular wall that, if symptomatic, can cause abnormal bleeding or pelvic pain. UFs can be removed via several different procedures, but myomectomy is the only procedure that leaves the uterus intact, allowing for future childbearing. However, myomectomy increases the risk of haemorrhage and postoperative blood transfusions. Tranexamic acid (TA) is an anti-fibrinolytic used to minimize perioperative blood loss. The efficacy of TA has been established for certain surgeries, but its effectiveness remains unclear for gynaecological surgery. The purpose of this systematic review is to determine if TA, compared to placebo, no treatment, or active comparator, is effective in reducing perioperative blood loss and the need for RBC transfusion in women undergoing myomectomy for fibroid removal.

**Methods:** MEDLINE, EMBASE, the Cochrane Library, Web of Science, PubMed, CINAHL, and the Transfusion Evidence Library were searched for full text RCTs without any language restrictions. To be eligible for inclusion, studies had to be RCTs including women of reproductive age undergoing myomectomy, with oral or intravenous TA administered perioperatively, and reporting outcomes of blood loss or need for blood transfusion. A total of 285 articles were found after duplicate removal.

**Results:** Two reviewers independently screened the articles based on title and abstract. Four studies met all eligibility criteria and were included in the review. Two studies compared TA to placebo, one compared TA to no intervention, and one compared TA with oxytocin. Overall, TA was not found to be effective in reducing blood loss or the need for transfusion when compared to placebo or oxytocin. However, for a subgroup of women undergoing myomectomy for the removal of multiple fibroids, TA was effective compared to no intervention in reducing both blood loss and RBC transfusion requirement.

**Discussion/Conclusions:** Compared to placebo or oxytocin, TA was not effective in reducing blood loss or the need for transfusion during myomectomy for fibroid removal, with the exception of
myomectomy for multiple UFs. Based on trial data, it is not recommended that TA be used as a hemostatic agent for myomectomy, except when multiple fibroids are being removed.
TACO prevention: how commonly are diuretics prescribed?

Submission ID

53

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Abstract Body (max. 350 words)

Background: Transfusion-associated circulatory overload (TACO) is one of the leading causes of transfusion-associated mortality. Several approaches to preventing TACO have been suggested. The purpose of this study is to determine how commonly diuretics are prescribed to patients while receiving a red blood cell (RBC) transfusion.

Design and Methods: This was a retrospective chart audit of 50 consecutive adult inpatient RBC transfusion orders at four academic institutions in July 2016. Only the first transfusion order for each patient was included. Individual orders for more than 2 units were excluded such that all transfusion orders were either 1 or 2 unit orders. Data collected included patient demographics and risk factors for TACO and transfusion order details. The primary outcome was the percentage of patients receiving furosemide peri-RBC transfusion. Secondary objectives included the dose, route, and timing of furosemide administration.

Results: Two hundred RBC transfusion orders were audited. The average age was 61.8 years and 52% were female. At least one risk factor for TACO was present in 55% of patients (28% were older than 70 years, 18% had a history of congestive heart failure, 16% had ejection fraction < 60%, 5% had diastolic dysfunction and 33% had renal dysfunction). Indications for transfusion were as follows: low hemoglobin 66%, active bleeding 17%, symptomatic anemia 12%, intraoperative transfusion 9%, postoperative transfusion 6%. The mean pre-transfusion hemoglobin was 72.8 g/L (SD 15.5 g/L). 82% were single unit transfusion orders. The transfusion order included the infusion rate in 44% of orders (mean infusion rate 0.5 units per hour). Peri-transfusion furosemide was ordered in 16% of cases with no difference in the presence of risk factors for TACO compared with patients not receiving
furosemide. The most common dose was 20mg (52%), the route was intravenous (90%) and timing was post-transfusion (74%). No transfusion reactions occurred in any of the patients.

**Conclusions:** Furosemide is not routinely ordered for RBC transfusion. When ordered, the most common prescription is 20mg given intravenously at the end of transfusion. As clinicians do order furosemide peri-transfusion, studies assessing the safety, efficacy, dose and timing of furosemide in preventing TACO are justified.
The Ottawa Criteria for Appropriate Transfusion in Hepatectomy (OCATH): Using the RAND/UCLA Appropriateness Method

Submission ID
18

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Abstract Body (max. 350 words)

Background: Hepatectomy is associated with a high prevalence of blood transfusions. A transfusion has the potential to be a life-saving intervention in the appropriate patient, but is associated with important adverse effects. Given the prevalence of transfusions, their potential for great benefit and harm, and the difficulty in conducting clinical trials, this topic is well-suited for a study of appropriateness. Appropriateness studies aim to determine the indications for which expected health benefits of an intervention exceed expected negative consequences.

Design and Methods: This study was conducted using the RAND/UCLA Appropriateness Method. An international, multidisciplinary panel of experts in hepatobiliary surgery, anesthesia, transfusion medicine, and critical care were identified. The panelists were sent a recently conducted systematic review on the topic, and asked to rate a series of 468 intraoperative and postoperative scenarios for the appropriateness of a blood transfusion. The scenarios were rated in two stages: by each individually, followed by an in-person moderated panel session.

Results: 48% of scenarios were rated as appropriate for transfusion, 28% inappropriate, and 24% uncertain. The key recommendations for intraoperative transfusion were: 1) it is never inappropriate to transfuse for significant bleeding or ST segment changes; 2) it is never inappropriate to transfuse for an intraoperative hemoglobin ≤ 75g/L; and 3) in the absence of significant bleeding or ST changes, transfusion for hemoglobin of ≥ 95g/L is inappropriate, and transfusion for hemoglobin of ≥ 85g/L requires strong justification. The key recommendations for postoperative transfusions were: 1) in a stable, asymptomatic patient, an appropriate transfusion trigger is 70g/L (without coronary artery disease) or 80 g/L (with coronary artery disease); and 2) it is appropriate to transfuse for a hemoglobin of 75 g/L either immediately post-operative, or with a significant decrease from the previous day (>15g/L).
**Conclusions:** Based on the best available evidence and expert opinion, criteria for the appropriate use of perioperative blood transfusions in liver resection have been developed. This provides clinical guidance for scenarios where a transfusion is clearly appropriate, clearly inappropriate, and for those that are equivocal. The areas of uncertainty and disagreement can inform the direction of future clinical trials.
The safety and efficacy of lysine analogues in cancer patients: A systematic review and meta-analysis

Submission ID
39

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Abstract Body (max. 350 words)

Background: Lysine analogues are effective agents used for the reduction of blood loss and blood transfusion. However, the safety of lysine analogues in cancer patients remains in question due to a potential increased risk of venous thromboembolism (VTE). Our objective was to investigate the safety and efficacy of lysine analogue administration in patients with cancer.

Design and Methods: Medline, Embase, and The Cochrane Library were searched from inception to June, 2016. Reference lists of retrieved studies were searched to identify additional publications. Randomized clinical trials in adult cancer patients for which a lysine analogue was administered for the purpose of blood loss reduction were included. The primary outcome was venous thromboembolic events. Secondary outcomes were other adverse events, blood transfusion, and blood loss. Two independent reviewers performed abstract and full-text selection, as well as risk of bias assessment using the Cochrane Risk of Bias tool.

Results: Overall, eleven studies involving 1,177 patients evaluated at least one of the primary or secondary outcomes. No increased risk of venous thromboembolism was observed for patients who received lysine analogues compared to control (Peto OR 0.58; 95% CI 0.26-1.28). The administration of a lysine analogue significantly decreased both transfusion risk (pooled RR 0.52, 95% CI 0.34-0.80) and blood loss (SMD -1.57, 95% CI -2.21 to -0.92). Among three eligible studies, no increased risk was observed for mortality (Peto OR 1.01; 95% CI 0.14-7.18) or infection (OR 0.58; 95% CI 0.27-1.27).

Conclusions and Relevance: The safety of lysine analogues in cancer patients has been inadequately studied. Based on the available literature, lysine analogue use has not been associated with increased risk of venous thromboembolism or other adverse events, while being effective in reducing blood loss and subsequent transfusion. More high-quality evidence in the form of randomized controlled trials are needed in this area before definitive conclusions can be drawn.
The Spread and Timing of Transfusions for Premature, Very Low Birth Weight Neonates: A Secondary Analysis of the ARIPI Trial

Submission ID

94

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: ARIPI was a Canadian RCT conducted to determine whether transfusing fresh RBC units, as opposed to older blood, was associated with improved health outcomes for premature, very low birth weight (VLBW) neonates requiring transfusion. The trial involved six NICU centres, and included 377 VLBW neonates who received at least one transfusion. The ARIPI study collected transfusion data on VLBW infants, not all of which has been analyzed. The purpose of this study was to perform a secondary analysis of the ARIPI data to determine red blood cell (RBC) transfusion patterns for VLBW neonates in the NICU with respect to the spread and timing of transfusion, as well as to determine whether centre differences exist in transfusion practice.

Methods: A descriptive analysis of the ARIPI data was conducted to determine the spread and timing of transfusions. Centre differences were tested using Moods median test, as the data were not normally distributed. Statistical testing was done in SAS, and graphs were generated in SAS and Excel.

Results: A total of 1922 transfusions were administered to the 377 infants, for a median of 4 transfusions (IQR: 2,7) per neonate.

The median number of transfusions ranged from 2 to 6 across the 6 NICU centres (p<0.001). Overall, the median time from birth to the first RBC transfusion was 7 days (IQR: 3,14), with the second transfusion occurring within 3 weeks of the initial transfusion. Ninety percent of subsequent transfusions had occurred by the 8th week of life. When stratifying by NICU, there were statistically significant differences in the timing of transfusions across the six centres (p0.01). There was also variability in the amount of time between transfusions (the spread of transfusions) across the six centres.

Discussion/Conclusions: For premature neonates, we demonstrated that the spread and timing of transfusions varied by NICU centre, and that the majority of transfusions occurred within the first 8 weeks of life. These findings provide insight on the transfusion patterns, and the variability of these patterns between centres, for premature VLBW neonates in a Canadian context. Exploring reasons for practice variation is needed to ensure optimal and appropriate use of red blood cells.
TRANFUSION PRACTICE IN SICKLE DISEASE PATIENTS IN OTTAWA

Submission ID

137

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Abstract Body (max. 350 words)

Background: Sickle cell disease is a genetic disorder of the beta globin chain in red blood cells that results in shortened red cell survival and decreased red cell deformity. Clinically this causes a haemolytic anemia and other complications including pain crises, acute chest syndromes and cerebral strokes. Red blood cell transfusion is an important part of the management of this disorder, either to treat or prevent complications. We conducted a retrospective review of red cell transfusions at the Ottawa Hospital (TOH).

Methods: Patients were identified using the sickle cell roster from the Hemoglobinopathy clinic and a historical list of all sickle cell patients treated at TOH since 2008. We retrospectively reviewed the electronic charts of all identified patients to determine the use of red blood cell transfusions. We recorded diagnosis, age, number of transfusion episodes, number of units transfused, type of transfusion (simple versus exchange), indication for transfusion and levels of hemoglobin S around the time of transfusion.

Results: From 2008 to 2015, 149 patients with sickle cell disease were cared for at the Ottawa Hospital. 92 patients were hemoglobin SS disease, 46 were hemoglobin SC disease and 9 were hemoglobin S-beta thalassemia. As of March 2016, the mean age of the patients was 32.8 years and 43% of the patients were male. A total of 77 (52%) patients were transfused at TOH during the period of the study. Among the patients transfused, 39 patients received exchange transfusions and 63 received simple transfusions, and 27 received both simple and exchange transfusions. The mean and median number of transfusion episodes were 8.7 and 1, respectively. The mean and the median number of red cell units transfused was 46 and 2, respectively.

Further analysis will be performed regarding the indications for both simple and exchange transfusions.

Conclusions: Red cell transfusions are a frequent procedure in patients with sickle cell disease but less than half of the patients followed in our sickle cell disease clinic required transfusion over the period of our study. Half of the patients transfused received at least one red cell exchange transfusion.
Abstract Body (max. 350 words)

Background: As a result of the Krever Report released on November 26, 1997, the role of a Transfusion Safety Officer (TSO) was established to enhance the safety and quality of blood transfusions in Canada. The TSOs fundamental role is improving patient safety in all aspects of transfusion practice.

This position comes with various accountabilities including technical/clinical, utilization management, quality and risk, education of health care professionals, and research. A guide to assist a health care professional’s transition into the role of a TSO is advantageous; however, there are limited resources to date.

Design and Methods: In 2014, the Clinical Project Coordinator-Transfusion Safety Nurse for the Ontario Regional Blood Coordinating Network (ORBCoN) visited various health care institutions in Ontario observing the TSOs daily activities and responsibilities. The TSOs identified that there was minimal guidance and limited resources during their transition to the role. Each acknowledged that a TSO might come from diverse backgrounds in health care, which could contribute to limitations in understanding of clinical or technical terminology and gaps in communication. Experienced TSOs from six Ontario hospitals engaged and participated in the development of this document.

Results: The resource provides information on the following:

- TSO Job Description
- Abbreviations & Glossary of Terms
- Committees and Organizations
- Useful links
- Investigation and Reporting of Transfusion Reactions
- Recalls/Withdrawals
- Product Administration Guidelines (monographs)
- Equipment used for infusion of blood
Conclusions: The Transfusion Safety Officer Resource Manual would serve as a valuable reference guide for Medical Laboratory Technologists, Registered Nurses and other health care professionals appointed into the TSO role.

Acknowledgements: ORBCoN gratefully acknowledges the funding support provided by the Ministry of Health and Long-Term Care (MOHLTC). ORBCoN would like to recognize the hospitals that generously shared documents and information that contributed to the creation of this resource manual.

- Kingston General Hospital
- Lakeridge Health
- London Health Sciences Centre
- St. Michaels Hospital
- Sunnybrook Health Sciences Centre
- Trillium Health Partners
- University Health Network
Transfusion-Associated Graft Versus Host Disease in the Extremely Preterm Neonate: A Retrospective Cohort Analysis

Submission ID
57

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Abstract Body (max. 350 words)

Background: Transfusion-Associated Graft Versus Host Disease (TA-GVHD) is a rare but generally fatal complication of blood transfusion due to donor lymphocytes initiating an immunologic reaction against host tissues resulting in bone marrow aplasia, skin infiltrates and pancytopenia, amongst other findings. The optimal approach to prevent TA-GVHD is irradiation of cellular blood components. Maintaining large inventories of irradiated red cells involves high costs, inventory management challenges and reduced shelf expiry. In addition, irradiated red cells are associated with hemolysis, hyperkalemia, and decreased post-transfusion recovery. The balance of the risk of these adverse features versus the prevention of a very rare complication has resulted in different local practices. Currently, our Transfusion Service does not provide irradiated red cells to preterm and low birth-weight neonates in the absence of another indication.

Methods: A retrospective quality assurance review of extremely preterm neonates <29 weeks gestation admitted to the Stollery Children’s Hospital Neonatal Intensive Care Units between 2009 and 2014 was performed. The electronic patient record and local database were used in a stepwise manner to identify deceased infants who had received non-irradiated cellular blood products and developed pancytopenia after initial transfusion. Laboratory and clinical parameters were then evaluated to identify features suggestive of TA-GVHD.

Results: A total of 467 infants (gestation: 25.4SD1.6 weeks; birth-weight: 835220g) were identified within the database. There were 114 deceased patients, of which 25 (22%) infants died within 24 hours after initial transfusion, too early for TA-GVHD development. New onset of pancytopenia was found in 8 (7%) infants after transfusion, however no infant demonstrated evidence a non-responsive marrow or clinical features consistent with TA-GVHD.

Summary: The transfusion of irradiated red cells to preterm or low birth-weight neonates is a controversial area due to lack of quality evidence regarding the risk of TA-GVHD in this population. This project determined that our practice of providing non-irradiated red cells to this patient group has not resulted in evidence of TA-GVHD. Although the numbers may not be adequate for definitive identification of a very rare risk, this information provides additional assurance regarding our risk benefit determinations and support for maintaining our current practice.
TRANSIENT HEPATITIS B IMMUNITY ACQUIRED FROM TRANSFUSION OF PACKED RED BLOOD CELLS: A Case Report Depicting Practice Guideline Rationale

Submission ID

96

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Abstract Body (max. 350 words)

Background and Case: Blood transfusion recipients of plasma or platelet components are known to passively acquire soluble viral antibodies, though this has seldom been documented with packed red blood cell (PRBC) transfusion given the minimal volume of accompanying donor plasma. Nevertheless, clinical practice guidelines discourage screening viral serology within six months of any blood transfusion. We report a case of a 38-year-old male who was confirmed to have acquired transient immunity against Hepatitis B following PRBC transfusion. Baseline investigations documented a non-immune Hepatitis B status. Two units of PRBC were transfused, following which unintended post-transfusion repeat testing of hepatitis immune status was performed. Hepatitis B serology ten hours following baseline investigations suggested that passive transfusion of Hepatitis B surface IgG antibody (HBsAb) had occurred, prompting further investigation.

Methods: Viral serology assays were determined on a Roche diagnostics e601 analyzer. Quantitative results are expressed as a signal: cut-off (S/CO) ratio to interpret the qualitative viral immunity status. PRBC were obtained from Canadian Blood Services. Retention segments from the PRBC units transfused were tested for HBsAb. The half-life of passively acquired HBsAb was also determined.

Results: The baseline HBsAb plasma concentration in the patient had a S/CO ratio of <2 (undetectable and non-immune). The post-transfusion concentration was found to be 55 S/CO, exceeding the threshold of 10 S/CO, therefore suggesting Hepatitis B immunity. Testing of the PRBC unit segments revealed that one unit had a HBsAb S/CO ratio of <2, while the other had a HBsAb concentration of 21,600 S/CO. Serial HBsAb concentrations were followed in the patient. The HBsAb antibody half-life was determined to be only 1.4 days with an anticipated Hepatitis B non-immune (<10 S/CO) status to be reached 4 days after the transfusion.

Conclusion: This case clearly depicts the passive transfusion of anti-viral antibodies with PRBC.
transfusion, a rarely observed or reported phenomenon. Our observation supports current practice guidelines discouraging anti-viral antibody testing within six months of transfusion, including PRBC. An unexpected finding was the short half-life of acquired HBsAb. Further investigation is needed to determine whether degradation or elimination of transfusion-acquired antibodies differs from that of endogenous antibodies.
Treatment of delayed hemolytic transfusion reaction with red blood cell exchange: a case report

Submission ID
112

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Abstract Body (max. 350 words)

Background: Delayed hemolytic transfusion reactions (DHTR) occur in approximately 1 per 2500 transfusions. Treatment includes supportive care, repeat transfusion, and possible automated RBC exchange (limited evidence).

Case: A 54 year old woman with multiple comorbidities including Crohn’s disease and cirrhosis was admitted to hospital for management of ascites. On post admission day (PAD) 9, her hemoglobin decreased to 63 g/L (baseline 96 g/L) without an obvious source of bleeding. The patient was typed as O, D+ with a negative antibody screen. She was transfused a unit of RBCs (O+, C-), which was well tolerated with an appropriate hemoglobin increment to 73 g/L. On PAD 14, her hemoglobin decreased to 65 g/L, which led to the transfusion of a 2nd unit of RBCs (O+, C+) without an apparent transfusion reaction and an appropriate hemoglobin increment to 77 g/L. On PAD 23, she received a 3rd unit of RBCs (O+, C+) for drop in hemoglobin to 69 g/L. Upon completion of the 3rd transfusion, the patient developed chills and a fever of 38.4 C. She received symptomatic treatment with rapid improvement. Post-transfusion testing revealed a positive DAT (IgG weak, C3d negative) and a non-specific antibody in plasma testing. The patient received 3 additional units of RBCs on PAD 25 and 26, which were O+C+, without overt symptoms. The hemoglobin decreased to 63 g/L, without an appropriate increment despite the additional transfusions. Her indirect bilirubin increased to 162.1 umol/L (baseline 7.7 umol/L), haptoglobin was below reference range, and creatinine increased to 186 umol/L (baseline 83 umol/L). Subsequently, plasma testing demonstrated an anti-C antibody by routine gel and an anti-e antibody using enzyme treated cells.

