Local Day – Canadian Advances in Transfusion Medicine Over the Years: Past, Present and Future

1A-01-01
ANNUAL GENERAL MEETING OF CSTM

No abstract available

1A-01-02
ORTHO AND BUCHANAN AWARDS AND LECTURES

No abstract available

1B-02-01
HISTORY OF TRANSFUSION MEDICINE IN CANADA

J Freedman

Laboratory Medicine, St Michaels Hospital, Toronto, Canada

Things are not always as they seem. We need to commit to examining as much of the relevant evidence as possible, even if it threatens our own interpretation – use a critical approach to all sources, and especially those that seem to confirm conventional wisdom; struggle to overcome personal bias, and, last but not least, resolutely refuse to believe something merely because we wish it to be true.

This talk will review the history of blood transfusion from ancient to modern times, focusing on Canadian contributions to the field. It will highlight some august luminaries who changed the way we practice transfusion medicine today and will discuss successes and failures and what we have learned from them.

"The history of medicine is in fact the history of humanity itself, with its ups and downs, its brave aspirations after truth and finality, its pathetic failures. the very bone and marrow of cultural history" (Fielding Garrison, 1870–1935).

1C-03-01
CANADIAN BLOOD SERVICES TURNS 20: PAST, PRESENT AND FUTURE

G Sher

Canadian Blood Services, Ottawa, Canada

Canadian Blood Services is celebrating its 20th anniversary in 2018. Much has changed in the last 20 years, and the organization is serving Canadian patients in a different environment than it did when it was created. While maintaining a core focus on blood and blood product acquisition and delivery, today Canadian Blood Services also plays a leadership role in the national system for organ and tissue donation and transplantation, conducts and supports world-class research and innovation, and continues to enable more stem cell transplants. One constant has been our work to bring scientific knowledge to bear on essential challenges related to transfusion and transplantation medicine and science in Canada.

Canadian Blood Services' approach to knowledge mobilization and innovation in research and development has created a convergence of essential expertise ranging from education to engineering, benchwork to business, data to discovery. Our model has been an essential engine in moving Canada's blood system from the crisis of contaminated blood in the 1980s and 1990s to the confidence Canadians express in their blood system today.

What does our future hold? Transfusion and transplantation practices are changing, technological innovation is upon us, political, fiscal and demographic trends are both driving innovation and posing new challenges, and private sector competition for raw materials in the form of commercial plasma collectors is a new reality. Like our international peers, Canadian Blood Services is relentlessly pursuing the value-driven transformations required to adapt to our changing contexts and maintain a secure supply of blood and blood products, remain relevant to generous but busy donors, and deliver "health-care dividends" to funding governments and taxpayers.

We know our traditional paradigms of operation and thinking must constantly evolve to ensure we are best able to meet patient requirements in a rapidly changing health-care environment. Meeting the needs of tomorrow's populations will necessitate collaboration and learning in new ways, taking advantage of new opportunities, and continuing the critical advancement of transfusion and transplantation knowledge and practice in Canada. We have an important history that guides and shapes the work we do, and a rich legacy of achievements over many years upon which future successes can be built. Innovating for the future will ensure we can find better answers for tomorrow, and continue to provide a secure system of life essentials for transfusion and transplantation that's reliable, accessible and sustainable for all Canadians.

1C-03-02
UPDATE ON NAC

JN Fesser

Pathology, Queen Elizabeth Hospital, Charlottetown, PE, Canada

The National Advisory Committee on Blood and Blood Products (NAC) is a group made up of predominantly physician experts in transfusion medicine from across Canada that serves to provide advice on utilization management and transfusion medicine practice to the provincial/territorial Ministries of Health, via the Canadian Blood Services Provincial/Territorial Blood Liaison Committee (CBS P/T BLC).

The CBS P/T BLC functions as the major forum for formal communications between CBS and its funders. This committee is composed of the provincial and territorial Blood Representatives (those individuals within the provincial/territorial Ministries who have been given primary responsibility for interactions between the province/territory and CBS) and selected representatives of the CBS executive and senior management teams.

By request of the CBS P/T BLC, NAC undertakes initiatives including the development of recommendations for blood component/product use, guidance statements for establishing uniform transfusion medicine practice, and developing plans to direct action under difficult circumstances. Recent initiatives include 1) updating of the National Plan for Management of Shortages of Labile Blood Components, releasing recommendations for the utilization of 2) CMV seronegative components, 3) irradiated components and 4) O negative red blood cell (RBC) units, and 5) providing guidance statements around testing for and management of prenatal patients with discrepant, weak or inconclusive serological RhD test results. Upcoming initiatives include developing position statements on 1) Factor XIII utilization, 2) autologous blood collection and 3) platelet use with consideration given to ABO and Rh group.

1C-03-03
UPDATE FROM THE QUEBEC TRANSFUSION ADVISORY COMMITTEE, THE COMITÉ CONSULTATIF NATIONAL DE MÉDECINE TRANSFUSIONNELLE

H Hume[1], A Wilson[2], A Trottier[3] and G Rivard[1]

[1]Université de Montreal [2]Centre Universitaire de Santé McGill, Montreal [3]Ministère de la santé et des services sociaux, Quebec, Canada

The "Comité consultatif national de médecine transfusionnelle" (CCNMT) is a transfusion medicine (TM) advisory committee to the Directorate of Biovigilance and Medical Biology (Direction de la biovigilance et de la biologie médicale, DBBM) of the Quebec Ministry of Health and Social Services (Ministère de la Santé et des Services sociaux, MSSS). Its membership consists of eight voting members (five physicians, two transfusion safety officers and the DBBM director) plus 4–5 non-voting members including representatives of Héma-Québec, the blood supplier Quebec. Its mandate is: (1) to review, study and discuss all aspects of transfusion practice and blood component/product utilization; (2) to make recommendations to the DBBM concerning blood products available to Quebec hospitals (additions, removals, indications), transfusion standards and guidelines and their application in Quebec hospitals or any other aspects of TM the committee considers pertinent and (3) to develop TM recommendations for Quebec hospitals. Recommendations to the DBBM concerning the addition or removal of blood products are made following an initial review of products by the National Institute for Excellence in Health and Social Services (Institut national d'excellence en santé et en services sociaux, INESSS); the INESSS review process includes a scientific committee with (among others) 2 CCNMT representatives. There were seven major issues addressed by the CCNMT in 2017–18.

(1) Recommendations to the DBBM of the INESSS reviews of plasma protein product (PPP) submissions; CCNMT supported the recommendations made by INESSS.

(2) Recommendation to the DBBM of the review by INESSS of a pathogen reduction technology, (Intercept[MC] Blood System) for plasma and platelets; INESSS recommended that this technology not be introduced into the Quebec blood system at the present time; CCNMT endorsed this recommendation.

(3) Collaboration with INESSS on the development and implementation of a guideline for the optimal use of intravenous and subcutaneous immunoglobulin (IVIg, SCIg) in neurology; the guideline document is available on-line at http://www.inesss.qc.ca/publications/guides-de-linesss.html; discussions concerning its dissemination and the implementation of a standardized IVIg/SCIg transfusion request form for the province are on-going.

(4) In collaboration with the Association of Hematologists and Oncologists of Quebec (Association de médecins hématologues et oncologues du Québec) the preparation of a position paper on the future of TM to be submitted to the MSSS; in particular the position paper advocates for an increase in the number of TM physicians in the province, an enhancement of the role of transfusion safety officers and the establishment of a provincial blood coordinating office.

(5) A survey of platelet usage in the province; a major finding was the need to facilitate the transfer of platelet units between Quebec hospitals; a working group has been established to address this issue.

(6) Promotion of patient blood management strategies: CCNMT continued its support for two pilot projects, one for preoperative anemia and the second for late cord clamping.

(7) In collaboration with the National Advisory Committee on Blood and Blood Products (NAC), completion of a position paper on recommendations for the irradiation of blood components in Canada.

These topics will be discussed and updated in the conference presentation.

1C-03-04

FROM SEROLOGY TO GENOTYPING: UPDATES IN BLOOD BANK TESTING

G Clarke[1,2]

[1]Canadian Blood Services [2]Lab Medicine and Pathology, University of Alberta, Edmonton, Canada

Since the 1980's there have been dramatic changes in the basics of blood bank testing for both donors and for patient pre-transfusion testing.

Antigen typing has been revolutionized by monoclonal antisera. Patient antigen typing is now routinely available as an adjunct to antibody identification. In addition, availability of monoclonal antisera has allowed for routine phenotyping for chronically transfused patients as well as many donors. This provides the potential to match for red cell antigens other than ABO and RhD (a stay out of trouble vs. get out of trouble approach to transfusion). Antigen typing of patients in the setting of a positive DAT has meant that a "dry match" can sometimes augment or even replace complex and time consuming auto and allo-adsorption as a method for finding the safest donor units for transfusion. Genotyping with prediction of phenotype is an extension of this strategy, allowing for antigen prediction and donor unit matching, even for patients who have been recently or chronically transfused.