Given ongoing hemolysis, the patient received 8 units of RBCs via exchange transfusion. The units were C and e negative and cross-match compatible. Her hemoglobin increased from 66 g/L to 98 g/L immediately following the exchange. Over the next several days, the hemoglobin slowly drifted down, but stabilized around 80 g/L, with improvement in her hemolytic markers and creatinine.

Conclusion: Red blood cell exchange can be an effective treatment strategy in severe cases of DHTR.
Use of intraosseous samples for ABO/Rh grouping and antibody screening

Submission ID

48

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Abstract Body (max. 350 words)

Objective: A study to compare ABO/Rh and antibody screening testing between intraosseous marrow aspirate and peripheral blood samples of patients.

Background: In rare cases where a peripheral blood sample could not be collected for CBC or Transfusion Medicine testing, intraosseous samples (bone marrow aspirate) can be used. This can be problematic in some trauma-caused or other resuscitation requiring cases and it may increase use of O-negative red cell units. We performed a study to validate ABO/Rh typing and antibody screening on 20 bone marrow aspirate specimens collected from intraosseous devices and we compared the results with same patient’s peripheral blood sample ABO/Rh testing and antibody screening findings.

Methodology: At least 2cc bone marrow aspirate and peripheral blood samples were collected separately in EDTA tubes on the same day from 20 Hematology/Oncology patients. Marrow aspirate samples were filtered by in-house made Spectra/Mesh Nylon filters to prevent bone or tissue debris contamination and further interpretation mistakes. This filtering also prevented clogging of our automated systems.

Blood and marrow aspirate specimens were run alongside each other for ABO/Rh testing by using our laboratory’s current ABO/Rh testing procedures. A separate solid phase antibody screening was also performed on each specimen by our Capture – R® system.

Results: ABO/Rh testing and solid phase antibody screenings revealed same results for each patient’s marrow aspirate and peripheral blood samples. There were no significant differences in agglutination reaction strengths between two samples. There was no present antibody in any of the samples which was also confirmed by checking of each patient’s history.

Conclusion: Filtered bone marrow aspirate samples can be used to perform ABO/Rh grouping and antibody screening analysis in situations where a peripheral blood samples cannot be collected. This could allow upfront ABO-compatible transfusion management of these patients and prevents unnecessary use of precious O-negative red cell units. In all cases, results should be confirmed with the first available peripheral blood sample.
Utilizing Electronic Health Records To Audit Red Blood Cell Transfusion Ordering Practices in Four Ontario Tertiary Care Centers

Submission ID
90

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Abstract Body (max. 350 words)

Background: Evidence for restrictive transfusion thresholds has prompted recommendations to order one red blood cell (RBC) unit at a time. Encouraging this practice may improve patient safety and RBC utilization, but manual chart audits to determine practice patterns are labour and time-intensive. Thus, we performed a retrospective cohort study utilizing a transfusion registry derived from electronic health records from four tertiary care hospitals in Hamilton to assess ordering practices and their effect on RBC utilization.

Methods: All inpatients age 18 who received an RBC transfusion from January 1st 2010-2015 were enrolled. Patients admitted with a trauma diagnosis, receiving >5 RBC units within 24 hours, receiving concomitant plasma and/or cryoprecipitate, and those with automatic pre-operative orders were excluded. Two cohorts were defined based on their first transfusion order request: patients who had a single RBC unit order or patients with multiple RBC units ordered. The primary outcome was total red blood cell utilization during hospitalization. Other outcomes included the proportion of patients transfused at different pre-transfusion hemoglobin values (taken within 24 hours) and orders with cancelled units. Data collection was censored at the end of the first hospital admission with RBC transfusion or death.

Results: We enrolled 10,076 patients, where 2,370 and 7,728 patients were in the single and multiple unit cohorts respectively. The total red cell utilization during hospitalization for the single unit cohort was lower compared to the multiple unit cohort (5,381 versus 27,625 units, median 2 units per patient in both cohorts, IQR 1-3 versus 2-4 respectively) (p<0.0001). Transfusion of multiple units occurred 55% of the time when the pre-transfusion hemoglobin threshold was 80 g/L. Multiple unit transfusions were ordered preferentially by hematologists (OR 2.97; 95% CI 2.11-4.18) and cardiovascular surgeons (OR 1.92; 95% CI 1.50-2.45). Ordering data suggests that 9.1% of two unit orders and 33.7% of three unit orders had cancelled units.

Conclusion: Multiple units at a time are ordered frequently and are occur at hemoglobin values above recommended thresholds. Auditing using electronic health records is complementary to manual chart reviews in identifying associations between RBC utilization and clinical services for
targeting quality improvement interventions.
When it comes to cord blood banking, what is the relationship between segments and bag

Submission ID

79

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Abstract Body (max. 350 words)

Background: New NetCord-FACT standards require that cord blood units (CBU) be tested post-thaw. Acceptance criteria include; viabilities for CD45+ and CD34+ cells greater than 40% and 70% respectively, potency confirmed (e.g. colony forming unit (CFU) growth) and proper understanding of the relationship between bag and segments. CBU at CBS Cord Blood Bank (CBB) are cryopreserved in a 25 mL bag along with a series of 4 attached segments. Segment#1 is closest to the bag while segment#4 is the furthest. Segments are used for post-thaw testing and HLA confirmatory typing. The objectives of the study were to test a new developed thaw protocol for post-thaw testing of segments, determine whether CBU would pass new NetCord-FACT standards and investigate the correlation between cord blood in the segments and the bag.

Methods: CBU (n=3) were processed at CBS CBB Ottawa manufacturing facility. CBU bags and segments were thawed in 37°C water bath and diluted (PlasmaLyte-A/4%HSA) 5-fold in 2 equilibration steps over 30 mins, after which an additional 2-fold dilution was done. Viability and potency were measured at 30 mins and 4 hours post-thaw.

Results: Thawed segment #1, #4 and whole bag were analyzed for viability at 30 mins. Viability of CD45+ cells between segment #1 (55.17.5%, p=0.7) and the bag were similar, but viability of CD45+ cells in segment#4 was much lower to that measured in bag (423 vs. 575%, p=0.01). CFU growth also was lowest in segment#4. However, there were no differences in the viability of CD34+ cells between segments and bag (mean of 95%, range 88-98%). Viability of CD34+ cells and CFU potency in bags were stable over 4 hours but significantly reduced for CD45+ cells though it still remained superior to the standard threshold (512%, p<0.05). Total cell counts estimated with segments were similar to that measured in bags. Confirmations of these results with additional units are ongoing.

Conclusions: Our results demonstrate that CBUs thawed with the thaw protocol meet the new NetCord-FACT standards. Our results also suggest that viability of CD45+ cells varies between segments and that segment#4 reflects poorly the viability of CD45+ cells in CBU bag.
2. Scientific

a. Oral Presentations

Improving appropriateness of RBC transfusion for iron deficiency anemia patients presenting to the Emergency Department

*One of top two abstracts

Submission ID

41

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Abstract Body (max. 350 words)

Background: Patients presenting to the Emergency Department (ED) with iron deficiency anaemia (IDA) are under recognized and over transfused. A three month audit of RBC transfusions at Sunnybrook Health Sciences Centre (SHSC) ED conducted in 2013 suggested that 58% of transfusions for IDA were appropriate.

Design and Methods: This is a retrospective quality improvement study assessing the rate of appropriate RBC transfusion in patients with IDA presenting to SHSC ED between April 2014 and December 2015. Only patients transfused by the ED were included. QI interventions included: education session (Nov 2013), presentation of QI project at ED rounds (Jan 2015), grand rounds presentation (March 2015), access to transfusion specialist for guidance (April 2015), emergency medicine podcast (May 2015), development of algorithm on IDA management in ED (April -October 2015), development of ED IDA toolkit (July - Nov 2015). Appropriateness was determined using an algorithm developed by two transfusion specialists with input from ED staff at SHSC. The process measure was monthly IV iron use in IDA patients managed exclusively by ED staff. Balancing measures included use of IV iron as per the algorithm and under transfusion defined as a patient with a hemoglobin < 60g/L who did not receive a transfusion.

Results: Assessment of 168 units transfused by ED over the study period revealed an improvement of RBC appropriateness to 91% (range 50% - 100%). IV iron use in IDA patients increased from only one dose between August and October 2013 to an average of 2.4 per month in 2014 and 4.8 per month in 2015. IV iron use did not follow the algorithm in 22% of cases. Eighteen out of 90 patients with a hemoglobin less than 60g/L were not transfused: 7 declined, 5 were admitted/referred to an inpatient team, 5 were asymptomatic and received IV iron and 1 was symptomatic.
**Conclusions:** An improvement in RBC transfusion appropriateness for IDA in the ED can be achieved and maintained with the implementation of simple educational and practical interventions. Involvement of the users (ED staff) in developing algorithms and ongoing communication between transfusion medicine and ED staff is key. These interventions can be adapted for implementation in other hospitals.
Bacterial Growth in Red Blood Cell Units Prepared with Different Additive Solutions

Submission ID

118

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Abstract Body (max. 350 words)

Background: Most studies of red blood cell concentrates (RBCC) prepared using different manufacturing processes and additive solutions (AS) are focused on changes on the RBC storage lesion and in vitro quality. So far, none of the studies have investigated whether RBCC manufacturing practices affect bacterial survival in contaminated units. Previous studies from Canadian Blood Services (CBS) and Héma-Québec (HQ) suggest that AS might have differential effects on bacterial growth. Thus, this study aims at comparing bacterial growth in RBCC prepared in four AS: SAGM, PAGGSM, AS-1, and AS-3.

Design and Methods: The study was conducted in parallel at CBS and HQ. Three ABO-Rh gender matched CPD whole-blood units were used to prepare three RBCC each suspended in SAGM, PAGGSM and AS-1, respectively. In parallel, one CPD2-RBCC was prepared and suspended in AS-3. Each RBCC was inoculated with one of four bacteria: Klebsiella pneumoniae, Staphylococcus epidermidis, Yersinia enterocolitica or Propionibacterium acnes, at a target load of 10 colony-forming units (CFU/mL) (n=4). On days 7, 14, 21, 28, 35 and 42, RBCC samples were taken to determine CFUs on blood agar. If growth was not detected during storage, at day 42, samples were inoculated in BacT/ALERT 3D culture bottles. The effect of AS and/or gender on bacterial growth will be analyzed once the experimental work is complete.

Results: Results from HQ show that S. epidermidis self-sterilized in all RBCC regardless of the AS. Although K. pneumoniae growth was not detected on blood agar, positive BacT/ALERT 3D cultures were obtained at day 42. P. acnes did not proliferate but survived RBC storage and was detected at concentrations <5 CFU/mL in PAGGSM-RBCC. At day 42, Y. enterocolitica grew similarly in AS-1 and PAGGSM-RBCC (3.3 ± 3.0x10^7 CFU/mL and 2.0 ± 0.8x10^7 CFU/mL, respectively), while a 1-log increase was observed for AS-3-RBCC (1.9 ± 0.5x10^8 CFU/mL) and 1-log decrease was obtained in SAGM-RBCC (2.0 ± 2.1x10^6 CFU/mL). Preliminary data at CBS show similar growth trends for all bacteria.

Discussion/Conclusions: Our results confirm that different AS have a differential effect on bacterial growth in RBCC. The clinical significance of these observations is unknown and merits further
investigation.
Before and After the Gate: Enhancing Detection of Alloimmunizable RHD Types in Child Bearing Age Females

Submission ID

61

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Abstract Body (max. 350 words)

Background: Accurate RHD typing in a child bearing age female (CBAF) establishes who warrants Rh immunoprophylaxis with restrictions to D- components. Historically, D+ status has been defined as ≥2+ reactivity regardless of reagent or platform, conflating with assumptions of wild type configuration and D tolerance. Due to concerns on gel-based overcalls on D typing, we prospectively characterized a cohort of 1000 CBAF for modality-related differences in reaction strengths and the associated odds of ascertaining potential D variants. We had adopted, and now maintain, a precautionary approach which incorporates tube testing after standard gel-based D typing for all gel results <4+. Genotypic adjudication applies to any discrepancy, as well as to a more encompassing gate for suspected weak D (all tube results ≤2+).

Design/Methods: The period before and after the concerted approach to CBAF D-typing was examined. D grouping in gel is automated (Provue), using monoclonal human IgM anti-D (MS-201), MTS Inc. In the enhanced testing era, all CBAF (defined as <45 years of age) with gel D types <4+ undergo parallel tube typing with monoclonal human IgM [MAD2] + polyclonal human serum IgG, (BioClone, OrthoClinical Diagnostics). Discrepancies (by internal modality or against external results), or tube results <3+, trigger a temporary classification as D-negative until genotype rules out a partial D allele.

Results: In the year before the enhanced approach to CBAF D typing (July 2014- June 2015), wherein D variants were suspected exclusively by inter-site discrepancies, 18 D variants were found, with 2 at-risk (alloimmunizable) genotypes. After the enhanced approach (01 Sept 2015 – 31 August 2016), 17 new D variants were found, with 8 (47%) at-risk (alloimmunizable) genotypes. Among these variants, median gel reaction strength (95% confidence interval) was higher in alloimmunization-vulnerable (vs tolerant) genotypes (3+ [2.6-3.2] vs 2+ [1.9-2.4], p=0.027).

Conclusions: Implementing complementary and modality-specific cut-offs for the assignment of D+ status may be worthwhile in CBAF in order to enhance the detection of sensitization-vulnerable variants. Historic modality-independent criteria for D+ status, and/or excess faith in high-strength reads, may miss genotypes at risk of seroconversion, and the larger potential consequence of hemolytic disease of the fetus/newborn.
Early γ-irradiation and subsequent storage of red blood cells in SAG-M additive solution potentiates the storage lesion and propensity to eryptosis

Submission ID
82

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Abstract Body (max. 350 words)

Introduction: Blood components (platelets and red blood cells) that contain low, but viable, levels of lymphocytes may be irradiated to prevent the proliferation of T-lymphocytes which are implicated in the development of transfusion-associated graft versus host disease, a rare but fatal condition. North American blood banking standards permit the irradiation of red cell concentrates (RCCs) at any time up to 14 days after collection and subsequent post-irradiation storage not exceeding their expiry date. A downside to this treatment, however, is the possible negative impact on RCC quality and shelf life.

Design and Methods: In a pool-and-split design, RCCs derived from three ABO-matched whole blood units were exposed to γ-irradiation (25 Gy) and were stored in SAG-M additive solution for 42 days. In vitro quality parameters (supernatant hemoglobin, cytosolic ATP and 2,3-diphosphoglycerate [2,3-DPG]) were examined in the RCCs at 4, 21 and 42 days of storage under blood bank conditions. RCC-derived microvesicles (CD235a events), phosphatidylserine (PS) externalization (annexin V fluorescence), intracellular Ca^{2+} activity (Fluo3 fluorescence) and cell volume (forward scatter) were determined using flow cytometry.

Results: As compared to untreated RCCs, γ-irradiated RCCs showed significantly altered microvesicle generation, supernatant hemoglobin and cytosolic ATP, but not 2,3-DPG, levels after 21-42 days of storage under blood bank conditions. γ-irradiation significantly enhanced intracellular Ca^{2+} activity and cell volume after 42 days of storage. PS externalization was not significantly different in the two study arms. PS exposure was, however, significantly more accentuated in γ-irradiated RCCs (421 days of storage) as compared to control RCCs after energy deprivation in vitro, a pathophysiologic cell stressor.

Conclusions: Early γ-irradiation of RCCs accelerates the red cell storage lesion and enhances the vulnerability to stress-induced apoptotic cell death, which may potentially diminish post-transfusion clinical benefits.
Acknowledgements: This research was supported by the Centre for Innovation of Canadian Blood Services, using resources provided in part by Health Canada, a Department of the Federal Government of Canada (to DVD and WPS) and the Burroughs Wellcome Fund in Innovation in Regulatory Science Award to DVD. SMQ and DC were supported by CBS postdoctoral and graduate fellowship awards, respectively.
GPIbalpha is required for platelet-mediated TPO production from liver and TPO-induced platelet generation from bone marrow

Submission ID
140

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Abstract Body (max. 350 words)

**Background:** Thrombopoietin (TPO) is a hematopoietic growth factor essential for thrombopoiesis. It is generated primarily in liver parenchymal cells with minor amounts produced in other tissues. The clearance of TPO is mainly through platelets and megakaryocytes via c-Mpl-TPO interaction and its subsequent internalization and degradation. Although it was reported that platelets may play a role in TPO production, the mechanism and the key platelet receptor involved in this process is largely unknown.

**Methods and Results:** Interestingly, we observed a 2-3 fold TPO decrease in the blood of GPIb-/- mice compared to syngeneic wild type (WT) and 3/- mice. Similar results were also observed in GPIb deficient Bernard Soulier Syndrome (BSS) patients. Given the enlarged size of GPIba-/- platelets, we investigated whether this is due to increased TPO clearance, and found similar levels of TPO internalization/clearance in WT and GPIba-/- platelets. Next we quantified TPO mRNA and found it
significantly reduced in livers of GPIba-/- mouse. Transfusion of WT, but not GPIb-/- platelets markedly increased TPO levels in circulation and mRNA transcription in the livers of GPIb-/- mice. To determine whether the extracellular portion of GPIb is required for the TPO generation, we utilized IL-4R/GPIb transgenic (Tg) mice in which most of the extracellular domain of GPIb is replaced by IL-4R. We found that the TPO levels in these Tg mice were also low. Similarly, transfusion of WT but not GPIb-/- or Tg platelets significantly improved TPO levels in Tg mice. In vitro studies further demonstrated that co-culturing GPIb-/- platelets with hepatocytes resulted in less platelet uptake and lower mRNA transcription as compared to WT control platelets. Unexpectedly, we found exogenous TPO can induce platelet generation in WT but not in GPIb-/- mice.

**Conclusion:** Our data shows for the first time that GPIb is required for platelet-mediated TPO production in the liver, and is also crucial for platelet generation in bone marrow following TPO stimulation. These data not only provide novel insight into platelet homeostasis, but also the mechanisms and effectiveness of current thrombocytopenia therapies such as TPO mimetics, as well as the mechanism and pathobiology of BSS.
Novel Anti-Fouling Coatings for Platelet Research and Clinical Diagnostics

Submission ID

134

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Abstract Body (max. 350 words)

Background: Platelets play key roles in hemostasis and thrombosis. Fibrinogen (Fg) binding to integrin IIb3 (GPIIbIIa) has historically been considered a requirement for platelet aggregation. Interestingly, we found that platelet aggregation persists even in the absence of Fg and VWF but not IIb3, suggesting unidentified IIb3 ligands are involved. Additionally, ligands of GPIb, another major platelet surface receptor, have not been fully explored. Identification of these interactions remains challenging as many bio-analytical methods suffer from high background signal or false positives due to non-specific binding (NSB) interactions. Furthermore, NSB remains detrimental to many clinical detection methods, such as MAIPA. The development of detection strategies that incorporate anti-fouling (resistance to non-specific interactions) properties is beneficial to the identification of these ligands and the advancement of analytical/clinical detection methods.