Antibody identification methods have also evolved. They have become more specific for clinically significant antibodies and more sensitive. Techniques such as gel cards and solid phase plates for antibody identification are more easily interpreted than tube methods and are amenable to automation.

Development of the computer assisted cross-match has allowed for rapid and safe compatibility assessment without the need for physical mixing of patient and donor blood. This opened the possibility for matching in locations remote from the blood transfusion lab, including the OR and ER, and also in distant communities where immunohematology expertise is limited. More recently remote review of antibody investigation panels and cloud storage of available antigen panels have emerged and are likely to further alter strategies for pre transfusion testing.

Next generation sequencing is a rapidly evolving tool that is likely to significantly impact transfusion medicine testing. With rapid, comprehensive and economical means of predicting donor red cell antigens, extended phenotype matching between patients and donors will be more feasible. Fully typed donor units may represent the majority of units on blood bank shelves.

1D-04-01

AN INTRODUCTION TO NEW AND RENEWED PRODUCTS FOR TRANSFUSION

D Devine[1] and G Sher[2]

[1]Canadian Blood Services, Vancouver [2]Canadian Blood Services, Ottawa, Canada

This is an exciting time for transfusion medicine in Canada, with new approaches and new products on the horizon. While some of these approaches are innovative to us, they have been well-tested in other countries or in historical times. This gives us some level of comfort as we consider implementation options. Most of the products

described below have not yet received regulatory approval, either for the manufacturer or for Canadian Blood Services, and as such remain in the research realm for now.

The major safety improvement under consideration is the implementation of pathogen inactivation technology. Only one technology is currently licensed for use with plasma in Canada, but others are anticipated to be licensed soon. The technologies currently in the global marketplace or in clinical trials are used to treat finished products, with one exception that treats whole blood units. Work is underway to determine the appropriate path to adoption of pathogen inactivation technology in Canada.

Platelet research has offered a very interesting suite of opportunities for Canadian hospitals. In addition to the ongoing discourse between Canadian Blood Services and the hospitals we serve around the management of platelet inventory to reduce wastage, last August we implemented a 7-day outdate for platelet products with an enhanced bacterial culture protocol to provide a safer product. These activities have reduced platelet wastage across the system. Two important areas of focus for platelet products are the use of platelet additive solution (PAS) to replace much of the plasma in the platelet concentrate, and the change in storage conditions of platelets from room temperature to 4°C for platelets to be given to actively bleeding patients. The use of PAS reduces the total plasma content, thereby decreasing antibody titres and providing additional nutrients for stored platelets. Cold-stored platelets may be a better product for bleeding patients, and permit storage beyond the current 7 days. These benefits could make cold-stored platelets an attractive product for smaller or remote hospitals with unpredictable platelet demand.

We continue to revamp our rare blood program, hopefully expanding the available products, their shelf-life once thawed, and our ability to conduct more extensive genetic analysis of blood groups. Trauma medicine is excited about recent studies using leukoreduced whole blood. Canadian Blood Services is also looking at starting clinical studies in Canada with this product in both trauma and planned surgery, perhaps returning us to a better version of the days before component therapy.

Renewed interest in freeze-dried plasma for both military and civilian medicine has Canadian Blood Services investigating the possibility of bringing systems for producing freeze-dried plasma to Canada. This product would permit the preparation of plasma immediately before use and improve the management of AB plasma in trauma protocols. It would also mean the end of conventional plasma bags broken during shipment or thawing.

And last, but not least, improving Canada's position for sufficiency of plasma-derived drugs is a high priority at Canadian Blood Services. To that end, we will be increasing the amount of plasma we collect for the manufacture of immune globulin products while we continue our work to assist the system with appropriate use of these drugs.

1D-04-02

NOVEL APPROACHES TO TEACHING TRANSFUSION MEDICINE

Y Lin[1,2]

[1]Department of Laboratory Medicine & Molecular Diagnostics, Sunnybrook Health Sciences Centre [2]Department of Laboratory Medicine & Pathobiology, University of Toronto, Toronto, Canada

The goal of the transfusion community is to provide high quality transfusion care. Traditionally, this has been defined as getting the right sample, getting the right test result, having the right equipment, getting the right bag with high safety standards and no waste of inventory and getting the right unit to the right patient. However, key to initiating this entire process is ensuring that the right decision to transfusion has been made. This is the focus of transfusion medicine education for clinicians. The current state of transfusion medicine knowledge shows the need for improvement. As technology advances, novel approaches to teaching transfusion medicine have been developed. This session will review examples of published transfusion medicine education experiences as well as highlight innovative methods and platforms for teaching transfusion to clinicians. Data evaluating the effectiveness of these approaches in changing transfusion behaviour will also be presented.

1D-04-03

CELLULAR THERAPY COMES OF AGE

D Wall

Division of Haematology/Oncology, The Hospital for sick children, Toronto, Canada

The field of hematopoietic stem cell transplant had seemed to have reached a comfortable approach to the treatment of both malignant and non-malignant disorders. Recently advances in cellular therapy are bringing transformative changes to these strategies. The first successful generation of CAR-T cells to treat B cell malignancies are becoming commercially available. These therapies place new requirements on the clinical cellular laboratory service – the clinical laboratory/cellular therapy

program will coordinate the collection of the raw cellular material for manufacturing by the commercial manufacturing site. Once the manufactured product is received back to the program, the product is stored and released for clinical use. In the eyes of Health Canada, the cellular therapy program responsible for collection, storage and release of such manufactured product carries full responsibility as a source establishment. Initially patient- or related donor- derived cells will be used for manufacturing these products but it is expected that 3rd party cells selected for specific HLA expression or by engineered cells to bypass the host immune system. Cellular therapy products targeting a range of malignancies and infectious diseases are in development and will be reaching the clinic in the near future. The 'cell pharmacy' requirements and management of these immune effector cells in the clinic are new roles for the cellular therapy laboratory. This talk will discuss the clinical practicalities of these new therapies and focus on blood bank/cellular therapy laboratory requirements to be able to support these exciting new products.

2A-01-01

APHERESIS DONOR ELIGIBILITY CRITERIA AND SELECTION IN PLATELET, PLASMA AND RED CELL COLLECTION

C Poole

Medical Division, South African National Blood Service, Johannesburg, South Africa

The collection of blood components by apheresis is a part of modern blood product service provision to patients in need. Apheresis technology can be used in the collection of platelets, red cells, plasma in the donor setting and the collection, reduction or replacement of platelets, red cells, plasma, haematopoietic stem cells, granulocytes and T-lymphocytes in the clinical setting.

The word apheresis is derived from Greek and means "to take away". The take away objectives of the talk include:

1. An overview of the advantages to patient and blood establishment of apheresis collection over non-automated, whole blood collections.
2. General considerations for an apheresis service in terms of legislative and regulatory compliance, patient guided demand for apheresis blood products, standard setting, fiscal oversight and technology partnerships.
3. Donor eligibility for apheresis platelet collection, apheresis plasma collection, apheresis red cell collection and concurrent collections (e.g. apheresis platelets and plasma)
4. Recruitment and selection

In general, donor eligibility for apheresis collection will include consideration of total blood volume (and weight as its proxy) for the determination of collection safety, pre-procedure blood counts relevant to the product being collected and frequency of apheresis single and concurrent donations.

Donor eligibility for platelet apheresis collection pre-and post-procedure platelet counts, monitoring of red cell and plasma loss over time and education and surveillance for use of antiplatelet medications.

Donor eligibility for plasma collection includes gender, pre-procedure total protein assessment, periodic serum protein electrophoresis assessment and periodic physical examination.

Donor eligibility for red cell collection includes threshold haemoglobin or haematocrit and, in double red cell collection, specific height, weight and haemoglobin considerations.

Recruitment and selection of apheresis donors includes analysis of relevant apheresis product demand, successful conversion of a whole blood donor to apheresis donation, appropriate informed consent, and education on time commitment and on potential adverse events.

2A-01-02

SHORT AND LONG TERM SIDE EFFECTS OF DONOR APHERESIS

M Neyrink[1], H Vrielink[2] and D Deeren[3]

[1]Hematology, AZ Delta Roeselare, Roeselare [2]Transfusion Medicine, Sanquin Blood Supply, Amsterdam, the Netherlands [3]Hematology, AZ Delta Roeselare, Roeselare, Belgium

In apheresis procedures, one or more blood components are obtained by machine processing of whole blood with return of the residual components of the blood to the donor during or at the end of the process. Side effects during this procedures can originate from the collection of blood, processing of the blood, and the return of the components. Type, frequency and severity of adverse events depend on several factors, e.g. condition of the donor, type and number of procedures performed, the way of venous access.