Methods: We developed a novel anti-fouling bio-analytical detection strategy for the identification of IIb3 or GPIb interactions. Our strategy is based on a trimethoxysilyl diethylenetriamine (DETA) organic-monolayer (coating) which forms covalent bonds to any hydroxylated (-OH) surface, such as glass, plastics and metals, and facilitates covalent linkage of either IIb3 or GPIb. Both coatings were synthesized on planer (glass slide) and spherical (3 m silica beads) surfaces. Fluorescence spectroscopy/microscopy and flow-cytometry were employed for the detection of binding interactions.

Results: GPIb coated surfaces bound both conformational and linear epitope specific anti-GPIb mAbs. IIb3 coated surfaces bound Fg as well as conformational and linear epitope specific anti-IIb3 mAbs. Furthermore, IIb3 coated beads were incorporated into murine wild-type and VWF/Fg-/- platelet aggregates, demonstrating the interaction with the yet unidentified x-ligand responsible for Fg/VWF-independent aggregation.

Conclusions: These data indicate IIb3 and GPIb adopt ligand binding conformations when immobilized on DETA. Moreover, DETA greatly resists non-specific interactions and maintains a very
low background signal regardless of detection method, even without employing a blocking agent (e.g. BSA). This work presents the first use of anti-fouling organic-monolayer attached platelet surface receptors and demonstrates the enormous potential that these synthetic coatings possess in research and diagnostics. Identification of novel IIb3 and GPIb ligands and evaluation of these coatings for auto- and allo-antiplatelet antibody detection are ongoing.
PATHOGEN-REDUCED PSORALEN-TREATED PLASMA RETAINS ROBUST ACTIVITY AFTER 5 DAYS POST-THAW STORAGE AT 1-6 °C

Abstract Body (max. 350 words)

**Background:** Optimal treatment of massive hemorrhage requires massive transfusion protocols (MTP) and readily accessible red blood cells, platelets, and plasma. Early and aggressive resuscitation with plasma and platelets has been associated with improved patient outcomes. Plasma thawed and stored at 1-6°C for up to 5 days (Thawed Plasma, TP) provides rapid plasma availability in MTP and reduces wastage. Conventional TP, however, carries the risk of window-period and/or emerging pathogen transmission and of bacterial outgrowth during storage. The INTERCEPT™ Blood System for pathogen reduction of platelets and plasma uses a photoactive psoralen (amotosalen) with UVA illumination (psoralen-treated) to cross link pathogen nucleic acids, including viruses, parasites, and bacteria, to prevent replication and infection.

**Design and Methods:** This study was designed to characterize the changes in protein concentrations over a 5 day post-thaw period in psoralen-treated fresh frozen plasma (FFP) and plasma frozen within 24 hours (PF24) intended to be used as readily available components in the treatment of massive hemorrhage. Psoralen-treated FFP and PF24 were thawed after ~3 to12 months of frozen storage and held at 1-6°C for 5 days. Global assessments of coagulation, as well as a range of hemostatic, anti-thrombotic and activation markers, were assessed.

**Results:** Day 5 thawed psoralen-treated FFP and PF24 contained comparable levels of factors II, V, VIII, IX, X, von Willebrands factor: RCo, fibrinogen, ATIII, protein C and protein S as Day 5 TP. Thrombin generation was robust on Day 5 (psoralen-treated FFP = 1,866±402 nM/min; psoralen-treated PF24 = 1,800±277 nM/min). Most factor activities on Day 5, including ADAMTS-13, were > 90% of Day 0 values, except for known labile factors V, VIII and protein S. All units contained >0.4 IU/mL protein S and alpha-2 plasmin inhibitor on Day 5. Global markers, including thrombin-antithrombin complexes, non-activated thromboplastin time and thrombin generation peak height did not indicate excessive activation of the coagulation cascade levels.
**Conclusion:** Psoralen-treated FFP and PF24 offer a pathogen-reduced alternative to conventional TP and demonstrated comparable procoagulant and antithrombotic activity after 5 days post-thaw storage at 1-6°C, offering improving safety from blood-borne pathogens.
b. Poster Presentations

Anaerobic Storage of Red Blood Cells

Submission ID

116

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Abstract Body (max. 350 words)

Background: During storage, red blood cells (RBC) are exposed to an increase in oxidative stress, which might affect their biological properties and their survival when trans fused. New Health Sciences Inc. (NHSi) has developed a novel storage system (Hemanext) that reduces RBC oxidative stress by reducing oxygen and carbon dioxide, aiming at improving RBC metabolism. The purpose of this work is to conduct an operational trial of this technology in routine processing and storage for RBC units stored in SAGM and in PAGGSM.

Methods: ABO compatible Whole Blood Units (WBU) were pooled and split before being treated using the Atreus Whole Blood Processing System (TerumoBCT). Paired RBC units were suspended in either SAGM (n=8) or PAGGSM (n=8) and then leukoreduced. Control and Hemanext RBC samples were taken before and after the O2 reduction process and on a weekly basis until they reach expiration date at day 42. Each sample and its corresponding control were analyzed and compared for Complete Blood Count (CBC), gas panels (tHb, Hctc, sO2, pO2, pCO2, pH, Na+, K+, glucose, lactate), free hemoglobin (Hb), spun hematocrit, ATP and 2,3-DPG.

Results: The Hemanext device reduced O2 levels below 20% SO2 for the entire storage period. The SO2 levels were reduced from 486% to 73% and pCO2 from 709mmHg to 71 mmHg after treatment and SO2 was maintained at 62% until day 42. The hemolysis rate at day 42 was slightly higher for PAGGSM-Hemanext units (0.30.1%) compared to PAGGSM-control (0.20.0%) and was markedly higher for SAGM-Hemanext (0.60.1%) than SAGM-control (0.30.0%). Hemanext storage significantly improved the 2,3DPG levels in RBC units with a maximum at D14 (16.00.5 mol/g Hb in PAGGSM and 11.63.2 mol/g Hb in SAGM vs 1.30.4 mol/g Hb in control).

Conclusions: The Hemanext device allowed anaerobic storage of RBC units, which had significant impacts on multiple in vitro metrics of red cell quality. This study demonstrates that Hemanext-treated RBC units stored in PAGGSM present better overall properties than SAGM at expiration.
Anti-D, Antibody Profiling

Submission ID

121

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Abstract Body (max. 350 words)

Background: When Canadian Blood Services is notified of an apparent anti-D identified in an RhD-negative transfusion recipient the associated donors are further examined. No products from these donors can be released until RhD typing is resolved. All donors are tested with anti-D reagent capable of giving a positive reaction with most weak D cells and partial D Category VI cells. Donor plasma is screened for irregular antibodies and donor units labeled with the antibody(ies) identified. Donor antibodies may be detected in transfused patients when the donor antibody titer is very high and when enhancement methods such as Gel-IAT, PEG-IAT or automated equipment are used. These methods also enhance autoantibodies with mimicking specificities such as anti-LW.

Design and Methods: Retrospective review of RhD-negative donors implicated in suspected RhD alloimmunization of RhD-negative recipients was performed. In 2016, NIRL received notification of 41 donors for investigation of weak D antigen related to 3 RhD-negative recipients with apparent anti-D post transfusion. Donor investigation included: RhD phenotyping with multiple reagents including the weak D test, extended RhCE phenotyping, and investigation for a Del phenotype by adsorption/elution with rare polyclonal anti-D. Donor RHD genotyping was performed if alloanti-D was confirmed in transfusion recipient. Advanced techniques to rule out or confirm anti-G or anti-LW include adsorption/elution, 0.2M DTT treatment or use of cord RBCs.

Results: 27 donors were tested and confirmed RhD-negative. 14 donors have not returned. Antibody investigation on 1 recipient identified anti-C and anti-K; anti-D, anti-G and anti-LW were excluded. Samples from other recipients were not provided.

Conclusions: When RhD negative donors are implicated in D alloimmunisation anti-G, anti-LW and passive anti-D must be considered. Strength of reactivity and antibody titer should be examined. Passive anti-D may be excluded by reviewing donor antibody investigations and repeating patient antibody screening. Donor investigations may include both serological and genotyping investigations. LW antigens are expressed strongly on adult RhD-positive RBCs and weaker on adult RhD-negative RBCs. Cord RBCs, RhD-positive or RhD-negative express LW similarly. Anti-LW may be distinguished from anti-D by testing cord RBCs, or by treatment of RBCs with DTT which denatures LW antigens but not RhD.
Antibody levels on murine erythrocytes are a key factor in inducing antibody-mediated immune suppression to erythrocyte alloimmunization and impacts both erythrocyte clearance and erythrocyte antigen loss

Submission ID

31

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Abstract Body (max. 350 words)

Background: Red blood cell (RBC) alloimmunization can be a serious complication of transfusion or pregnancy causing hemolytic disease of the fetus and newborn (HDFN). Polyclonal anti-D has been used to prevent HDFN and this mechanism has been referred as antibody-mediated immune suppression (AMIS). Although this therapy has been highly successful, the mechanisms of anti-D remain poorly understood. The major theories behind AMIS are based upon erythrocyte clearance, immunological deviation, and antigen (Ag) modulation on the RBC surface. None of the anti-D monoclonal antibodies that have been assessed have been as effective as polyclonal anti-D for AMIS induction. Recent studies have demonstrated that it is possible to recapitulate the anti-RBC polyclonal antibody’s properties using blends of monoclonal antibodies targeting different epitopes. In the present work, we studied the impact of the quantity of antibodies bound on RBC on AMIS induction and their effect on RBC clearance and Ag-loss mechanisms.

Design and Methods: Transgenic HOD mice contain RBC expressing an antigen composed of hen egg lysozyme (HEL), in sequence with ovalbumin (OVA) and the human Duffy transmembrane protein [HOD]. HOD-RBCs labeled with a fluorescent dye (PKH26) were transfused into C57BL/6 mice. After 24h different concentrations of anti-OVA polyclonal antibodies were administered. Mice were bled at 2, 24, 48 and 72h and the percentage of HOD-RBC in circulation and HODAg levels on RBC survival were assessed by flow cytometry. HEL-specific antibody responses were measured by ELISA 7 days after HOD-RBC transfusion.

Results: Anti-OVA IgG when achieving a high level of opsonization of the RBC induced AMIS. High quantities of anti-OVA IgG induced rapid clearance of HOD-RBCs and induced HOD Ag-loss. However, intermedia levels of these antibodies induced partial HOD-RBCs clearance, but complete Ag-loss. In addition, AMIS induced by anti-OVA antibodies showed better correlation with their ability to induce Ag-loss than RBC clearance.

Conclusions: The quantity of antibodies opsonizing an RBC is a key factor to induce AMIS impacting both RBC clearance and Ag-loss mechanisms. These results help explain the superiority of polyclonal antibodies to monoclonal therapeutics for AMIS induction and could influence the development of effective therapies to replace anti-D.
Assessment of the stability of bacterial frozen stocks used in quality control testing procedures

Submission ID
33

Authors/Co-Authors & Affiliations
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Abstract Body (max. 350 words)

Background: The preparation and maintenance of bacterial frozen stocks is an essential practice to perform quality control (QC) testing. At Canadian Blood Services, bacterial stocks are prepared every year for use in various procedures including the QC master lot testing release of BactT/ALERT culture bottles, and the development and validation of new protocols. Although it is known that microbial stocks prepared in 15% glycerol could remain viable for decades when stored at -80°C, stability of bacterial stocks at Canadian Blood Services was initially established with an expiration date of one year. This study was aimed at assessing the stability of frozen stocks over a period of four years as a measure to increase efficiency associated with QC testing practices.

Experimental Design: Aerobic and anaerobic species including Gram positive (Bacillus cereus, Propionibacterium acnes, Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pneumoniae) and Gram negative (Bacteroides fragilis, Klebsiella pneumoniae, Serratia marcescens, and Yersinia enterocolitica) bacteria were used in this study. Bacterial suspensions were prepared by adjusting cultures of each organism in Trypticase Soy broth supplemented with 15% glycerol to a 0.5 MacFarland standard, which corresponds to bacterial levels ranging from $10^6$ to $10^7$ colony forming units/ml (depending on the species). Aliquots of the suspensions were frozen at -80°C, and the initial bacterial load of the suspensions was assessed by thawing an aliquot (up to a week after freezing), and plating the last three serial dilutions on duplicate blood agar plates. The stability of the enumerated stocks was assessed on a yearly basis over four years.

Results: No significant differences in viability or counts for any bacterial species were observed over the four years of testing ($p>0.01$). Furthermore, no differences in the stability of stocks were observed between Gram positive and Gram negative strains, or between aerobic or anaerobic species.

Conclusion: Enumerated bacterial stocks may be stored at -80°C for up to four years, with no significant loss or effect on the bacterial loads or viability. Future implementation of this protocol would improve the efficiency of routine QC protocols involving bacterial testing at Canadian Blood Services.
Cell wall modification during biofilm formation might confer Staphylococcus epidermidis advantageous growth in platelets

Submission ID

22

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Abstract Body (max. 350 words)

Background: Bacterial contamination poses the greatest safety threat to platelet transfusions. Staphylococcus epidermidis, a predominant contaminant, forms matrix-embedded cell aggregates (biofilms) in platelets. Typical biofilm-negative S. Epidermidis strains display a biofilm-positive phenotype in platelets. Bacterial cell wall remodeling occurs during biofilm formation and we hypothesize that peptidoglycan, a major S. Epidermidis cell wall component, is remodeled during platelet storage. This study was aimed at studying changes in biofilm matrix composition and peptidoglycan patterns of S. Epidermidis grown in platelets.

Design and Methods: Three biofilm-positive S. epidermidis (ST10002, AZ39 and AZ22) and a biofilm-negative strain (ST11003) were used herein. Biofilms were grown in glucose-supplemented Trypticase Soy Broth (TSBg) (24h/37C/static) or platelets (5 days/20-24C/agitation). Production of polysaccharide intercellular adhesin (PIA), a polysaccharide-based biofilm matrix, was assayed by immunoblot (N=2). Proteinaceous composition of the S. epidermidis biofilm matrix was evaluated by MALDI-TOF analysis.

Results: In TSBg, a PIA-based biofilm matrix was detected in S. epidermidis ST10002 while a protein-based matrix was present in AZ39 and AZ22. S. epidermidis ST11003 did not form biofilms in TSBg. The four strains were biofilm-positive in platelets and susceptible to proteinase K disruption revealing a proteinaceous matrix. MALDI-TOF analysis of five HPLC peptidoglycan muropeptides from biofilms grown in TSBg revealed that all of them were D-Glu amidated and one was also O-acetylated. Three of these muropeptides, including the amidated/O-acetylated one, were missing in the HPLC peptidoglycan profile of platelet cultures. Selected peptidoglycan muropeptides from biofilms grown in platelets are undergoing MALDI-TOF analysis.
**Conclusion:** Platelet storage induces structural changes in the *S. epidermidis* cell wall and biofilm matrix composition. While amidation decreases the negative charge of the peptidoglycan, increasing antimicrobial resistance, peptidoglycan O-acetilation is linked to pathogenesis. Investigation of bacterial physiological changes induced during platelet storage is important to propose new strategies to reduce bacterial contamination.

**Acknowledgements:** The network Centre for Applied Development (netCAD) for platelet supply.
Combination of liposomes and rejuvenation treatment for minimizing hypothermic storage lesion of red blood cells

Submission ID
83

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: Liposomes have been shown to minimize RBC membrane damage occurring during 42-day hypothermic storage (HS), while rejuvenation solutions have been shown to restore RBC metabolism. This study aimed to evaluate the effect of combining liposomes and rejuvenation treatments on the quality of stored RBCs.

Methods: Five leukoreduced packed RBC units obtained from the CBS netCAD were pooled and split. The units produced were segregated into four experimental groups sham control (S), liposome-treated (L), rejuvenesol-treated (R) and liposome + rejuvenesol-treated (L+R). The pRBCs were incubated for 1 h at 37°C with HEPES-NaCl (sham), liposomes (DOPC:CHOL, 7:3 mol%, 2 mM lipid), Rejuvenesol and liposomes plus Rejuvenesol (1mM lipid). The in vitro quality was accessed by hemolysis, deformability, aggregation, ATP and 2,3-DPG at day 42 HS.

Results: Hemolysis was significantly decreased in all treatments compared to sham control (0.60 ± 0.06%): L (0.53 ± 0.01%, p=0.042), R (0.43 ± 0.02%, p=0.004), L+R (0.48 ± 0.06%, p=0.020). Ektacytometry analysis showed an increase in maximum elongation in R (0.55 ± 0.01, p=0.010) and L+R (0.55 ± 0.01, p=0.010) treatments compared to S (0.53 ± 0.01) but not L (0.53 ± 0.01, p=0.936). RBC rigidity increased in all treatments compared to sham (1.19 ± 0.07): L (1.28 ± 0.06, p=0.025), R (1.44 ± 0.17, p=0.010) and R+L (1.44 ± 0.06, p=0.004). RBC aggregation amplitude was significantly increased by R treatment only (24.07 ± 1.67 vs. 19.12 ± 1.38 au, p=0.004). ATP levels were significantly higher in all treatments compared to sham. The levels of 2,3-DPG were no longer detectable in S and L treatments at day 42. The combined treatment was comparable to R (2.38 ± 3.26 vs. 2.62 ± 2.20 mol/g Hb, p=0.868).

Conclusion: Both rejuvenation and liposome treatments improved the quality of stored RBCs compared to sham control. The combined treatment (L+R) did not have a greater impact in improving in vitro quality of stored RBCs compared to rejuvenation alone. Lipid concentration on the combined treatment was a limiting factor of the study. Further investigation should address whether rejuvenation solutions affect liposomes ability to interact with RBC membranes.

Acknowledgements: University of Alberta, Canadian Blood Services, Biomet.
Comparison of the MTS Anti-IgG Card to the MTS Buffered Gel Card with the 0.8% RESOLVE Panel C Ficin Treated

Submission ID

76

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Abstract Body (max. 350 words)

Introduction: While reviewing our techniques, we noticed a lack of conformity for the identification of antibodies in Gel enzyme (Ficin) technique. We routinely use the MTS Anti-IgG Card (GelIg) card whereas the manufacturers monograph recommends the use of MTS Buffered Gel Card (GelB). However, the monograph also states that antibodies requiring Anti-IgG to be detected will not be detected by the GelB card. Consequently, we decided to validate and compare both cards to determine if our technique needed to be changed.

Conception and Methods: We used plasma samples stored between 2 and 8°C for a maximum of 14 days. The cards were tested in parallel according to the manufacturers’ specifications. The samples were tested in 4 different labs. Our observations were based on the following criterias:

Sensitivity: Strength of reaction
Specificity: Reactivity with the identified antibody
Presence of non-specific reactions

Result: 44 samples were tested including 17 different antibodies. Strength of reaction were between weak and 4+. Some samples could contain more than one antibody.

Sensitivity:
4 anti-K were not found with the GelB card. These antibodies reacted between weak and 2+ with the GelIg card.
7 samples demonstrated lower sensitivity with the GelB cards (reaction between weak and 3+).
Lower sensitivity was observed with the following antibodies: Non-specific (3), anti-D (1), anti-C (2), anti-K (1) and anti-Jka (1).
33 samples showed equal sensitivity between the two cards.

Specificity:
The 4 anti-K not found in the sensitivity analysis also failed the specificity test
1 anti-Jka showed a higher specificity with the GelB card
1 anti-Jka demonstrated a lower specificity with the GelB card
33 samples showed equal specificity between the two types of cards.