Not all side effects are exclusively related to the apheresis procedure, but can also appear in whole blood donations. Although the overall morbidity of apheresis donations is low, side effects are important because they can impact the return rate of the donor to a donor center.

Many of the side effects during apheresis are related to venous access. Adequate venous access is needed for a good draw and return flow between donor and machine. Peripheral venipunctures can cause local problems such as hematomas, bruising, burning pains due to peripheral nerve injury, but also thrombosis and phlebitis. Use of central venous catheters can lead to pneumothorax, infection, air embolism, hemorrhage and arrhythmia.

Overreaction of the body to certain triggers (e.g. stress, pain, dehydration) can lead to vaso-vagal reactions with severe hypotension and bradycardia. These events are experienced as very unpleasant and have negative effect on the return rate of the donor. Hemodynamic changes during apheresis procedures can also lead to hypovolemia, especially in smaller donors. Hypotension can furthermore be enhanced by the use of ACE inhibitors (blood pressure lowering drugs) by the donor.

During apheresis procedures, sodium-citrate solution is added to the donors' blood entering the apheresis device as anticoagulant. Anticoagulation is achieved by binding the ionized calcium. Citrate is completely resolved in the plasma, therefore with the return of the components to the donor, depending on the procedure more or less citrated plasma is re-infused and as result, the ionized soluble calcium concentrations in the donor are more or less reduced. Therefore it is likely that mild symptoms of hypocalcemia due to citrate infusion frequently occur especially when more plasma is returned. Long term effects of citrate have been published as well. Frequent plateletapheresis donors showed significant osteoporosis, especially in the metabolically very active lumbar spine (Karin Amrein). Beside chelation of calcium to citrate, also magnesium is bound, resulting in significant drops in magnesium levels.

Rare side effects during apheresis procedures are hemolysis and air embolism. Hematopoietic stem cell donors are mobilized with medication such as filgrastim or plerixafor. This medication has its own side effects sometimes confusing with apheresis caused events.

Low ferritin levels in apheresis donors are in the spotlight. Although no erythrocytes are collected in platelet/plasmapheresis procedures, a loss of 20–30 mg of iron per apheresis procedure is normal due to loss in the apheresis disposable and test tubes. Therefore, relative high levels of anemia in frequent apheresis donors are be observed despite normal hemoglobin values at time of donation.

2A-01-03

ESTABLISHING AN APHERESIS SERVICE IN A RESOURCE-LIMITED SETTING: CAMBODIA

B Pheng[1], S Sok[1], P Bunpa[1], V Kao[1], K Ou[1], S Varoeun[1], S Eav[1], M Yong[2] and H Vrielink[3]

[1]National Cancer Center [2]Maternity, Calmette Hospital, Phnom Penh, Cambodia [3]Transfusion Medicine, Sanquin Blood Supply, Amsterdam, Netherlands

Cambodia (South East Asia) became independent from France in 1953, but the road to self-governance was very difficult. Civil war (1967–1975) lead to genocide, economic destruction, massacre of intellectuals and 1.7 million deaths. This situation ended in January 1979 leaving the healthcare very limited with only nine physicians survived. Since then, the country experienced significant and consistent economic growth. The Cambodian flagship hospital is Calmette Hospital, which has been modernized enormously during the last decade.

The National Blood Transfusion Center (NBTC) started in 1993. Its role is to collect, process, store and distribute blood components to all Cambodian hospitals free of charge. The Cambodian Red Cross participates in donor recruitment, educational programs, and technical support. Despite all efforts, there is shortage of blood supply which forces to rely on whole blood collections from family donors (70%). Apheresis is not available at NBTC.

Apheresis started in Calmette hospital in 2012 with the donation of a MCS+ device (Haemonetics) and training by Hans Vrielink. The first apheresis procedure was a leukoreduction in a CML patient with leukostasis. Since then 57 hemato-oncology patients were treated with leukoreductions. In our hands, leukapheresis in combination with hyperhydration and cytoreductive medications showed better outcome in terms of acute mortality rates compared to patients not receiving leukapheresis. By following ASFA guidelines, TPE was also approved. Eighteen patients with severe myasthenia gravis or Guillain Barré syndrome were treated with plasma exchange (IgGs are much

more expensive compared to TPE and have limited resource). TPE significantly improved survival rate compared to patients who did not received TPE (all died).

A Cobe Spectra (Terumo BCT), was donated by prof Yoshihisa Kodera, Aichi Medical University (Japan), on behalf of the Asia Pacific Blood and Marrow Transplantation Group in 2015.

Since 2017, platelet collections by apheresis have been approved for active bleeding cases with severe thrombocytopenia, e.g. extra-uterine pregnancy, appendicitis, subdural bleeding, ureteral stone with hematuria, and acute intestinal occlusion. Since then, 20 plateletapheresis procedures (all family donors) were performed for 15 patients applying a dual needle procedure. In approximately 70 min in average 280×10^9 platelets in 300 ml were collected. No side effects of plateletapheresis were seen. Shortly, collection of leukoreduced platelets will be initiated.

In the near future, apheresis collection of HPCs for autologous and allogeneic transplantation in hemato-oncology patients will start in the National Cancer Center (NCC) of Calmette Hospital.

Challenges are technical problems with apheresis equipment and lack of apheresis application awareness among colleagues. Many physicians are not convinced that apheresis can be of help for their patients despite evidence-based indications. Some prefer basic supportive care and steroids rather than apheresis. However, with strong commitment of hematologist team at NCC of Calmette hospital, apheresis is considered the technology of choice for saving life and will be performed following the ASFA guidelines if there is proper indication.

However, having only two apheresis machines for one country is not sufficient. For apheresis to be sustainable, successful and response to the need, more machines and human resources capacity are needed.

Academy Day – Education and Training

2A-02-01
MORE THAN JUST A MANIKIN: OPPORTUNITIES FOR SIMULATION IN CLINICAL TRANSFUSION MEDICINE

A Petrosoniak[1] and K Pavenski[2]

[1]Emergency Medicine, St. Michael's Hospital, University of Toronto [2]Laboratory Medicine, St. Michael's Hospital, University of Toronto, Toronto, Canada

Simulation was first introduced to healthcare as an enhanced training modality to augment traditional educational methods. Healthcare simulation is a technique that serves to replicate real experiences in a fully interactive manner. A strength of simulation is that practice can occur in a nonpunitive environment without posing a threat to patient safety. Ideal simulation cases consist of rare, high-stakes scenarios that cannot be practiced on real patients. Furthermore, SBME facilitates team-based training and provides an opportunity for participants to reflect upon their performance and discuss non-technical skills during structured debriefings. These benefits are not without challenges related to cost, time and training required for successful implementation.

Simulation has been used in transfusion medicine although its adoption has been slow. Most commonly it is used to enhance transfusion education and assessments among nursing and medical trainees. More recently, simulation-based medical education (SBME) has gained popularity among staff physicians and nurses in the field of transfusion medicine. Clinical situations most commonly used in transfusion simulations include administration of blood components, management of transfusion reactions and management of massive hemorrhage.

Healthcare simulation is now widely adopted and its applications have broadened and matured. Within transfusion medicine, educational methods now include a vast array of options from focused task-training for procedural skills (e.g. rapid infuser use), to multi-disciplinary team training using high-fidelity manikins (e.g. resuscitation of the bleeding trauma patient). The improved integration of standardized patients in training and evaluation modules, now enables trainees to practice important skills such as consent for blood product administration and navigating ethical dilemmas related to transfusion.

More recently, simulation has gained popularity as a quality improvement intervention and testing modality (such as specific PPID technology). Simulation offers a unique approach to testing new and existing processes without impacting patients. Moving simulation into the actual (in situ) clinical environment represents an exciting shift towards blending SBME and quality improvement to ultimately improve patient outcomes. We will discuss two local studies that utilized in situ simulation to identify and evaluate latent safety threats related to massive hemorrhage protocols

within the trauma bay and the operating room. The findings informed change at local, departmental and institutional levels. The future of simulation in transfusion medicine will seek to enhance educational opportunities and simultaneously evaluate and improve patient and system-based outcomes.

Academy Day – Organisation and Quality

2B-03-01
QUALITY: WHAT I KNOW NOW THAT I WISH I'D KNOWN THEN

MA Smith

Quality and Regulatory Affairs, New Zealand Blood Service, Auckland, New Zealand

This presentation is a personal reflection on 18 years as a Quality Manager in the blood industry in Australia and NZ. Over that time, regulation and quality systems thinking has evolved significantly. When implementing a quality system, it is easy to focus on the detail of compliance without stepping back to consider where the biggest risks and challenges lie. This presentation will highlight, with the wisdom of hindsight, some of the areas that can present particular challenges.