Presence of non-specific reaction:
7 samples showed non-specific reactions with the GelIg cards that were not seen with the GelB
Conclusion: In our hands, the GelB cards were not sufficiently sensitive and specific to represent an advantage over the Gellg cards. On the other hand, they did not show non-specific reactions often seen with Gellg cards. Overall, we chose to remain with the Gellg cards despite the presence of non-specific reactions.
Development of biocompatible gold nanosensors for the detection of quality markers and the characterization of blood products

Submission ID

108

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Abstract Body (max. 350 words)

Background: To ensure availability of biological products, blood banks have developed and validated multiple storage conditions for each product line to maximize shelf life and quality. In the case of labile products, their metabolism is known to remain active during storage, leading to storage lesions. microRNAs (miRNAs) levels are modulated by these storage-related damages, which makes miRNAs ideal candidates as potential biomarkers of quality monitoring. Lately, nanoparticles have been widely used and studied for biosensing applications. The objective of this work is to develop a biocompatible gold nanosensor for sensitive, selective and direct detection of biomarkers to assess the quality of blood products to be transfused.

Methods: Gold nanoparticles (GNPs) surrounded by a fluorescent silica shell were prepared using a wet chemistry method. miRNA-223 was chosen as a potential target, since it is strongly expressed in platelet concentrates and its concentration fluctuates according to storage lesions. A custom molecular beacon was designed and used as a probe for the specific detection of miRNA-223 targets. The fluorescent transducer probe was conjugated at the surface of GNPs using an EDC/Sulfo-NHS cross-linking reaction. The hybridization reaction between the target and the probe initiates an energy transfer mechanism which can be recorded by fluorescence emission.

Results: GNPs (49 ± 6 nm) surrounded by a thick fluorescent silica shell (22 ± 2 nm) were prepared and used as nanosensors because of their luminescence properties and long-term stability. Conjugation of the probe onto the nanoparticles was confirmed by fluorescence spectroscopy and microscopy, as well as nanoparticle tracking analysis. The fluorescent response of the molecular beacon was studied and showed a reproducible and linear relationship ($R^2 = 0.97$) with miRNA-223 concentration, down to a 10 nM limit of detection.

Conclusions: Biocompatible fluorescent GNPs were prepared and used as tools for blood product characterization. The conjugation of a molecular beacon at the surface of nanoparticles was achieved and characterized using spectroscopic and microscopic techniques. The functionalization of the probe is still being optimized. The fluorescence response of the molecular beacon was successfully characterized for the detection of a model miRNA target.
Effect of the preprocessing storage temperature on cold blood potency

Submission ID
44

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Abstract Body (max. 350 words)

Background: Umbilical cord blood has been proven to be an important alternative source of hematopoietic stem cells (HSC) for transplantation. Public cord blood banks are operated under guidelines established by national regulatory agencies and many of them obtain an accreditation from Netcord FACT and/or AABB. Despite the standardization of cord blood banking procedures, some parameters such as the preprocessing storage temperature remain unregulated. In many cord blood banks including the Héma-Québec cord blood bank, the cord blood units (CBUs) are kept at room temperature (RT) for up to 48 hours before volume reduction and cryopreservation.

However, a recent study suggested that a preprocessing storage of 72 hours at RT might have deleterious effects on the HSC reconstitution capacity. We thus examined the effect of a preprocessing storage period of 48 hours (in agreement with regulatory guidelines for unrelated CBUs) at RT or 4C on HSC potency in vitro, using the expression of aldehyde dehydrogenase (ALDH) in CD34+ cells as a marker of long-term repopulating cells and the classical CFU assay, and in vivo using the Nod-scid gamma (NSG) mouse model of engraftment.

Methods: CBUs (n=16) were divided into two smaller bags after a small aliquot of blood was taken for initial analyses and incubated for 48 hours at 4C or RT. Aliquots of cord blood were taken at the end of the incubation period. The CD34+ ALDHbr content was determined by flow cytometry and CFU assays were done using Methocult. CBUs were then volume reduced and cells were cryopreserved until their reconstitution potential was assayed in NSG mice.

Results and Conclusion: The results obtained demonstrate that, as recently reported, the CD34+ALDHbr cell content in CBUs correlates well with CFUs. The results also show that the preprocessing storage temperature (RT vs 4C, 48 hours) prior to CBU banking does not significantly affect HSC potency, as evaluated in vitro by CD34+ALDHbr and CFU assays and in vivo, as evaluated in the NSG engraftment assay. ¹ I. Louis et al, Transfusion 2012;52:2401 ² Storms et al, Blood 2005, 106:95 ³ Shoulars et al, Blood 2016, 127:2346
Enhancing Blood Donor Skin Disinfection Using Natural Oils

Submission ID

24

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Abstract Body (max. 350 words)

Background: Effective donor skin disinfection is essential to prevent bacterial contamination of blood components. Platelet concentrates are the most susceptible product to contamination, mainly with skin flora bacteria such as *Staphylococcus epidermidis*. We have proved that cell aggregates of *S. epidermidis*, known as biofilms, are resistant to complete inactivation by the two skin disinfectants currently used at Canadian Blood Services, 2% chlorhexidine-gluconate (CHG) and 70% isopropyl alcohol (IPA). Essential oils have been shown to synergistically enhance the antibacterial activity of CHG. The aim of this study was to test plant-extracted essential oils in combination with CHG or CHG-IPA for their ability to eliminate *S. epidermidis* biofilms.

Design and Methods: Essential oils extracted from *Artemisia herba-alba*, *Lavandula multifida*, *Origanum marjoram*, *Rosmarinus officinalis*, and *Thymus capitatus* were tested for skin irritation in a rabbit model. *S. epidermidis* biofilms were exposed to each oil alone, in combination with CHG or CHG-IPA. Then, residual viable cells of *S. epidermidis* were quantified by serial dilutions, plating and colony counting. Oil qualitative and quantitative compositions were analyzed using gas chromatography-mass spectrometry.

Results: Rabbit skin irritation was observed with all oils at concentrations higher than 30% and therefore concentrations of 10%, 20%, and 30% were chosen for the anti-biofilm assays. All oils, with the exception *O. marjoram*, had a significant anti-biofilm activity at the three tested concentrations (p<0.05). Interestingly, *L. multifida* was the only oil with a synergistic effect with CHG, and had the highest anti-biofilm activity when combined with CHG-IPA (p = 0.0051). Gas chromatography-mass spectrometry revealed that the main component of the *L. multifida* oil (45.1%) was linalool, a natural occurring terpene alcohol found in plants. Skin penetration and toxicity assays of the *L. multifida* oil and linalool should be performed to demonstrate their suitability as human skin disinfectants.

Conclusion: The plant-extracted *L. multifida* oil and its main component linalool increased the anti-biofilm activity of CHG-IPA. Upon further validation, these components could potentially be used to improve blood skin disinfection.
Acknowledgements: Canadian Blood Services and Health Canada and the High Ministry of Education Saudi Arabia for funding.
Evaluation of Beckman Coulter StatSpin Centrifuges For Supernatant Hemoglobin Determination in Whole Blood and Red Cell Concentrates

Submission ID

141

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Abstract Body (max. 350 words)

Background: Beckman Coulter (BC) StatSpin Express centrifuges are compact with pre-set centrifugation speeds/times available for rapid processing in clinical settings. It is unknown to what degree the pre-set programming impacts separation of free hemoglobin (Hb) and extracellular vesicle bound Hb within the supernatant fraction, from which aliquots are removed for plasma hemoglobin or hemolysis testing. A change in sedimentation of the sample could artificially increase or decrease the supernatant Hb (sHb). This study evaluates the effect of pre-set BC StatSpin Express 3 and 4 centrifuges on sample preparation for sHb analysis.

Methods: One CPD/SAGM LR Red Cell Concentrate (RCC) was stored to day 27 and one CPD whole blood (WB) unit was stored to day 7 and 22. At each test point for each unit, fourteen BD VacutainerTMK3EDTA tubes were filled with 7 mL samples. Two samples were prepared using each pre-set program on the StatSpin Express 3 and 4, and a conventional centrifugation program (Eppendorf 5810R, 2200xg at 4C for 10 min). Each tube was visually inspected before a supernatant aliquot was removed to measure sHb using the HemoCue Plasma/Low Hemoglobinometer.

Results: No significant visual differences between tubes spun using different pre-set programs were observed; excluding RCC samples using the StatSpin Express 4 which did not have clear cell interfaces. Ultimately, this did not affect sHb values. StatSpin 3 and 4 RCC samples at the different settings had mean sHb of 0.6 to 0.8 g/L, which was not significantly different (p=0.07) than those spun with the conventional centrifuge (mean=0.7 g/L). StatSpin 3 and 4 WB samples at the different settings had mean sHb of 0.4 to 0.5 g/L (day 7) and 0.7 to 0.9 g/L (day 22), which was not significantly different (p=0.29, p=0.26) than the conventional centrifuge (mean=0.5 g/L, mean=0.8 g/L).

Conclusions: BC StatSpin Express 3 and 4 centrifuges used at any of the evaluated manufacturer pre-set programs are suitable for separating RCC and WB to measure sHb when a 7 mL volume is
prepared. However, further testing is required to validate the pre-set programs for measurement of other supernatant components and volumes.
Evaluation Of Platelets In 100% Plasma Treated With Amotosalen-UVA

Submission ID

51

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Abstract Body (max. 350 words)
The INTERCEPT Blood System for platelets is FDA approved for the ex vivo preparation of pathogen-reduced apheresis platelet components (PC) to reduce the risk of TTI, including sepsis, and to potentially reduce the risk of transfusion-associated GVHD. The initial FDA licensure was for INTERCEPT treatment of PC suspended in plasma and platelet additive solution (PAS)-3, collected on the Amicus separator. The label was expanded in 2016 to allow for INTERCEPT treatment of PCs suspended in 100% plasma, collected on the Trima separator. This in vitro study was performed to support a US label extension for apheresis platelets in 100% plasma.

The objective of this prospective, multi-center, in-vitro, non-inferiority study was to evaluate the Day (D) 5 pH and platelet dose of INTERCEPT platelets suspended in 100% plasma.

Apheresis donations (n=425) were collected using the Trima (Terumo BCT), 61.2%, and Amicus (Fenwal Inc.), 38.8%, separators. Input PCs containing an average of $4.9\pm1.310^{11}$ platelets, in 364±37mL of plasma, were treated by the end of D1 using the small volume (SV), large volume (LV) or Dual Storage (DS) INTERCEPT processing sets. Samples were collected from the input PCs and from components post-treatment and D5 post-donation. The acceptance criteria for the study were (1) the INTERCEPT pH failure rate on D5 is not inferior to the historical control failure rate of 13/668 (approximately 1.946%) using a non-inferiority margin of 3% at the 2-sided 0.05 alpha level and (2) at least 75% INTERCEPT PCs contain 310$^{11}$ platelets with 95% confidence.

D5 INTERCEPT PCs in 100% plasma contained, on average, 3.8± 0.9 platelets in 301±64mL. The dose and volume recovery post the INTERCEPT process were 86.8±4.8% and 92.5±1.8%, respectively. The mean Day 5 pH was 7.1±0.2 with 461 of 464 components having a pH ≥ 6.2.

INTERCEPT-treated PCs met the US CFR requirements for Day 5 pH and dose. Furthermore, non-inferiority between the Day 5 pH failure rates (13/668) of INTERCEPT platelets and Historical Controls (Tudisco et al, 2005) was achieved.
Evaluation of the functional properties of buffy coat-derived monocytes for monocyte monolayer assay

Submission ID

109

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Abstract Body (max. 350 words)

Introduction: Current clinical application of monocyte monolayer assay (MMA) to predict haemolytic significance of red blood cell (RBC) alloantibodies require that the assay be performed with fresh blood monocytes. This study developed protocols for the isolation and cryopreservation of monocytes, then compared the performance of buffy coat-derived monocytes with peripheral blood monocytes with regard to the ability to phagocytose sensitized RBCs and secrete cytokines upon stimulation with lipopolysaccharide (LPS) in-vitro.

Materials and Methods: Peripheral blood mononuclear cells (PBMCs) were isolated by Histopaque-10771 density gradient (Sigma). Pooled buffy coat PBMCs were suspended (1:1) in cryopreservation media, (RPMI-1640: fetal bovine serum (FBS): dimethyl sulfoxide (DMSO), 2:2:1) and aliquots frozen to –80°C before transfer to liquid nitrogen storage. The cells membrane integrity was determined by trypan blue exclusion. PBMCs were cultured on coverslips treated with poly-L-lysine solution and the resulting monocyte monolayers incubated with either 5% anti-D-sensitized RBCs or LPS. Phagocytic index (PRBC) was determined microscopically (number of phagocytosed RBCs/ 100 monocytes) whereas cell supernatants were analyzed for cytokines using multiplex fluorochrome technique.

Results: Our protocol consistently yielded over 60% PBMC isolation (buffy coats; 67 ± 6%, peripheral blood; 76 ± 8%) with low contamination (RBCs 5%, platelets < 15%, neutrophils 5%). Recovery of PBMCs post-wash was constantly above 80% (86.4 ± 4.7%). The average monocyte ratio increased from 7 ± 2%, 29 ± 5% and 93 ± 2% before isolation, post-isolation and post-adhesion respectively. Freshly isolated PBMCs were 100% viable whereas frozen PBMCs showed 93.5 ± 1.2% viability. Cryopreserved monocytes resulted in a phagocytic index of 79.6 ± 5.9% compared to both fresh buffy coat (PRBC; 76.7 ± 10.9%) and peripheral blood monocytes (PRBC; 82.4 ± 10%). Significantly increased secretion of TNF-α, IL-8, IL-1β, IL-6, MIP-α and MIP-β from cryopreserved buffy coat monocytes was observed compared to both fresh buffy coat and peripheral blood monocytes.

Conclusion: We demonstrate that monocyte isolation and cryopreservation does not affect the viability and phagocytosis ability of monocytes. However, cryopreserved buffy coat PBMCs showed up-regulated cytokine secretion pointing out that cryopreservation could modulate various genes.
involved in cytokine production.

Acknowledgments: University of Alberta, Canadian Blood Services.
Hemovigilance Monitoring of Septic Transfusion Reaction (STR) Risk with the INTERCEPT Pathogen Inactivation and Large Volume, Delayed Culture Platelet Bacterial Protection Systems

Submission ID
88

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Abstract Body (max. 350 words)

Introduction: Amotosalen/ultraviolet A (UVA) light (INTERCEPT Blood System, Cerus Corporation) pathogen reduction (PR) and delayed, large volume, bacterial culture with the BacT/ALERT System (DLVBC) (BioMerieux, Inc) represent respective best-in-class systems to reduce the risk of septic transfusion reactions (STR) due to platelet concentrates (PC). Where implemented, hemovigilance (HV) programs continue to receive reports of suspected STR, most of which have low imputability as other causes are more likely or insufficient information is available to impute system failure.

Methods: United Kingdom, French, Swiss, and Belgium HV reports, and Cerus Corporations adverse event records were reviewed to assess the residual risk and imputability of STR with amotosalen/UVA-treated or DLVBC-screened PC.

Results: Approximately 1.35 million DLVBC-screened and ~2.3 million amotosalen/UVA-treated PC were distributed. No septic fatalities were reported with either technology. The French, Belgium and Swiss HV programs monitored >2.83 million conventional, non-DLVBC-screened PC and recorded 58 STR and 9 fatalities. Concurrently, zero definite and 2 possible STR were reported with 548,915 amotosalen/UVA-treated PC, significantly fewer than with conventional PC (20.3 STR per million vs. 0.0 per million, P<0.05). One definite, 1 possible, 7 undetermined/indeterminate non-fatal STR and 5 contaminated near miss PC were reported with 1.35 million DLVBC-screened PC between 2010 and 2015, for a reduced false-negative rate compared with the prior five years (3.7 STR per million vs. 16.3 per million, P<0.05). HV programs highlight a major weakness for reporting STR. Stringent criteria are used to determine definite imputability, including evidence of patient infection, PC contamination and irrefutable evidence of a donor source, with confirmation of strain identity. Reports with incomplete investigations are considered undetermined or indeterminate, or possible sepsis. Some of these cases are almost certainly due to bacterial contamination of PC.

Conclusion: Best-in-class pathogen reduction and bacterial culture systems reduce STR risk, although underreporting and inadequate clinical data may result in underestimation. Investigation of suspected STR should include Gram stain and culture of the residual PC and rigorous follow-up of the donor, co-components and recipients in order to prove causality.
Hepatitis E Prevalence in Canada - a Large Blood Donor Survey

Submission ID

19

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Abstract Body (max. 350 words)

Background: Hepatitis E (HEV) is a non-enveloped RNA virus which is a common cause of infectious hepatitis in developing countries. The illness is similar to hepatitis A both in transmission (fecal-oral) and in symptoms. Most infected individuals recover completely, but immunocompromised transfusion recipients may develop chronic hepatitis. Formerly thought to be a disease of travelers, HEV is increasingly recognized as an endemic zoonotic illness in developed countries. Aside from a previous, limited prevalence survey carried out at Canadian Blood Services (CBS) and HemaQuebec (HQ), this is the first large national survey in Canada.

Design and Methods: In collaboration with HQ and the American Red Cross (ARC), samples from approximately 50,000 whole blood Canadian blood donors are being collected. Clinics are randomly selected and all donations from selected clinics with available plasma samples are tested at the ARC laboratory in Gaithersburg, MD, using the cobas HEV (ID-NAT) Test on the cobas 8800 system. All NAT-reactive donors will be notified by letter, deferred from donating for 6 months and in-date products collected from the donor, and any frozen red blood cells or plasma from the previous 6 months will be destroyed. Recipients will be traced in the event of any products transfused in the previous 6 months.

Results: As of December 14, 2016, 12,969 samples (7,264 CBS and 5,705 HQ) have been tested. All were HEV NAT negative. It is anticipated that final results of the study will be available by the spring of 2017.

Discussion /Conclusions: A previous HEV-RNA prevalence study of 14,000 donors found no donors posing risk for HEV transfusion transmission to recipients in Canada, but it did not include donors from all areas in Canada and the larger sample size of the present study is required to better define the risk. Based on the previous study, with a seroprevalence of 5.6%, it is evident that donors have been exposed to HEV, either through travel or endemically in Canada. Once completed, this study will inform transfusion policy as this virus of emerging importance to transfusion medicine is monitored.
Host Coagulation Initiated on the Virus Surface

Submission ID
69

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Abstract Body (max. 350 words)

Background: News reports of dengue (DENV), Zika, chikungunya, and Ebola infections are reminders that viruses are a prevalent threat to both healthcare and blood collection systems. To address the lack of defences against these and other emerging pathogens, we hypothesized that many viruses have common host-derived constituents within the surrounding membrane bilayer, termed envelope. To explain numerous virus-hemostatic disease links, we previously showed that the envelope of three herpesviruses acquire tissue factor (TF) and anionic phospholipids (aPL) from the host, both vital in physiological blood coagulation. Viral TF and aPL accelerate the activation of clotting factor (F) X to FXa by FVIIa, leading to clotting and cell signaling. Using herpes simplex virus type 1 (HSV1) as a model virus, our lab has shown that both in vitro and in vivo infection is inhibited when the virus lacks TF. Furthermore, HSV1 has evolved to modulate TF function through virus-encoded glycoprotein C (gC). Our current objectives are to: a) determine if other enveloped viruses obtain TF and/or aPL; and b) dissect the involvement of viral TF/gC on virus-mediated clotting.

Methods: TF+/TF-HSV1 variants and DENV propagated in cell cultures were purified and characterized. Immunogold electron microscopy was used to simultaneously visualize TF, aPL and a virus-encoded marker on the virus surface. Plasma clotting induced by HSV1 was characterized in human plasma. FX activation by virus and the effect of solublized gC (sgC) was followed in a FXa chromogenic assay.

Results: Individual HSV1 and DENV particles incorporated TF and aPL into their envelope. Viral TF and gC were required for optimal FX activation, and TF was essential for gC-mediated enhancement. This was confirmed using purified membrane-bound TF, in the presence or absence of sgC. In plasma, gC enhanced TF-dependent clotting induced by HSV1, which was mitigated by an alternative FX-activating clotting pathway.

Conclusions: For the first time, enveloped viruses from distinct families are shown to acquire the host coagulation initiating factors, TF and aPL, supporting the idea that targeting viral TF may facilitate broad-spectrum anti-viral development. Virus surface TF and aPL may explain the correlations to a variety of hemostatic imbalances.
How mass-scale red cell genotyping of blood donors is helping fulfill the demand of antigen-matched blood: our strategy.

Submission ID

74

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Abstract Body (max. 350 words)

Hema-Quebec faces an increasing demand for antigen-matched blood units for ongoing erythapheresis in anaemia patients, as well as punctual demand for ethnically diversified recipients. The supply of these units depends on our capacity to forecast and maintain a versatile inventory. Over the last few years, the genotypes and phenotypes requested by the hospitals have become increasingly complex. This required diversity exposes our reference laboratory to unnecessary thawing of rare blood units or worse, the incapacity of filling an urgent order. The implementation of mass-scale red cell genotyping of our blood donors using a specific selection algorithm is aimed at increasing our capacity to satisfy the hospitals needs regarding particular, complex or rare blood groups. In order to match our inventory with the hospital requirements, our selection algorithm allows for a selection of all ABO-Rh groups for black donors, as well as O and A groups for non-Caucasian donors. Every selected donor has given blood at least three times in the last 12 months and has no known genotypes on files. Since June 2016 and up to this day, using the ID CORE XT platform with the Luminex xMAP technology, we have genotyped a total of 748 donors. At maturity, following our ramping up and process optimization, we expect to genotype 5000 donors per year, out of approximately 326,000 total annual donors (based on 2015-2016 data). While our strategy have been helping stock blood units with useful common combinations, it also allowed us to stock numerous rare units, such as 18 hr⁺,+w/−, 10 hr⁺, 7 partial c, 5 partial C, 3 k−, 2 Kp(b−), 3 Yt(a−), 2 U var, 2 U- and 2 Lu(b−), 2 Js(b−), 1 Jo(a−), 1 Hy− and 1 Co(a−). In summary, it is clear that most of the operating blood banks face new challenges regarding antigen-matched blood units in regard to rarity and ethnical diversity. These challenges must be addressed with innovative donor recruitment strategies, strategic testing and characterization, and screening for high demand phenotypes and genotypes. We believe that mass-scale red cell genotyping of blood donors constitute a great tool to address these challenges.
Impact of additive solution on the quality of red blood cell concentrates derived from whole blood riboflavin/UV light treatment

Submission ID

68

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Abstract Body (max. 350 words)

Background: It is well accepted that pathogen inactivation (PI) has both pros and cons: improvement of blood product safety by inactivating a variety of pathogens vs. quality impairment of pathogen-reduced products. Recently, efforts have been aimed at understanding the molecular mechanisms triggered by the PI in order to modulate the process to improve blood component quality. Here, the impact of the RBC additive solution on the quality of red cell concentrates (RCCs) derived from WB riboflavin/UV light treatment was evaluated.

Design and Methods: Two ABO-matched whole blood units were pooled and split into two identical units which were treated with riboflavin and UV light (Mirasol technology). The RCCs were produced by the buffy coat method in SAG-M or AS-3 additive solution, respectively, and RCC quality was assessed on days 7, 14, 21, and 42 of storage by measuring metabolic parameters, hemolysis development using the Harboe method, osmotic fragility reported as the sodium chloride concentration that produced 50% hemolysis (mean corpuscular fragility; MCF) as well as the supernatant levels of potassium and microvesicles using a potassium electrode and flow cytometry against 1,000 control beads, respectively. Four independent repeats were carried out.

Results: Data obtained in the RCC in SAG-M derived from whole blood PI treatment were similar to results published before; however, RCCs produced in AS-3 exhibited a significant (p<0.01) 4.5-fold reduction of hemolysis development on day 42. This AS-3 effect was reflected in a significantly (p<0.01) reduced release of microvesicles showing a 5- and 15-fold difference on day 21 and 42, respectively, between SAG-M and AS-3. Similarly, the potassium levels in the supernatant decreased about 1.5-fold (p<0.05) compared to the SAG-M units. A significant (p<0.05) improvement of membrane integrity expressed by the mean corpuscular fragility at day 42 of storage further supported the hemolysis data. Metabolic parameters such as pH, glucose and lactate were not impacted by the choice of additive solution.

Conclusion: Replacement of SAG-M with AS-3 significantly improved the RCC quality upon whole blood PI treatment suggesting a protective mechanism of AS-3 to the red cell membrane making it a
promising solution for whole blood riboflavin/UV light PI.
Increased proliferation and maturation of erythroid progenitors treated with hemin

Submission ID

122

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Abstract Body (max. 350 words)

Human hemin, the oxidized form of heme, is a therapeutic agent approved as a clinical treatment for acute attacks of porphyria, commercialized as Normosang and Panhematin. While the molecule has relatively well described stimulatory effects on erythroid progenitors, we are interested in understanding the underlying mechanisms of such pro-proliferative and differentiating effects that could perhaps support a larger spectrum of clinical applications.

We first started to test the activity of porcine BioXtra hemin on the K562 erythroleukemia cell line. As expected following the treatment of K562 cells with 30M of hemin, we observed an increase of the red pigment of the cells, noticeable following a simple cell centrifugation, consistent with differentiation towards the erythroid lineage and accumulation of human hemoglobin. Interestingly, a decrease in cell proliferation was also observed following treatment.

We then tested the effect of a hemin treatment on the proliferation and differentiation of cord blood CD34 hematopoietic stem cells. We first observed increased median fluorescence intensity (MFI) of the CD235 marker on cells treated with 30M hemin BioXtra compared to untreated controls, through flow cytometry analysis. Moreover, the number of total and CD235+ expressing cells treated with 30M hemin was increased by 8.1 and 9.7 fold, respectively, compared to controls, after 25 days of culture. Interestingly, the pro-proliferative effect was noticeable from the 14th day of culture. These results indicate a positive effect of hemin on erythroid progenitor cells maturation and expansion.

These results, combined with recent clinical evidence, suggest that better understanding of hemin action at the cellular level might benefit other classes of patients as well as potentially complement the development of in vitro-derived blood substitutes.
Insulin-like growth factor-2 released by osteoblasts promotes the growth of cord blood cells

Submission ID
37

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Abstract Body (max. 350 words)

Background: Expansion of cord blood (CB) hematopoietic stem and progenitor cells (HSPC) is investigated as a mean to accelerate engraftment following HSPC transplantation. Serum free medium (SFM) conditioned with mesenchymal stromal cell-derived osteoblasts (OCM) increases expansion of CB CD34+ cells and progenitor 2-fold vs. control SFM (Dumont et al., 2014). The growth factors responsible for OCM activities are unknown. Herein, we investigated the implication of insulin-like growth factors (IGF-I, -II) on the growth promoting activity of OCM.

Design and Methods: Q-PCR assay was used to measure IGFs expression in osteoblast and mesenchymal stromal cells (MSC). The functional contribution of IGFs to the growth promoting activities of OCM on CB cells was investigated by inhibition of IGF-1 receptors with AG-1024 (0-10 uM).

Results: Q-PCR revealed a large increase in the relative expression of IGF-II in osteoblasts by day 4 of osteogenic differentiation, compared to MSC (100.2 ± 66.9, n = 2), whereas there were no notable changes in IGF-I expression. IGF-II mitogenic activities are largely mediated through the activation of the tyrosine kinase receptor IGF-1R, which can be inhibited in culture with the selective kinase inhibitor AG-1024. Addition of AG-1024 reduced cell growth in dose-dependent manner in both SFM and OCM cultures (p<0.05). However, reductions in OCM cultures were more pronounced with preliminary results revealing a 25.6 ± 8.2% (meanSD) decrease in expansion of total cells vs. 17.4 9.6% for SFM control (n=3). Production of immature CB CD34+/CD45RA- cells was also significantly reduced in SFM (36.8 ± 3.6%, p<0.05) and OCM (43.2 ± 8.5%, p<0.05) cultures treated with AG-1024.

Discussion: Our results indicate that IGF-1R signaling is important for optimal growth of CB cells even in SFM cultures. IGF-2 released by osteoblasts in OCM may be partially responsible for the growth promoting activity of OCM on UCB cells. We are currently investigating the levels of IGF-2 in OCM and whether the increased cell growth seen in OCM is due to increased level of beta-catenin downstream of IGF-1R. Such finding would provide a molecular mechanism explaining how IGF-2 present in OCM, partially mediates the survival and proliferation of CB cells.
Loss of hematopoietic stem cell activity in cord blood units due to processing delay could impair engraftment in patients

Submission ID
95

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: Cord blood (CB) hematopoietic stem cells (HSC) are a curative treatment option for many patients. CB units are typically stored at room temperature (RT) prior processing and must be cryopreserved by 48 hrs post-collection. The impact of such delays on HSC function is unclear. The main hypothesis is that extended delays reduce the potency of CB due to loss of HSC activity. We set to test this hypothesis through serial transplantation and limit dilution (LD) transplantation assays in immunodeficient mice.

Study design: CB units were split with one half processed immediately (baseline 8-17 hrs) and the second after storage at RT for 40-44 hrs. Units were processed into buffy coat following standard banking procedures. Thawed CB cells were transplanted into NSG mice to track their engraftment activities. Serial transplantation (3 donors tested) was performed to test the self-renewal activity of HSC, and LD assay (2 donors) was used to estimate the frequency of bone marrow (BM) engrafting cells.

Results: Analyzes of human chimerism in primary serial transplants revealed a reduction in short-term platelet (p=0.11, n=3) and leucocyte (p<0.001) engraftments. This deficits accentuated over time as supported by lower levels of platelets (175 ± 109 vs. 380 ± 153 hPlts/μL, p=0.17), leucocytes (10 4% vs. 17 8% CD45+ cells, p=0.06) and BM chimerism at 16-18 weeks (49 ± 10% vs. 59 ± 6% CD45+ cells, p=0.17). Strikingly, BM engraftment in secondary recipients was even more perturbed in stored group (2 ± 2% CD45+ cells vs. 23 ± 17%, p<0.05), indicative either of impaired HSC self-renewal activity and/or reduced number of HSC. LD transplantation assays revealed large reductions in the net number of human platelet engrafting cells in stored units (74 ±12% reduction vs. baseline, p=0.004) and in the net number of Scid repopulating cell (55 ± 38% reduction, p=0.23).

Conclusion: Human platelet, leukocyte and BM engraftment were reduced following prolonged storage of CB before processing. The serial and LD transplantation assays demonstrated that this is the result of loss of HSC activity and HSC numbers. These results warrant stricter storage guidelines since prolong processing delays could contribute to impaired engraftment in patients.
MODELLING THE IMPACT OF EXTENDED SHELF-LIFE PLATELETS IN CANADA

Submission ID
38

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Abstract Body (max. 350 words)

Background: Platelets distributed to hospitals in Canada (excluding Quebec) have a shelf-life of five days to minimize the risk of transfusing a contaminated unit. Shelf-life may, however, be extended to seven days with enhanced bacterial testing. Canadian Blood Services (CBS) has developed a plan to introduce seven-day shelf-life for platelets. Enhanced bacterial testing required as part of this program, however, will increase the cost of producing platelets. These additional testing costs may be offset through lower product wastage. Thus, we present a study to determine the end-to-end wastage rates for platelets across the blood supply chain.

Design and Method: A simulation model of the platelet supply chain was created. The model includes all CBS production centres, as well as 288 hospitals that received platelets in 2015/16. The simulation model mimics the flow of platelet products from collection through testing and distribution at CBS and then onto hospitals where platelets are stored and either transfused or outdated. The model was validated against historical data. It was then modified to simulate a shelf-life of seven days for platelets. A set of experiments was conducted to evaluate the impact of extended shelf-life platelets on product availability and wastage rates.

Results: Simply extending the platelet shelf-life from 5 to 7 days will result in a 30% reduction in wastage, while maintaining current availability. Further decreases to product wastage can be obtained if:
1. Collections are modified to ensure that increased units are available for distribution on Mondays and Tuesdays;
2. Platelet testing is completed within 48 hours of collection;
3. Platelet production is adjusted so that collections turned into platelets more closely match the ABO/Rh profile of units demanded by hospital customers;
4. Product substitution for platelets is permitted at both hospital transfusion locations and CBS distribution sites.

When extended shelf-life platelets are adopted, along with changes to the operational elements of the platelet supply chain, reductions in product wastage of between 40% and 70% can be anticipated.

Discussion/Conclusions: There are operational benefits to be gained from extended shelf-life platelets. However, extended shelf-life platelets are best optimized through coordinated efforts to streamline the supply chain.
New Bacterial Detection Algorithm Supports Extension of Platelet Storage from 5 to 7 Days at Canadian Blood Services

Submission ID

21

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Abstract Body (max. 350 words)

Background: In anticipation of extending platelet shelf-life from five to seven days, Canadian Blood Services will be implementing a new bacterial testing algorithm. This spiking study was aimed at evaluating whether bacterial detection is improved when platelet screening with the BacT/ALERT system is performed at 36 or 48h post blood collection instead of 24h as currently required. Enhancing bacterial detection with the addition of an anaerobic culture bottle and a 6h post-sampling quarantine was also assessed.

Design and Methods: Five bacteria, including four aerobes (Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae and Serratia marcescens) and one anaerobe (Propionibacterium acnes) were used herein. Groups of four 7-8 day old platelet pools (two for P. acnes) were tested for sterility and were inoculated at target bacterial loads of 0.003-3 colony forming units (CFU)/ml, followed by incubation under standard conditions for 7 days (N=4). At 24, 36, and 48h post-inoculation, and every 24h thereafter, 8-ml samples were injected into a BacT/ALERT aerobic and an anaerobic culture bottle. Samples were also taken at each testing time to determine bacterial loads. Positive bottles were subcultured to confirm the identity of the inoculated species.

Results: Positive culture results were obtained with fast growing aerobic bacteria (e.g., K. pneumoniae) at loads 0.004 CFU/ml when sampled at 24h post-spiking. Importantly, pools inoculated with slow growing bacteria (e.g., S. epidermidis) at initial levels <0.02 CFU/ml were only captured with sampling performed at 36h, or 48h, or 3 days post-spiking. Also notably, 24h platelet cultures inoculated with 0.04 CFU/ml of K. pneumoniae were captured within the 6h post-sampling quarantine. Using anaerobic bottles allowed detection of P. acnes and showed a trend towards faster detection of two aerobic bacteria. However, anaerobic cultures had a false positive rate of 0.9%.

Conclusions: A new testing algorithm with delayed sampling and a 6h post-sampling quarantine, along with increased sampling volume, will improve platelet safety and supports the extension of platelet shelf-life to 7 days at Canadian Blood Services. Very low bacterial levels could still be missed however with platelet sampling at 36 or 48h.

Acknowledgements: Volunteer donors and Canadian Blood Services Sites for platelet supply.
Novel Silencing JR/ABCG2 Alleles Resulting in a Jr(a-) Phenotype

Submission ID

119

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Introduction: Jr is a high prevalence antigen in the JR blood group system occurring in >99% of the general population. The Jr antigen may cause transfusion reactions and hemolytic disease of the fetus and newborn. There are >20 ABCG2 null mutations resulting in the Jr-null phenotype. Family studies were performed after anti-Jra was detected during prenatal screening of a Pakistanis woman. Two different novel silencing mutations not previously reported were discovered.

Design and Method: The propositus and her brother’s red cells were phenotyped with unlicensed anti-Jra antisera by the indirect antiglobulin test and prenatal screening was performed by polyethylene-glycol (PEG) indirect antiglobulin test and gel solid phase (GEL-IgG) testing. Genomic DNA was isolated and JR/ABCG2-coding exons and flanking regions were amplified and sequenced as previously described. Briefly, fragments encompassing exons 4, 5, 7, 9 and 13 of ABCG2 were amplified by polymerase chain reaction (PCR) using target specific primers. Traditional Sanger methods were then used to sequence amplicon libraries and sequencing results were compared to reference libraries/SNP databases.

Results: The propositus had anti-Jra confirmed in her plasma and she and brother 1 were shown to be Jr(a-) by serological methods and genotyping. Brother 2 was shown to have weak Jr(a) expression by serological methods. Amplification and sequencing of JR/ABCG2 exons 4, 5, 7, 9 and 13 showed the following changes in the propositus and brother 1: Heterozygous for insertion of an A at c.420 in exon 5 resulting in a frameshift and premature stop codon and heterozygous for deletion of TA at c.986 in exon 9 resulting in a frameshift and premature stop codon. Brother 2 showed no change in exon 5 and was heterozygous for deletion of TA at c.986 in exon 9 resulting in a frameshift and premature stop codon.

Conclusions: Novel JR/ABCG2 alleles harboring 2 different silencing mutations has been identified in a prenatal patient and in two of her siblings. The JR/ABCG2 genotype: ABCG2*01N.420_421insA/*01N.986_987delTA results in a predicted Jr(a-) phenotype. This family study identified a donor compatible with this prenatal patient and a rare Jr(a-) donor for enrollment in the Canadian Blood Services rare donor program.
Platelet desialylation correlates with efficacy of first-line therapies for immune thrombocytopenia

Submission ID

63

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Abstract Body (max. 350 words)

Immune thrombocytopenia (ITP) is a common autoimmune bleeding disorder. Despite considerable investigation, the pathogenesis of ITP remains incompletely understood, and for many patients, effective therapy is still unavailable. Using murine models and in vitro studies of human blood samples, we recently identified a novel Fc-independent platelet clearance pathway, whereby antibody-mediated desialylated platelets can be cleared in the liver via asialoglycoprotein receptors,
leading to decreased response to standard first-line therapies targeting Fc-dependent platelet clearance. Here, we evaluated the significance of this finding in 61 ITP patients through correlation of levels of platelet desialylation with the efficacy of first-line therapies. We found that desialylation levels between different responses to treatment groups were statistically significant ($p < 0.01$). Importantly, correlation analysis indicated response to treatment and platelet desialylation were related ($p < 0.01$) whereby non-responders had significantly higher levels of platelet desialylation. Interestingly, we also found secondary ITP and certain non-ITP thrombocytopenias also exhibited significant platelet desialylation compared to healthy controls. These findings designate platelet desialylation as an important biomarker in determining response to standard treatment for ITP. Furthermore, we show for the first time, platelet desialylation in other non-ITP thrombocytopenias, which may have important clinical implications and deserves further investigation.
Platelet Desialylation: A Novel Immune Tolerance Pathway with Therapeutic Potential in Decreasing Alloimmunization in Transplants and Transfusions

Submission ID
133

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

GPIb and GPIbIIIa (integrin IIb3) are two abundant platelet surface receptors that are commonly targeted by auto- and allo-antiplatelet antibodies in thrombocytopenias. Interestingly, we found GPIb was significantly less effective at inducing an antibody response than GPIbIIIa, unless in the presence of a co-infection (viral or bacterial). Given that GPIb is the most heavily sialylated protein, we hypothesized that removal of charged terminal sialic residues will unmask and alter the glycosylation profile to enhance antigen presentation and antibody production. However, unexpectedly, we found upon platelet desialylation, antibody generation was suppressed rather than enhanced. This was true in both iso (WT (wild-type) platelets into 3-/ or GPIb-/ mice) and allo (C57BL/6 WT platelets into BALB/c mice) anti-platelet responses. To assess whether desialylated platelets had immunomodulatory function beyond decreased immunogenicity, we transfused WT BALB/c mice with WT BALB/c desialylated or non-desialylated platelets during the course of immunization with allogeneic C57BL/6 WT platelets. We found a significant decreased antibody response against alloantigen H-2Kb in mice that were transfused with desialylated but not WT platelets. The suppressed antibody response was specific to platelet antigens, as there was no significant difference between the two groups following challenge with sheep red blood cells. Utilizing state-of-the-art non-invasive, in vivo Multispectral Optoacoustic Tomography imaging, we tracked, in real-time, increased pooling of desialylated ICG-labeled platelets to the liver and surprisingly the gut in mice following transfusion. In contrast, non-desialylated ICG labeled platelets remained in circulation. Correspondingly, intravital microscopy revealed increased adherence and
arrest of desialylated platelets in mesenteric veins but not arteries compared with non-desialylated platelets. Thus increased desialylated platelet sequestration and clearance in the liver/gut may have immunosuppressive effects against platelet associated antigens as part of normal platelet homeostasis. These findings may also be exploited as a therapeutic target to decrease alloantigenicity in transfusions/transplants (e.g. desialylated platelets carrying coagulation factors for hemophilia therapy).
Purified prothrombin substitutes for prothrombin complex concentrates in reducing bleeding in both normal and coagulopathic mice

Submission ID

86

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Abstract Body (max. 350 words)

Introduction: Prothrombin complex concentrates (PCC) are fractionated plasma products that reverse warfarin anticoagulation, and may be useful as general pro-hemostatic agents. Which protein constituent is most important in PCC procoagulant activity is unclear. PCC are enriched in the vitamin K-dependent proteins (VKDP) prothrombin, FVII, FIX, and FX, and proteins C and S. Here, we compared commercial PCC, three or four factor (3F- or 4F-) VKDP (mixtures of purified prothrombin, FVII, FIX, and FX), or purified prothrombin alone as bleeding treatments in normal or coagulopathic mice.