Resourcing the Quality Team with adequate levels of staff and skills is crucial. Consider what tasks the team will be doing, the level of support the Team will need to provide to the organisation. The Team will likely require training in areas such as auditing, root cause analysis, risk analysis etc. They may also need specific technical training in areas such as calibration. Structure of the team needs to be considered, especially where there is wide geographical spread.

Unless the business is actively educated about quality it may be difficult to achieve the desired level of regulatory compliance. Encourage departments to take responsibility for their own quality and compliance: "quality from within". Provide extra support where concepts are difficult, e.g. many people find validation and change control challenging.

Most things are not black and white and yet staff typically want black and white answers. Risk underpins everything and regulators are taking a more risk-based approach than they did 20 years ago. It is important to establish organisational risk management policies and procedures as well as a standard methodology for risk assessment. Encourage staff to think about levels of risk in everything they do and to apply appropriate controls.

Documentation can quickly become unmanageable if not carefully planned and managed. People tend to create documents without thinking about the ongoing burden of maintenance. Process mapping and identification of critical control points is the key to determining exactly what documentation is required. Use risk assessment to identify appropriate controls.

Quality needs to develop an effective interface with those responsible for procurement and supplier management. Suppliers may not always understand the GMP constraints customers work under and procurement staff may not fully appreciate the risks involved in sourcing critical products.

Information technology is a large and complex area that is not well understood by many outside the profession. There can also be challenges in getting the required level of GMP compliance from IT departments and providers. This is therefore another important interface for the Quality Team. Although highly beneficial for certain functions, computer systems are not necessarily the answer to all problems and it is easy to underestimate the amount of work involved in specifying, implementing and validating them.

As far as possible, it is helpful to engage with the regulator and ensure a two-way flow of information. Regulators have an education role but, if new to the blood industry, may require training in the manufacture of blood components. Educating them about the risks involved in blood manufacture is an ongoing process.

2B-03-02
DEVELOPING THE QUALITY TEAM

LA Bust

Africa Society for Blood Transfusion (AfSBT), Cape Town, South Africa

Background: The size and structure of the Quality Department in a blood transfusion service should be tailored to suit each organisation. The Quality Manager

should lead a team of dedicated professionals that guides the organisation towards its objectives of supplying quality products and services and achieving accreditation or certification. This individual must have adequate authority to carry out quality responsibilities and must report to the top executive and be independent of line functions.

Discussion: When appointing staff to the Quality Department it is important to select candidates with the appropriate qualifications and experience. Desirable personal attributes include: good organisational skills, meticulousness, diplomacy, strong ethical values and conflict resolution abilities.

Quality personnel should undergo ongoing training to remain current. Training can be through formal certificate or diploma courses, informal short courses or e-learning on the internet. Topics for training could include quality principles (such as the Five Whys, Pareto Analysis, the Seven Tools of Quality, Six Sigma etc), documentation principles, auditing techniques, risk management and quality indicators. Training on job management skills is also beneficial and could include project management, communication techniques and time management. Personnel should also be encouraged to research appropriate quality topics and conduct in-house training sessions for other departments.

Ongoing development of Quality personnel should include exposure to other organisations and their systems, learning and networking through congress attendance, and regular competency assessments with feedback. Succession planning within the department is important.

The Quality Department cannot achieve accreditation or regulatory compliance on its own and teamwork is required. Support for the department should be garnered by appointing Quality ambassadors/ champions in technical departments and regional zones. The Quality Department should also understand the needs of the departments it serves and aim to keep quality systems simple and user-friendly so as not to overly impose on routine workloads.

Conclusion: Quality is crucial in blood transfusion due to the nature of our work and our products being infused directly into the veins of human patients. An effective Quality Management System provides a strong foundation for the rest of the organisation. The Quality Department, with support from top management, needs to develop a culture so that all employees think and act quality on a daily basis. All employees should feel part of the overall quality team. A pervading quality culture will lead to continual improvement and contribute to sustainability of the organisation.

2B-03-03

WHEN THINGS GO BADLY – MANAGING QUALITY PROBLEMS AND COMPLAINTS IN TRANSFUSION MEDICINE

T Vuk

Quality Management, Croatian Institute of Transfusion Medicine, Zagreb, Croatia

According to many of its characteristics and features, transfusion medicine is a specific area of medical science. This particular position also entails the great responsibility of transfusion services to provide accessible and safe transfusion therapy. Despite the tremendous progress in terms of quality and safety in transfusion medicine and the fact that most of the activities in transfusion chain take place without any problems, some risks are still present. Biological origin of blood products may be the cause of transfusion-transmissible infections and immune-mediated transfusion reactions, while the complexity of the process and a large number of participants in transfusion chain facilitates the occurrence of errors.