Design and Methods: Coagulopathy was induced using the previously described Blood Exchange-induced Coagulopathy Approach (BECA). In BECA, four sequential exchanges of whole blood for washed red cells reduce all coagulation factors in plasma by 80%. BECA mice were transfused with treatment solutions immediately prior to: tail vein transection; intravascular laser injury; or liver transection. Blood loss, thrombus size, or extravasated clot weight were determined, respectively. Normal mice were similarly challenged by liver transection. Human normal pooled plasma (hNPP) was diluted to mimic coagulopathy and combined with the treatment solutions, and prothrombin times (PT) and thrombin generation assays (TGA) were performed. Dose response studies were used to select appropriate doses for treatment solutions.

Results: PCC, 4F-VKDP, or prothrombin alone reduced tail vein blood losses indistinguishably from murine plasma. Three factor (3F-) VKDP mixtures were as effective as 4F-VKDP unless prothrombin was omitted. PCC, 4F-VKDP, and 3F-VKDP lacking prothrombin increased thrombus size equivalently following intravascular laser injury. PCC, 4F-VKDP, or purified prothrombin alone reduced liver injury bleeding equivalently relative to vehicle, but 3F-VKDP lacking prothrombin, or purified FIX did not, in both normal and BECA mice. Supplementation of diluted hNPP with prothrombin alone, PCC, or 4F-VKDP decreased PT and increased TGA values more effectively than 3F-VKDP lacking prothrombin.

Conclusions: Prothrombin is the dominant procoagulant component of PCC and is sufficient to
recreate PCC control of hemorrhage in coagulopathic mice. In vitro coagulation assays confirm this functional profile in human plasma.

**Acknowledgements**: Funding was provided by Canadian Blood Services (CBS) and Health Canada (grant to HN, ELGP, and WPS). SMQ was supported by a CBS postdoctoral fellowship award.
RESIDUAL RISK OF CYTOMEGALOVIRUS AFTER LEUKOREDUCTION IN THE CANADIAN BLOOD SUPPLY

Submission ID

11

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: Human cytomegalovirus (CMV) is a common herpes virus which infects white blood cells (WBCs). Frequently a mild infection or asymptomatic, the virus remains latent in WBCs and their precursors. Pre-storage leukoreduction reduces the risk of febrile reactions and alloimmunization against leukocyte antigens, as well as reducing risk from leukocyte associated viruses. At Canadian Blood Services, CMV antibody negative product is available on request for high risk patients. We estimated the residual risk of CMV in leukoreduced red blood cell (RBC) and platelet products.

Design and Methods: The residual risk of CMV was estimated as the product of the probability of filter failure \( p(f) \) and probability of the unit containing CMV infectious particles \( p(\text{viremia}) \). We assume risk is due to incident cases and correlates with filter failure. \( p(f) \) was the number of filter failures (residual white blood cell count of \( 5 \times 10^6 \) or greater) for a product divided by the number of units tested in 12 months. \( p(\text{viremia}) \) was obtained from publications. Confidence intervals were estimated as the product of the 97.5% confidence limits for \( p(f) \) and \( p(\text{viremia}) \).

Results: \( p(\text{viremia}) \) was estimated to be 0.12%. In 2015/16 there were 10 filter failures of 8,057 RBC units tested (0.001241157). The residual risk was 1 in 679,810 RBC units (95%CI: 1,979,022 - 280,347). Approximately 80% of platelet units released are pooled platelets and 20% apheresis platelets. The residual risk was the sum of the two risks proportional to units released. There were 6 filter failures of 1,207 pooled platelet units tested (0.004971002) and 5 filter failures of 1,409 apheresis platelet units tested (0.003548616). The residual risk of platelet products was 1 in 185,667 (95%CI: 762,777 – 62,814)

Discussion/Conclusions: The residual risk of CMV in leukoreduced products is very low (without antibody testing), but a few recipients may be exposed each year. About 40% of donors have positive tests for CMV antibody, thus many recipients are likely also to have been already infected. Most recipients are at low risk of clinically significant sequelae. Thus the chance of receiving an infectious unit AND becoming infected AND developing clinically significant disease is very small.
Safety and Utilization of Blood Components Prepared With Amotosalen-UVA Pathogen Reduction Technology (A-PRT) in Patients With Massive Transfusion Exposure

Submission ID

87

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Introduction: Massive transfusion (MT) requires transfusion of large volumes of platelets (PC), plasma, and RBC with risk of transfusion-transmitted infection (TTI). PRT reduces risk of TTI. Plasma and PC prepared with A-PRT (INTERCEPT, Cerus, Concord, CA) were evaluated for safety and utilization in MT.

Methods: Two studies were conducted. An active HV study was performed in 5 European centers using A-PRT plasma. Patients with a diagnosis of trauma, massive bleeding, or large volume plasma exposure (LVPE, 10 or more FP within 24 hours) were assessed for adverse events (AE) and transfusion-related mortality. A second single center retrospective review of two-treatment periods (21 months each) compared conventional PC (C-PC) with A-PRT PC utilization and safety (mortality and hospital days) for patients with MT (defined as 10 RBC/24 hours). Descriptive statistics characterized continuous variables, and Kaplan-Meier estimates were used to estimate mortality and hospital days.

Results: Of 9,667 patients exposed to A-PRT FP, 3,012 had trauma (n = 115), massive bleeding (n = 2,608), and LVPE (n = 675) with median exposure to 9, 4, and 16 A-PRT plasma components, respectively. Patients without a diagnosis of trauma, massive bleeding, or LVPE (n = 6,655) had median exposure to 3 A-PRT plasma units. 0.3% of patients with trauma, massive bleeding, and LVPE had an AE related to A-PRT plasma and 0.2% of patients had a SAE with 0.1% deaths. For patients without trauma, massive bleeding, or LVPE: 0.5% had an AE related to A-PRT plasma, 0.2% had a SAE with 0.1% deaths. Retrospective review of the 306 patients with MT (156 C-PC, 150 A-PRT PC) showed use of PC, plasma, and RBC was not significantly different on the day of MT or within 7 days after MT. In hospital mortality (27.6 and 24.0%), and median hospital days (27 and 23 days) were not statistically different for C-PC and A-PRT PC respectively.

Conclusions: MT with PRT plasma and PC did not result in increased morbidity or mortality. Support of MT patients with PRT components did not result in more component utilization or time to hospital discharge.
Testing the Efficiency of Riboflavin and Ultraviolet Light Treatment for Inactivation of High Titers of Biofilm-Derived Staphylococcus epidermidis in Platelet Concentrates

Submission ID

23

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Abstract Body (max. 350 words)

Background: The predominant platelet concentrate (PC) contaminant Staphylococcus epidermidis forms surface-attached aggregates (biofilms) in PCs, which have been linked to missed detection during routine PC screening. This study was aimed at evaluating the efficacy of riboflavin-UV treatment to inactivate S. epidermidis biofilms in buffy coat (BC) PCs.

Design and Methods: Biofilm and non-biofilm cells from S. epidermidis ST-10002 (PC contaminant) and S. epidermidis AZ-66 (skin isolate) were individually inoculated into whole blood (WB) units at a concentration of ~10^6 colony forming units (CFU)/mL (N=4-5). One spiked and three unspiked WB units were processed to produce a BC-PC pool. Riboflavin was added to the pool, which was split into two bags: one for UV treatment and the second was left untreated as a control. Bacterial loads were measured before and after treatment. Changes in in-vitro PC quality were assessed by flow cytometry (CD62 expression as response to ADP) and dynamic light scattering.

Results: Bacterial counts were reduced during BC-PC production from ~10^6 CFU/mL in WB to 10^3-10^4 CFU/mL in PCs (p <0.0001). Riboflavin-UV treatment resulted in significantly higher reduction of S. epidermidis AZ-66 than strain ST-10002 (≥ 3.5 log reduction and 2.6-2.8 log reduction, respectively, p <0.0001). No differences in S. epidermidis inactivation were observed in PCs produced from WB inoculated with biofilm or non-biofilm cells (p >0.05). Platelet activation was enhanced in PCs produced with WB inoculated with biofilm cells compared to non-biofilm cells (p <0.05).

Conclusion: The efficacy of riboflavin-UV treatment was similar in PCs produced from WB inoculated with S. epidermidis biofilm or non-biofilm cells. Levels of biofilm-derived S. epidermidis ≥ 10^3 CFU/mL were not completely inactivated by riboflavin-UV; however, further testing is necessary with lower (real-life) bacterial loads.

Acknowledgements: Volunteer blood donors and the Network Centre for Applied Development (netCAD) staff for blood collection and PC manufacturing. Dr. E. Maurer for dynamic light scattering data interpretation and staff in Dr. M. Scott laboratory for logistical support.
Use of Buffy Coat Derived Leukocyte Enriched Products for Evaluation of a Plasma Reduction Stem Cell Manufacturing Protocol

Submission ID

27

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Abstract Body (max. 350 words)

Background: An update in human progenitor cell (HPC) apheresis system technology led to higher collection volumes resulting in greater DMSO load and unacceptably long transfusion times for patients. A volume reduction step was therefore warranted to remedy these issues. The objectives of this study were to develop suitable mock HPC (mHPC) products and evaluate the effectiveness of the BioSafe PeriCell volume reduction technology on white blood cell (WBC) recovery and viability.

Methods: As HPC products are not readily available for development purposes, mHPC were created from peripheral whole blood buffy coats (BCs). Fresh ABO matched BCs were pooled and concentrated. mHPCs were diluted in compatible plasma to capture the full range of input volumes and WBC concentrations corresponding to the median, 5th and 95th percentiles of past HPC products. Six mHPC products were tested; three high and three low WBC concentrations, each at high, low and median volumes. Units were reduced on the Sepax2 (PeriCell Protocol, CS.430.1 kits). Unit volume, WBC concentration and WBC 7-AAD CD45 % viability were determined before and after each reduction. Finally, one mHPC was run in triplicate to assess the reproducibility of the method.

Results: The mHPC products had a mean starting 7-AAD CD45 % viability of 76 ± 8% [64-85] and a hematocrit of 14 ± 5% [9-19] which is well below the maximum allowable limit of the PeriCell. No significant differences in WBC recovery or change in viability were seen between the 6 mHPC products. Aggregate data showed that the mean WBC recovery of the volume reduction process was...
97 ± 8% [64-105] with a 3 ± 3% [-2-11] change in viability. The method was found to have a CV of 2.0% and measurement of technical reproducibility was very high (98 ± 2% WBC recovery). The change in total WBC count and WBC viability of the processed products were not different (p>0.05) than the un-manipulated control samples.

Conclusions: BC-derived mHPC products can be a suitable alternative when HPC products are not available. The volume reduction protocol evaluated was highly reliable and had minimal impact on total WBC counts and WBC viability.
Using a Logic Model to Develop an Out of Hospital Transfusion Program in the Fraser Health Authority

Submission ID

113

Authors/Co-Authors & Affiliations
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Abstract Body (max. 350 words)

The Holmberg House Hospice (HHH) is a separate facility from the Abbotsford Regional Hospital and Cancer Centre (ARHCC), but is located on the same property. It is a hospice plus model that strives to limit patient transfer to the acute care facility for medical interventions such as intravenous infusions. HHH expressed a desire to include red blood cell and platelet transfusions in its scope of care.

HHH engaged stakeholders which included the Transfusion Medicine Laboratory (TML), medical staff, and nursing staff to confirm support for the development of this program. The goal is to ensure that the benefits outweigh the risks in a situation analogous to a home transfusion. The biggest risk is the unavailability of immediate, emergency care in the event of an adverse reaction to the transfusion. Elements of the program include a criteria for patient eligibility, validation of component transportation containers, and targeted education for clinical and technical staff at HHH and ARH TML.

A set of evaluation criteria to measure the effectiveness of the program will be developed using a logic model. A logic model presents the relationships between the inputs, activities, and outputs. It also assesses the short-term, intermediate, and long-term effects of the program by measuring the intended outcomes. The inputs of this program include: policy development, procedures, human resources, and blood component transportation. The activity is the transfusion of blood components. The outputs are the assessments of patients’ symptoms and the number of eligible and ineligible patients referred. The intended outcomes for this program include, realizing the patients’ goals of life and reducing the use of medical or acute care beds.

Authors: Diana Kobes, Darlene Mueller, and Dr. Grant Sigurdson

Acknowledgements: Attila Almos, Dr. Neil Hilliard, Dr. Doug Morrison, Baljit Singh, Ruth Topolnicky, Bella Wang, Daphne Williscroft
VIA FreezeTM Research Controlled-Rate Freezer as a High Throughput Tool for Evaluating Mesenchymal Stem Cell Cryopreservation Methods

Submission ID
142

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Abstract Body (max. 350 words)

Background: Cryopreservation methods for Mesenchymal Stem Cells (MSCs) commonly use a standard freezing protocol (10% DMSO, 1C/min freezing rate, liquid nitrogen storage). While recent studies suggest that increased freezing rates improve post-thaw MSC recovery and viability, evaluation of alternative protocols is complicated and time consuming. Development of high throughput screening methods could allow for decreased costs and higher efficiency evaluation. The VIA FreezeTM Research Controlled-Rate Freezer (Asymptote Ltd.) can freeze samples in 96 well-plates allowing for higher throughput evaluation.

Methods: Freezing rate consistency across the plate was evaluated for three different freezing profiles using a thermocouple submerged in cryoprotectant solution. Thawing efficiency from -40 to 10C was also evaluated. To detect percentage intact cells post thaw a fluorescence assay was used (SYTO 13, Ethidium bromide). This study evaluated the addition of three concentrations of a dimethyl sulfoxide solution (2%, 5%, 10%) to a pellet of cultured human bone-marrow derived MSCs. Triplicate aliquots (100 L) in a 96 well-plate were frozen at 1C/min using the VIA FreezeTM with ice nucleation at -5C. Plates were thawed using a 37C water bath.

Results: The VIA FreezeTM maintained a consistent freezing rate for 100 L volumes across wells in a 96 well-plate from -10 to -40C for 0.5, 1 and 2C/min rates (0.48 ± 0.01C/min, 1.06 ± 0.02C/min, 2.07 ± 0.02C/min respectively, n=3/rate) with overall freezing rates from -10 to -90C of 0.45 ± 0.02C/min, 0.83 ± 0.01C/min, and 1.02 ± 0.09C/min respectively. Differences in thawing times between outer wells (2 min) and inner wells (7-9 min) were observed. Differences in intact cells between concentrations (2% and 10%) were found (47 ± 7%, 85 ± 6% respectively, n=3/group, p=0.002).

Conclusions: The VIA FreezeTM can be used to process small volume samples at freezing rates of 0.5 to 2C/minute in a 96-well plate. Thawing rate differences between inner and outer wells indicate that only inner wells should be used for optimization studies. This study demonstrated that
differences due to cryosolution concentration can be detected using a fluorometer-based assay. Adaptation of this high throughput system could be used for optimizing cryopreservation protocols for other cell types.
Weak D genotyping: Héma-Québec’s experience.

Submission ID

73

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Abstract Body (max. 350 words)

Following the recommendations of the College of American Pathologists (CAP) Transfusion Medicine Resource Committee (TMRC) and the American Association of Blood Banks (AABB) (Sandler et al., 2015), Héma-Québec started offering weak D genotyping service in June 2016 to every hospital in the province of Quebec obtaining unusually weak serological results for women under age 45. Weak D genotyping is of particular interest in pregnancy, as it may allow for the prevention of unnecessary injections of Rh immune globulin (RhIG), as well as the prevention of transfusion of scarce RHD-negative red blood cells (RBCs), when RHD-positive RBCs could have been safely used. The PCR-sequence-specific primers (SSP) and restriction fragment length polymorphism (RFLP) assays used allows for the analysis of types 1, 2 and 3, as these types can safely be considered RhD-positive. We also analyse the RhD-negative weak D type 42 for statistical reasons, as it is prevalent in our population (St-Louis et al., 2011). Two hundred forty-six weak D genotypes have been determined to this day with frequencies of 19% (type 1), 5% (type 2), 10% (type 3), 27% (type 42) and 39% other than 1, 2, 3 or 42. Further investigation was initiated to determine the molecular identity of the others. Out of 91 samples, 71 (78%) were confirmed to be legitimate serological weak D, mainly of types 4.1, 4.2 and 4.3. Surprisingly, 20 samples were discovered to be suspected-normal D (2 samples) or confirmed normal D (18 samples). Along with Sandler et al. (2015) data, our findings highlight the difficulties in our hospitals in interpreting the serological weak D. Trend analysis was conducted regarding the reagents and technologies used by each hospital, the origin of the request and the ethnicity of the concerned patient, but no significant correlation could be identified at this point. Altogether, our findings allow to share the frequency of weak D types 1, 2, 3 and 42 obtained in serological weak D, <45 years old Quebec’s women, and also highlight the need for further investigation of standard practices amongst our hospitals regarding the management and interpretation of atypical D typing.
3. Administrative

a. Oral Presentations

British Columbia Centre for Disease Control and Canadian Blood Services Transfusion Transmissible Infection Data Sharing Initiative

Submission ID
85

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Abstract Body (max. 350 words)

Background: Blood borne pathogens can potentially result in transfusion-transmissible infections (TTIs). Currently, routine Canadian Blood Services (CBS) blood donor screening includes HIV, HBV, HCV, HTLV, syphilis, West Nile virus, and selective Chagas screening for at-risk donors. Donors are not laboratory screened for other potentially transfusion transmissible pathogens.

Design and Methods: As a joint initiative, British Columbia Centre for Disease Control (BCCDC) and CBS developed a process that ensures timely reporting of positive test results of blood borne pathogens not currently included in CBS donor screening to CBS. The process involves automated extraction of positive laboratory test results from Panorama, the provincial public health information system, and storage of encrypted data on a secure BCCDC file transfer protocol (FTP) server, which is accessible only by BCCDC and CBS. On regular business days, CBS will retrieve and link the data to PROGESA, the CBS donor information system, using a previously validated anonymized data linkage process, to identify potential at-risk donations. CBS medical staff will review the data and assess need for further action, such as possible donor deferral.

Results: Final review and approval of the reporting and data transfer process by BCCDC, Panorama Data Governance, and CBS has occurred. CBS has created a local operating procedure to integrate the process into current BC and Yukon centre practices. A demonstration trial to confirm data transfer and FTP access was successful. The process should be operational and preliminary data available by CSTM 2017.

Discussion/Conclusions: This mechanism complements existing reporting of suspected TTIs by BCCDC to CBS, which is based primarily on physician reports to public health, which are then
reported to CBS, and extends the scope of laboratory surveillance of blood borne infectious disease of potential risk to blood safety beyond the current panel of routinely screened pathogens at CBS. It may provide one of the best illustrations in the world of integration of close-to-real time, public health infectious disease laboratory data, with donor screening measures employed by blood suppliers, to achieve risk reduction of TTI.

**Acknowledgements:**
We would like to acknowledge the collaboration of colleagues: Drs Mel Krajden, Muhammad Morshed, Jason Wong, Jeffry Sze and Alice Cheung
Expanding the reach of Transfusion Camp: a novel approach to assessing and addressing the transfusion medicine knowledge gap

Submission ID

84

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Abstract Body (max. 350 words)

Background: There is considerable evidence that postgraduate medical trainees lack transfusion medicine (TM) knowledge. Transfusion Camp, a unique longitudinal program consisting of five one-day sessions over the academic year was established in 2012 for University of Toronto postgraduate medical trainees. In 2016-2017, it was expanded to include other university sites. The objectives of this report are to assess TM knowledge across postgraduate medical training programs and to describe the novel approach of expanding the reach of Transfusion Camp.

Method: Building on its initial local success, the University of Toronto Transfusion Camp established an infrastructure and partnership with Canadian Blood Services. Starting in July 2016, didactic lectures given in Toronto were webcast to five satellite sites for remote live-attendance and recorded for later viewing by two other sites. The team-based learning seminars were delivered by local TM specialists in Toronto and at satellite sites. Pre-Transfusion Camp TM knowledge was assessed using the BEST-TEST.
Results: For 2016-17, >170 trainees from eight universities are participating in this education program. 110 trainees who attended day-one completed a pre-camp exam using the BEST-TEST to evaluate their transfusion knowledge. The average score for this cohort was 10.13 (2.91) out of 20. No significant differences were observed between Universities (ANOVA, p=0.55) but a significant increase was observed with increasing years of training (8.92 (2.93, n=38), 10.13 (2.69, n=39), 11.64 (2.61, n=28) and 10.80 (2.39, n=5) for PGY1, PGY2-3, PGY4-5 and PGY6-7, respectively, ANOVA, p=0.0017). Scores varied between specialties (Figure 1). The program, lectures and team-based learning seminars, have been highly rated by participants from both live and remote sites.

Conclusions: Transfusion Camp has the potential to be a national education program for postgraduate medical trainees in Canada. It provides the opportunity to understand the current TM knowledge gap, provides access to TM education opportunities by leveraging TM expertise, and promotes the networking of TM specialists with trainees who will administer blood products in the future. Finally, we hope that the program will narrow the TM knowledge gap and lead to improved transfusion practice.
High resolution auditing capability empowered by process mining: Characterising inventory flow through an automated blood dispensing refrigerator using a novel process mining approach.

Submission ID
106

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Abstract Body (max. 350 words)

Background: Auditing plays a significant role in transfusion medicine practice as it allows for continuous quality improvement of processes, and is a requirement in various accreditation schemas. Auditing also has the potential to be resource intensive, especially if manually done, could be subject to the Hawthorne effect, and may not be able to be done if the observed process is too complex. Process mining has been used in other industries and has recently been adapted for use in transfusion inventory analysis by Quinn et al. (Transfusion, 2017, in press) and Cheng (Transfusion, 2017, in press). The study used process mining to audit how the fridge (HemoSafe) was being used for the red cell (RBC) inventory, compares it to what was anecdotally known, and used no significant human resources.

Methods and Materials: Analysis was done using an institution-wide RBC data extract from the laboratory information system for the period of March 1, 2014-September 30, 2015. After using the TRUISM framework for data validation, process mining was performed and process maps were generated. A manual process map was also generated by subject matter experts for comparison.

Results: Approximately 2655 RBC units were transferred to the fridge location from the Victoria General inventory, of which 568 were crossmatched, 174 (6.6%) were transfused primarily to 11A (128/174, 73%) and 10A (32/174, 18%) which were operating theatres; other ward destinations accounted for <5 transfusions. The other transactions were complex, ranging from transfers, errors in issuance, and quarantine (data not shown). Comparison of the manually generated process map demonstrates an underestimation of the complex looping structure of the actual process (data not shown).

Conclusion: We demonstrate the use of process mining to audit how RBC units are being used at an automated blood dispensing fridge. The study highlights how it can be used to understand complex transactions in an inventory sub-location, and illustrates the potential application of this technique to understand inventory flow at other institutions.
Abstract Body (max. 350 words)

Background: In 2006, a regional network model was funded by the Ontario Ministry of Health and Long-Term Care (MOHLTC) to support a provincial blood utilization strategy in Ontario. At that time, many of the 158 Ontario hospitals with transfusion services did not have access to standardized best practices around the management of blood for transfusion.

Method: Three regional offices were created. Four priority goals were identified: utilization, education, inventory management and communication. In 2013, a fifth priority - quality was added. Measures for success were defined.

Results: To address utilization improvement, six audits were conducted using standardized tools (IVIG, plasma, PCC, RBC, platelets). Provincial guidelines and a request form for IVIG were implemented. Resources, events and online courses were developed (8,848 tests completed in 2016) to provide standardized education for physicians, nurses and technologists on utilization and safe administration of blood and to provide wider access to expert knowledge. Improvements in inventory management included a provincial program to optimize inventories and minimize wastage.

Annual RBC outdates were reduced by over 8,000 units (76%) between 2006-2016. Annual provincial RBC utilization declined by over 20,000 units during this period. In 2013, provincial redistribution of PPP commenced with an average annual savings of $313,357 realized. A provincial blood shortage plan (initial release 2008) provided guidance to hospitals through standardized tools. A robust communication network was established including annual visits to hospitals in Ontario (in partnership with CBS staff) and the development of a website to provide a central communication hub. In 2016, ORBCoN launched a provincial transfusion quality improvement plan to further
improve RBC utilization.

**Conclusion:** Evaluations and monitoring of performance indicators have demonstrated that hospital personnel have been satisfied with the support provided by ORBCoN.

Over a ten year period, the establishment of ORBCoN has proven that a coordinated regional network model can be successful and effective within a geographically large and diverse province such as Ontario.

Acknowledgements: ORBCoN acknowledges funding received from the Ontario MOHLTC and for the vision and support of our three sponsors - Dr. Jeannie Callum, Prof. Emeritus Nancy Heddle and Dr. Antonio Giulivi and for the collaboration and support of our many transfusion colleagues across the province.
Safety-Related Adverse Transfusion Reactions: What Reactions are Reportable to Health Canada?

Submission ID

120

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Background: The Blood Regulations were implemented in 2014, consistent with the recommendations from the Krever inquiry. Under the new framework, blood establishments must report to Health Canada any serious and/or unexpected adverse reaction, related to the safety of the blood. Safety in this context specifically refers to quality and efficacy. This encompasses reactions whose root cause is donor-related, as well as reactions that are related to regulated activities, including importation, processing, storage, distribution, transformation, and transfusion of blood.

Methods: The present discussion centers reported or postulated mechanisms that may underlie safety-related transfusion reactions, based on the Blood Regulations and a review of the literature.

Results: Blood may be associated with a wide range of safety-related adverse transfusion reactions, including: anaphylaxis/allergic reactions, transfusion-associated acute lung injury (TRALI), infections, hemolysis, graft-versus-host disease, metabolic disorders, hypotension, and lack of efficacy. Root causes may include transfer of donor-derived agents or molecules, e.g., infectious agents causing infection, or anti-HLA antibodies leading to TRALI. Adverse reactions can also be related to issues with regulated activities such as processing, storage, transformation, etc., such as mislabelling of the ABO type of a component, leading to a hemolytic reaction.

Discussion: Since the Blood Regulations were implemented, there have been questions regarding which adverse reactions fall under the scope of the Blood Regulations, and must be reported to Health Canada. The root cause of a blood safety-related transfusion reaction may not be immediately apparent in the healthcare setting. Blood establishments investigating a transfusion reaction should consider whether the reaction could be related to a donor-derived factor, or whether any regulated activities conducted in their site could have comprised the root cause of the adverse reaction. Additional research and better reporting of safety-related adverse reactions could help identify new mechanisms or trends in blood safety, and thus help improve the safety of blood transfusion for Canadians.
Transfusion Medicine Calls - Impact on Technologist Time.

Submission ID

127

Authors/Co-Authors & Affiliations

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Abstract Body (max. 350 words)

Introduction: Staffing levels are often dictated by testing numbers and volumes of component/product handled. In this era of fiscal restraint, these parameters may not accurately reflect the true workload of blood bank (BB) technologists.

Methods: An audit of technologist call to transfusion medicine (TM) physician forms was performed between 1800h January 20th until 0800h January 30th to assess workload burden. Call forms were evaluated by site; shift and type of call. The call types were categorized as a) Components/ products not meeting approved criteria; b) massive hemorrhage related; c) reaction related; d) transplant issues; e) antibody/testing issues; f) process issues and g) inventory issues.

Results: A total of 94 documented calls were evaluable. 64% were from tertiary sites with dedicated TM staff but 26% and 10% were at community and rural sites with crosstrained staff. The majority of calls (43%) occurred on evenings, 37.5% on days and 19% on nights. Conservatively, if each call took 5 minutes, this accounted for 7 hours and 50 minutes of technologist time. See Table 1 for call type breakdown.

Conclusion: This data indicates that testing volumes and component/product numbers should not be the only considerations for staffing requirements. It is also likely an underrepresentation as ward calls by technologists were not captured. Mechanisms such as online physician decision support trees may help and for example could have saved 42 (45%) technologist calls to TM physicians in Category A.

Table 1 Call Type Breakdown

<table>
<thead>
<tr>
<th>Site</th>
<th>Components</th>
<th>IVIG/RhIg</th>
<th>Fibrinogen</th>
<th>PCC</th>
<th>MHP</th>
<th>Transfusion reactions</th>
<th>Transplant related</th>
<th>Testing issues</th>
<th>Process Issues</th>
<th>Inventory Issues</th>
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</thead>
<tbody>
<tr>
<td>1 Academic/tertiary</td>
<td>13</td>
<td>6</td>
<td>8</td>
<td>4</td>
<td>11</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>2 Academic/tertiary</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td>3 Community</td>
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<td>0</td>
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<tr>
<td>4 Community</td>
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<td>1</td>
<td>0</td>
<td>6</td>
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<td>0</td>
</tr>
<tr>
<td>5 Community</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
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<td>6</td>
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<td>6 Rural</td>
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<td>0</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>3</td>
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<tr>
<td>Totals</td>
<td>17 (18%)</td>
<td>12 (13%)</td>
<td>9 (10%)</td>
<td>4 (4%)</td>
<td>18 (19%)</td>
<td>8 (9%)</td>
<td>4 (4%)</td>
<td>10 (11%)</td>
<td>8 (9%)</td>
<td>3 (3%)</td>
</tr>
</tbody>
</table>
b. Poster Presentations

"Anti G Testing and Titration Strategy in Prenatal Patients"

Submission ID

71

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Abstract Body (max. 350 words)

Background: It is important to differentiate anti-G from anti-D in pregnancy to ensure appropriate Rh Immune Globulin (RhIG) prophylaxis. Anti-G looks like anti-D and anti-C. When detected concurrently additional testing is necessary to distinguish them. Identifying or excluding anti-D determines RhIG eligibility. Anti-G testing and titration including case selection, serological methods and reporting has been standardized among the CBS perinatal testing laboratories.

Testing Strategy: At the start of a new pregnancy anti-G is suspected if anti-D and anti-C titres are:

- equal strengths; OR
- anti-C titre is < 2 tube difference from anti-D titre; OR
- anti-C titre is higher than anti-D titre.

Anti-D must be differentiated from anti C and anti G. Differentiation of anti-C from anti-G is not required as it does not affect RhIG eligibility.

A combination of R1R1, R2R2 and rr cells are used to determine the presence or combinations of anti-D, anti-C and anti-G.
If anti-G and anti-C are confirmed or if differentiation from anti-C is not performed, an anti-G and anti-C are reported. A combined anti-G+C titre is performed using an rr cell. If anti-G is reported and anti-C and anti-D excluded, an anti-G titre is performed using an R2R2 cell. After RhIG prophylaxis an rr cell is used for the anti-G titration.

When anti-D is excluded, RhIG prophylaxis is recommended for potential fetal maternal hemorrhage, for the 28-week routine dose and at delivery of an Rh positive baby, regardless of titre strength. Repeated exclusions for immune anti-D and anti-C (if initially excluded) are not performed until next pregnancy.

**Conclusion:** The standardized strategy outlined allows for detection, antibody identification and consistent follow up of prenatal patients with anti-G antibodies, with or without an immune anti-D. This group of patients with complex serology must be tested appropriately to ensure that RhIG is offered and immune anti-D development prevented. For pre transfusion testing, distinction of anti-G from anti-C plus anti-D is less important as C and D negative red cells can be readily provided for these patients.
A new antibody in your patient .... was the donor really antigen negative?

Submission ID

72

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Abstract Body (max. 350 words)

Background: Each year CBS is notified of patients who have developed unexpected antibodies following transfusion of antigen negative donor units. These cases are investigated systematically and the investigation steps are outlined.

Methods: Investigation of the patient to confirm the presence and identity of the antibody; and investigation of the implicated donor(s) to confirm the phenotype and identify and quantify any donor antibodies present.

Recipient investigations: A review of blood products transfused prior to detection of the antibody including Intravenous immune globulin, Rh immune globulin, plasma and platelet products or donor red cell units with an antibody that could contribute to a passive recipient antibody. Antibody identification, DAT and phenotype is confirmed. In case of an apparent anti-D after transfusion of D negative red cells, anti-LW and anti-G are excluded.

Donor investigations: Donor antigen phenotyping is confirmed for the antigen corresponding to the patient antibody. Any discrepancies in phenotyping or variations in reaction strength result in testing donor cells with a variety of antisera and red cell antigen genotyping. For RhD negative patients with apparent anti-D, all implicated donors have repeat testing to confirm RhD negative status. DEL testing by RHD genotyping is performed and serological testing for DEL by adsorption elution with rare polyclonal anti D is done in selected cases. Donor antibody titration is performed when the donor is known to have an antibody resulting in a passive recipient antibody.

Results: In 2016 three such investigations were completed on 41 donors. One patient had acquired passive anti-D from an O RhD negative donor with high titer anti-D; one patient had a transient anti-D possibly from IVIG therapy. The third patient had an anti-Bga.

Conclusion: Investigation of new and unexpected antibodies in patients following transfusion of antigen negative red cells requires a multifaceted investigation that includes confirmation of patient
antibody identification, exclusion of passive antibody and donor antigen investigation through serological and genotyping studies.
Affecting decreased hospital requests for CMV-seronegative blood components in BC and Yukon Region

Submission ID

128

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Abstract Body (max. 350 words)

Background: Cytomegalovirus (CMV) is a transfusion-transmissible herpes virus. Cumulative evidence indicates an equivalent, very low risk of transfusion-transmitted (TT)-CMV achieved by leukoreduction of blood components and/or sourcing cellular components from CMV-seronegative donors. Canadian transfusion guidelines from the National Advisory Committee on Blood and Blood Products (NAC), increasingly reflect the equivalence of these two methods. Here, we summarize the impact of collaborative efforts by the British Columbia and Yukon (BC&Y) transfusion medicine community to adopt NAC recommendations for appropriate use of CMV-seronegative blood.

Design and Methods: Canadian Blood Services (CBS) BC&Y hospital order data for CMV-seronegative product requests from 2004/05 to 2015/16 were obtained from the CBS data warehouse. Between fall 2015 and June 2016, these data were shared and discussed, in the context of results of cumulative, published evidence; evolving clinical practice in different jurisdictions; and NAC guidance on appropriate use of CMV seronegative blood, at face to face meetings with: blood transfusion service (BTS) staff and clinician representatives of Vancouver area hospitals; provincial Blood Coordinating Office (PBCO) and Transfusion Medicine Advisory Group (TMAG), to align provincial and NAC guidance and promote clinical adoption and, the provincial Hospital Communication Forum, including hospital BTS laboratory technicians and nurses, to affect change in hospital ordering practice. Monthly CMV seronegative request data were provided to BC&Y hospitals, with follow-up by the CBS BC&Y Hospital Liaison Specialist.

Results: From April 2009 to March 2015, a relatively stable monthly average of 1,536 CMV-seronegative requests were received from BC&Y hospitals (annual range over this period: 17,448-19,105). Average monthly requests decreased by 24% to 1164 units between April 2015-March 2016, followed by a steeper 32% decline to 788 units, between April-Dec 2016. Between the latter two
time periods, CMV-seronegative platelet requests decreased 25%; the corresponding decrease for RBCs was 49%. Over this time, there have been no reports of TT-CMV in BC&Y region.

**Discussion/Conclusions**: Regional collaborative consultation, data-informed feedback, and educational efforts by multiple stakeholders CBS, hospital BTSs, PBCO and TMAG have complemented a recent trend that has seen a marked decrease in hospital requests for CMV-seronegative blood, with no evident compromise in patient safety.
Characterizing commitment and knowledge of stem cell donors following initial recruitment: a preliminary analysis

Submission ID

65

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Abstract Body (max. 350 words)

Introduction: Previous research has outlined that stem cell donor ambivalence at multiple points in the donation process is associated with attrition. Higher ambivalence at time of recruitment has been shown in registrants who believed recruitment staff to be less informative, felt uninformed, and had unanswered questions.

Stem Cell Club is a federal non-profit that recruits Canadians as stem cell donors. Here, we characterize the commitment level and knowledge of our donors following registration, and their experience registering.

Methods: From 10/16-12/16, newly registered stem cell donors at six stem cell drives run by Stem Cell Club in Ontario and British Columbia were invited immediately following recruitment to participate in the survey. Questionnaires employed the seven-question Simmons Ambivalence Scale (SAS, Cronbachs =0.68), and responses were dichotomized for each item to reflect whether participants expressed any ambivalence (1) or no ambivalence(0). An ambivalence scale was formed by averaging the dichotomized responses. A fourteen-question true/false informed consent quiz assessed registrants knowledge according to World Marrow Donor Association suggested procedures for informed consent at time of registration. Likert scales were employed to assess registrant experience and perceived knowledge.

Results: Of the 228 stem cell donors (30% non-Caucasian males) registered during the study stem cell drives, 100 (44% of registrants) completed the post-drive survey and consented to be included in this analysis (27% of survey participants were non-Caucasian males). 88% of registrants reported feeling at least moderately informed about stem cell donation, 90% agreed or strongly agreed that recruiters were very knowledgeable, and 18% reported unanswered questions following the drive. Mean SAS score was 0.190.22, with 44% of registrants scoring 0/7, 20% scoring 1/7, and 36% scoring 2/7. Mean informed consent quiz scores were 8213%, with the lowest scores on questions regarding donation process and side effects.
**Conclusions:** In summary, we describe the ambivalence of donors recruited by Stem Cell Club, and our performance on metrics known to influence ambivalence. These data will guide quality improvement efforts, including revisions to our recruiter training program to improve registrant experience and address observed registrant knowledge gaps. Study recruitment remains ongoing.

**Acknowledgments:** This work was supported by a Canadian Blood Services BloodTechNet grant.
Combining Blood and Stem Cell Drives

Submission ID

105

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Abstract Body (max. 350 words)

Background: Stem cell drives and blood drives facilitate education and recruitment of eligible individuals as potential unrelated stem cell donors and as blood donors, respectively. Running combined blood and stem cell drives allows recruiters to cross-promote and recruit the same individuals for both programs.

Previously, we reported our model of the stem cell drive including five stations: pre-screening, informed consent, registration, swabbing and reconciliation (Fingrut et al, CSTM 2015). However, no model of combined blood and stem cell drives has been described. Here, we present our approach and describe development of a checklist to standardize combined drives.

Methods: Our model was designed to recruit donors for Canadian Blood Services. It adapts the stem cell drive model to include blood donation promotion and education. Further, it adds a blood education station, at which individuals are guided to book an appointment to donate.

Results: In our model, prescreening stem cell donors is revised to promote both blood and stem cell donation, and to redirect older individuals and women to the blood station. Reconciliation is revised to direct registrants to visit the blood education station and consider donating. Tasks that recruiters perform at the blood education station include: educating potential donors on the need for blood donation; describing the donation procedure; guiding potential donors to ascertain their eligibility; redirecting ineligible donors; assisting in booking clinic appointment via Canadian Blood Services sign-me up forms and online applications; and informing on what to bring to their appointment. Where applicable, recruiters can redirect ineligible potential blood donors to register with OneMatch, donate blood for research, provide financial donation, or promote blood donation to their social networks. A checklist was designed, including the above tasks, and is published on www.stemcellclub.ca

Conclusion: In summary, we present the first published model of combined blood and stem cell donor recruitment in Canada. Our model is relevant to anyone who spearheads donor recruitment in conjunction with Canadian Blood Services. Our checklist provides guidance to recruiters and standardizes the blood educations station across drives. Currently, we are developing an online module to disseminate our approach to recruiters across Canada.
Development of a Multimedia Library to Support Stem Cell Donor Recruitment

Submission ID

64

Authors/Co-Authors & Affiliations

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Melody Salehzadeh, Stem Cell Club
Yizhuo Gau, Stem Cell Club

Abstract Body (max. 350 words)

Introduction: Unrelated stem cell donors can be recruited online or at stem cell drives, where they provide informed consent and a tissue sample (buccal-swab) for HLA-typing. Stem Cell Club is a federal nonprofit that runs stem cell drives across Canada to improve the quality of membership on Canada’s stem cell donor-database. Previously, we reported on development of a resource outlining materials needed to run a Stem Cell Drive (Fingrut, CSTM 2016). Here, we report on the development and launch of a multimedia library to enhance the stem cell donor recruiter toolkit.

Methods: Stem Cell Clubs from across Canada were invited to design and submit multimedia materials to support stem cell donor recruitment. Materials had to target recruitment of the most needed stem cell donors according to the literature: young and ethnically-diverse males. Posters were published in an editable format (JPG, PPT, or DOC) to allow recruiters to modify and include event details.

Results: As of January 2017, our multimedia library includes 19 poster designs, 1 vertical banner, 2 horizontal banners, and 4 button designs. All materials are published on http://stemcellclub.ca/promo.html. Themes include superheroes, patient campaigns, puzzle piece matching, swab cartoons, and recruitment slogans such as Will you Marrow me?.

Conclusions: This presentation outlines the development and launch of a multimedia library for use by all donor recruitment organizations. These materials will support donor recruiters to promote stem cell donation and participation in stem cell drives. The library will continue to be expanded at regular intervals. Needs assessments will be conducted to inform future multimedia development to support stem cell donor recruitment, including need for stem cell donation infographics.

Acknowledgements: This work was supported by a Canadian Blood Services BloodTechNet Grant
Development of a Series of Training Videos for Stem Cell Donor Recruiters

Submission ID
30

Authors/Co-Authors & Affiliations
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Warren Fingrut, MD., University of Toronto

Abstract Body (max. 350 words)

Background: Unrelated stem cell donors are recruited at stem cell drives, where recruiters guide registrants to provide informed consent and a tissue sample (buccal-swab) for HLA-typing. Studies have shown that registrant experience, including impression of recruiter knowledge, impacts registrant's commitment as donors, highlighting the need for well-trained, competent recruiters. Stem Cell Club is a federal nonprofit that runs stem cell drives to recruit Canadians as stem cell donors. Previously, we reported the development of our online training program for stem cell donor recruiters (Fingrut, CSTM 2016a). A needs assessment survey identified the need for a series of videos to supplement our recruiter training program (Fingrut, CSTM 2016b). This survey included 52 Stem Cell Club donor recruiters across Canada, where 94% agreed or strongly agreed that videos covering all aspects of stem cell drive operations would be helpful and would be used to review material prior to a drive. Here, we describe the development of these training videos.

Methods: Videos were designed to demonstrate the roles of the recruiter across the stations of the stem cell drive, including recruiting donors, performing eligibility assessment, guiding donors through registration and swabbing, and reconciling swab kits. Scripts were written by the authors in accordance with best practices for stem cell donor recruitment and World Marrow Donor Association guidelines for recruiter training (Schmidt 2013). A third-party videographer was retained for video recording and editing. A combination of narration and role-playing was used to emphasize important concepts and reinforce procedural techniques.

Results: The video series consists of six segments: i) Prescreening; ii) Redirecting Ineligible Donors; iii) Securing Informed Consent; iv) Registration and Error Checking; v) Swabbing; and vi) Reconciliation. In total, these videos have a runtime of 40 minutes. The videos are published online at http://www.stemcellclub.ca/training/. In the two months since publication (12/2016-01/2017), a mean of 31 recruiters (range=16-67) have used each of these training videos.

Conclusion: We have developed a new resource to enhance our recruiter training program and address an identified training gap. Future videos will be developed, to cover pre- and post-drive topics.

Acknowledgments: We acknowledge funding from a Canadian Blood Services BloodTechNet grant.
Engagement of Transfusion Medicine Technical Leaders in the Development of a Provincial Transfusion Medicine Data Portal

**Submission ID**

117

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**Abstract Body (max. 350 words)**

**Background:** The BC Provincial Blood Coordinating Office (PBCO) houses a provincial Central Transfusion Registry containing comprehensive transfusion-related data for all blood products since 1999. This data has been provided to designated transfusion medicine (TM) leaders at scheduled intervals, and on request. These leaders identified the need to establish a means to pull information in an on-demand fashion for timely decision-making purposes. Engagement of stakeholders was critical to assess how best to enable them to access and utilize this powerful data set.

**Method:** Through the TM leaders, PBCO held multiple dedicated sessions to share system options, brainstorm the most relevant metrics, develop a usable interface and provide regular updates. This group understood the current data, and was invested in improving access and analysis of the information. Understanding the varied needs of the larger end user group supported creation of a TM Data Portal that provides timely access to relevant high-level overviews and detailed datasets to support work including patient care, inventory management and quality improvement initiatives.

**Results:** Engagement success was measured based on feedback collected after each update and through surveys following initial training of new TM Data Portal users. Responses indicate users found the system easy to navigate, expressed surprise and interest at the depth and breadth of data, and were pleased with the relevancy of information. Several TM leaders involved early in the development have remained the most frequent external users to date.

**Discussion:** Early, frequent and appropriate engagement of key stakeholders throughout the development phase helps to create a stronger connection and greater awareness for the new users. Time, as always, is a consideration when engaging busy health care leaders at any point in this process. Ongoing engagement to support system use, training additional users, and developing innovative training tools continues following the TM Data Portal launch in 2016.

**Acknowledgements:** PBCO is grateful to the Transfusion Medicine Leaders in BC (TRG and TMAG) for their support and collaboration on this project.
Ontario’s Transfusion Transmitted Injury Surveillance System: New Tools to Reduce Complexity in Adverse Transfusion Event Reporting

Submission ID
91

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Abstract Body (max. 350 words)

Background: Reporting of adverse transfusion events (ATEs) for hospitals is complex. In Ontario, some ATEs require mandatory reporting to Canadian Blood Services (CBS), or to the manufacturer of a plasma derivative (MPD) or directly to the Canadian Vigilance Program, all regulated by Health Canada (HC). In addition, some ATEs are reported to the voluntary Ontario Transfusion Transmitted Injuries Surveillance System (TTISS-ON) as part of the national hemovigilance system run by Public Agency of Canada (PHAC). Some ATEs are reported to both agencies. Determining what, who and how to report an ATE can be confusing for the hospital Transfusion Medicine Laboratory (TML)/Blood Banks and may require completion of multiple reporting forms. To simplify this process in Ontario, a project to create a comprehensive, easy-to-use reporting guide, applied to a single reporting form, was undertaken by the TTISS-ON education committee.

Design and Methods: Two reporting algorithms were designed: one for ATEs resulting from a blood component; and, one for ATEs resulting from a plasma derivative. The guide was reviewed by HC, CBS and MPD representatives for input and finalization. The reporting form, currently used by TTISS was accepted as a single initial reporting form. Both the paper based reporting guide and form were converted to on-line web based tools.

Results: The guide includes the algorithms, instructions and target contact information. The web-based version prompts the user for the type of blood product transfused, reaction severity, whether the reaction is associated with something that the hospital TML did to the product that could have affected the product quality, and the type of reaction that occurred. Upon answering these questions the system indicates to whom the reaction should be reported. The ATE information can be entered on line into the TTISS database, and the electronic reporting form saved and printed for further reporting to other agencies as indicated by the guide.

Conclusion: A common electronic ATE reporting form and Ontario Guide for Reporting Reactions,
available in print or electronically, comprise streamlined tools that help hospital TML/Blood Banks report ATEs to the right sources, thereby fulfilling safety-minded hemovigilance mandates.

Acknowledgements: HC, CBS, MPD.
Platelet Immunology Investigations and Results in Canada

Submission ID

26

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Abstract Body (max. 350 words)

Background: The CBS Platelet Immunology Laboratory performs investigations of patients from across Canada for assessment of platelet refractoriness, diagnosis of fetal/neonatal alloimmune thrombocytopenia (FNAIT) and diagnosis of post transfusion purpura (PTP). The number and variety of anti HPA and anti HLA antibodies detected from 2014-2016 are reported. Significant variation in the rate of positive antibody investigations is observed suggesting variability in patient selection for testing.

Methods: HLA antibodies are detected and classified using One Lambda LABScreen products. A Luminex instrument identifies and records the fluorescent intensity of the Phycoerythrin on each microsphere. HPA antibodies are detected using Immucor’s PAK kits which are ELISA based techniques used to screen for antibodies directed against platelet glycoprotein antigens IIBIIIa, IbIX, lalla and IV.

Results: 466 investigations were performed on samples referred from 9 provinces (NL, PEI, NB, NS, ON, MB, SK, AB and BC). 168 samples were sent for diagnosis of FNAIT; 281 for platelet alloimmunization and 17 for PTP. For those patients investigated for platelet alloimmunization, on average 59% had anti HLA antibodies (range: 50 – 100%). For those investigated for FNAIT, on average 39% had anti HPA antibodies (range 14 – 100%). Anti HPA antibodies identified included anti HPA1a (33%); anti HPA1b(27%); anti HPA 3a (5%); anti HPAA5a (3%) and anti HPA 5b(32%). Anti HPA 1a was identified in one patient (6%) with post transfusion purpura.

Discussion: An increasing number of anti HPA and anti HLA antibody investigations have been tested in the last 12 months. The presence of anti HLA/HPA antibody (ies) in samples tested shows significant regional variability. Differences in criteria for investigation of platelet refractoriness may contribute. The frequency of positive tests for maternal anti HPA antibodies is also variable and may also reflect different diagnostic thresholds for investigation of neonatal thrombocytopenia. The regional variation in anti HPA antibodies detect suggests varying referral patterns for this disorder. The particular antibodies identified in FNAIT investigation also differ in number compared to those expected based on published reports, possibly highlighting Canada’s ethnic diversity and associated variation in typical HPA types.
Prospective Blood Product Order Screening By Technologists: Educating and Empowering to Keep Our Patients Safe

Submission ID

78

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Abstract Body (max. 350 words)

Background: Prospective transfusion order screening (PTOS) uses established hospital transfusion guidelines to flag potentially inappropriate transfusion orders. The correct indication, dose, and timing of the infusion are factors worthy of consideration. The blood transfusion laboratory (BTL) technologist is crucial to the success of this process. However, there is often difficulty engaging technologists. This responsibility may seem intimidating and may be misconstrued as being beyond the MLT scope of practice. Education is vital to enabling the successful fulfillment of these expanding responsibilities for technologists. As part of the Ontario Transfusion Quality Improvement Plan toolkit, the educational module Prospective Blood Product Order Screening; What, Why, Who and How? was created to specifically educate technologists.

Design: Physiology of tissue oxygenation, symptoms of decreased tissue oxygenation and the goals of a red cell, platelet and plasma transfusion are reviewed including review of primary and secondary hemostasis. Content includes a comprehensive description of the screening process as well as professional guidelines confirming the MLT scope of practice. Real screening situations are included to illustrate the steps involved to enhance technologist judgment and understanding. This module will be encouraged to achieve the core competency of order screening.

Results: This pilot project has been informally reviewed by technologists with positive feedback including:
Well written, informative
Cases are very good examples to demonstrate the screening process
This would have been very helpful; I wish we had this when we initiated screening
By popular request, these tools are shared before their formal wide release.

Conclusions: With the advent of PTOS, the BTL technologist will become more actively involved in a therapeutic role. This new role is vital to the successful implementation of PTOS and to improve patient safety and resource stewardship by the common means of conservative transfusion practices. Education for technologists is necessary to build confidence and eliminate misconceptions regarding this new responsibility. We will assess the usefulness of the educational component after release to determine if it encourages/assists technologist engagement through knowledge and
understanding.
The Development of a Provincial Transfusion Related Adverse Reaction Reporting Tool using a Multidiscipline Collaborative Process

Submission ID
115

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Abstract Body (max. 350 words)

Background: The Health Canada Blood Regulations provide regulatory requirements specific to blood, and are harmonized across Canada. The Regulations apply to all establishments that handle blood, and align oversight according to the risk of activities each establishment performs. The Regulations require that Transfusion Services (TS) report serious or unexpected adverse recipient reactions to Health Canada when the root cause is attributed to a regulated activity performed by their establishment and the quality and/or safety of the blood component is affected. In British Columbia (BC), TS report recipient adverse reactions to the BC Provincial Blood Coordinating Office (PBCO) who submits the non-nominal data to the Public Health Agency of Canada. In addition, TS report specific adverse reactions attributed to the safety of the blood components directly to Canadian Blood Services (CBS).

The requirement to report to Health Canada added another layer of decision-making to an already complex system.

Method: A BC working group was struck, including a CBS Physician, Clinical Nurse, Technical Practice Leader and members from PBCO. The varied backgrounds proved beneficial as each offered insight into the complexity of investigating, categorizing and reporting adverse reactions and highlighted critical components in determining front line needs. The working group met monthly to develop a comprehensive, easy-to-follow job aid.

Results: A job aid was developed that categorized the adverse recipient reactions by:

- Adverse recipient reactions, not related to the quality and/or safety of blood components;
- Serious and/or unexpected adverse reactions attributable to the quality and/or safety of blood components;
- Death related to a transfused blood component.

Each category provides details of the reporting requirements and timelines. Part two of the job aid offers guidance in reporting of recipient adverse reactions to plasma protein products, which are not covered by the Blood Regulations, but must be reported appropriately.
Discussion: This provincially coordinated and collaborative approach avoided duplication of work, and optimized resources towards mandatory compliance in the appropriate reporting of transfusion related adverse reactions. A multidisciplinary working group helped ensure development of a tool that helps all disciplines understand the reporting requirements of the multiple agencies.

Acknowledgements: Health Canada, TRG and TMAG.
The Mock Stem Cell Drive: Development and Evaluation of a Practical Workshop to Train Stem Cell Donor Recruiters

Submission ID
66

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Abstract Body (max. 350 words)

Introduction: Unrelated stem cell donors are recruited at stem cell drives, where recruiters guide registrants to provide informed consent and a tissue sample (buccal-swab) for HLA-typing. Studies have shown that registrant experience, including impression of recruiter knowledge, impacts donor attrition rates, highlighting the need for well-trained, competent recruiters. Stem Cell Club is a federal nonprofit that runs stem cell drives to recruit Canadians as stem cell donors. Previously, we reported the development of an online training program for stem cell donor recruiters (Fingrut, CSTM 2016a). We also developed a series of videos, designed to supplement this training program (presented separately). A needs assessment survey identified the need for a mock stem cell drive to supplement our recruiter training program (Fingrut, CSTM 2016b). >88% of 55 stem cell donor recruiters polled agreed or strongly agreed that development of this practical workshop would improve training, and that they would personally use this resource.

Methods: A workshop was developed, assessing skills required to lead each component of the stem cell drive, from planning through to post-event tasks. Recruiters who had completed Stem Cell Clubs online training modules and videos were invited to complete the workshop in person or via videoconference, administered by the author. The workshop was designed to simulate realistic situations, requiring recruiters to demonstrate needed skills and troubleshoot issues. A post-workshop survey evaluated participant perceptions of workshop utility.

Results: The workshop includes scenarios assessing skills across drive setup and supplies; pre-event preparation; prescreening; redirecting non-optimal donors; securing informed consent; registration; swabbing; reconciliation; and post-event tasks. An outline is published online at www.stemcellclub.ca/training. In the two months since launch (12/2016-01/2017), 8 recruiters have completed this workshop (mean completion time=60 minutes). In post-workshop survey, participants unanimously felt the workshop prepared them to lead drives, facilitated development of core skills, and improved their confidence with the material.

Conclusion: In summary, we describe the successful development, launch, and evaluation of a recruiter training workshop to address an identified training gap. This workshop is relevant to any organization who trains stem cell donor recruiters.

Acknowledgments: This work was supported by a Canadian Blood Services BloodTechNet grant.
Validation of an Online Training Program for Stem Cell Donor Recruiters

Submission ID
104

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Abstract Body (max. 350 words)

Background: Unrelated stem cell donors are recruited either online or at stem cell drives, at which recruiters guide registrants to provide informed consent and a tissue sample (buccal-swab) for HLA-typing. Registrant experience at time of recruitment has been shown to impact their commitment as donors, with higher ambivalence seen among registrants who believed recruitment staff were less knowledgeable. This highlights the need for well-trained, competent recruiters. Previously, we reported the development of our online training program for stem cell donor recruiters (Fingrut, CSTM 2016). Here, we validate this online training against in-person training.

Methods: An informed consent and quality control quiz was developed and administered to new volunteer recruiters following completion of either online or in-person training session. The informed consent quiz assessed required registrant knowledge at time of recruitment, per World Marrow Donor Association guidelines. The quality control quiz assessed the ability to identify and correct common errors that can occur during stem cell drives.

Participants consented for their anonymized quiz scores to be included in the analysis. Recruiters who had previously completed training or had attended a stem cell drive within the previous six months were excluded. Results were scored against pre-set rubrics. Informed consent and quality control scores were summed for each participant in each group. Two-tailed t-tests were used to identify significant changes in quiz scores between online and in-person groups.

Results: From 09/15-09/16, 160 volunteer recruiters across Canada completed the online training (n=160). A further 58 volunteer recruiters completed an in-person training session on 10/01/2015, facilitated by a certified recruiter trainer.

Mean informed consent quiz scores and mean quality control quiz scores were significantly higher in the cohort who completed online training compared to in-person training (respectively, mean=937% vs 788%,p<0.00001; mean=8911% vs 8012%,p<0.00001).

Conclusion: Our results demonstrate that online recruiter training is feasible and effective in instructing volunteers in informed consent and quality control procedures necessary to recruit stem cell donors. Our work supports continued development and implementation of online recruiter
training programs. Limitations of online recruiter training include recruiters being unable to ask questions or practice handling recruitment material prior to their first drive.
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