For all these reasons, it is important to ensure the proper functioning of all activities in the entire process of transfusion medicine, from vein to vein, and monitor them with different control mechanisms.

Quality management system and haemovigilance significantly contribute to the safety and quality in transfusion medicine. These systems have the role of preventing things going badly and when this happens they allow preventing or mitigating the damage by a correct and rapid response.

The best approach to managing quality problems is preventative approach, through comprehensive risk management, education, definition of critical control points, permanent quality monitoring and vigilance, audits, identification of opportunities, etc.

In blood banks, quality problems are often manifested on blood products, and possible causes include: biological origin of blood products, human errors, suboptimal planning and organization of work, poor quality of materials and equipment used in product realization. In hospital transfusion units, problems are most commonly related to pre-transfusion testing, particularly errors in pre-analytical phase, and to the selection or issue of blood components for transfusion. Some problems in transfusion medicine are related to clinical transfusion practice and activities that are not directly under the jurisdiction of blood transfusion service (BTS), however BTS can affect them through hospital transfusion committees, education of clinical staff, and so on.

Even with the maximum commitment to quality, not all products and services are always in line with the customer requirements and expectations. Therefore, customer complaints are valuable source of information for service providers and manufacturers. Solving the problems that led to the complaint gives customers a sense of trust in further collaboration.

When solving problems, it is very important to follow a standardized protocol, with clearly defined responsibilities and prescribed sequence of activities, to use the appropriate problem solving tools, and to ensure adequate information within and outside the institution. Quality problems and complaints should be resolved in a timely manner and all procedures must be documented and traceable. In order to carry out the appropriate corrective actions and make them effective, it is necessary to carry out a root cause analysis of the problem. When analyzing the risks and problems associated with a particular product, materials and equipment, the impact on other products should be investigated, including the assessment of the need for product recall. The ultimate goal of all this activities is a continuous quality improvement.

2B-04-01

INTRODUCING THE I TRY IT PROGRAM

B Custer

No abstract available

2B-04-03

TTID RESEARCH FROM THE I TRY IT PROGRAM

A Al Riyami

No abstract available

Academy Day – Immunohaematology

2C-05-01

WHAT'S NEW IN THE KELL AND GERBICH BLOOD GROUP SYSTEMS

PC Ligthart

Immunohematology, Sanquin Blood Supply, Amsterdam, Netherlands

The 36 antigens of the Kell blood group system are expressed on a single pass glycoprotein encoded by the KEL gene. Most Kell blood group antigens have either a high (24 antigens), or a low frequency (11 antigens) in most ethnic populations. The K antigen has a frequency of around 10% in the Caucasian population and approximately 2% in people of African descent. In almost all cases the underlying genetic variation is a single nucleotide polymorphism, causing amino acid changes in the Kell glycoprotein, which can influence glycosylation and expression levels. Genotyping of these alleles is therefore quite easy and can be done on a large scale. Antibodies against Kell antigens have been reported to cause severe, immediate or delayed transfusion reactions. During pregnancy, Kell antibodies may cause severe forms of haemolytic disease of the foetus and the newborn, making intra uterine transfusions to the foetus necessary. This has been explained by the fact that Kell antibodies can suppress the development and proliferation of red cell precursors in the bone marrow. Many mutated KEL alleles have been identified that either cause a very low expression of Kell antigens (K mod phenotype) or no expression of Kell antigens (K null phenotype). The presence of these alleles can cause discrepancies between phenotype and genotype. Kell is expressed in complex with the XK protein. An impaired expression of XK also leads to low Kell expression. Furthermore, a link between the Kell protein and protein 4.1 has been described. This protein is a part of a membrane complex in which also the membrane structures that carry the Gerbich antigens are present.

The 11 antigens of the Gerbich blood group system are expressed on two different single pass glycoproteins that are encoded by one gene (GYPC). The presence of two different start codons cause the transcription of two different proteins; glycophorin C (GPC) and the shorter glycophorin D (GPD). Some of the antigens are expressed on either GPC or GPD, while others are expressed on both. The absence of antigens Ge2 and Ge3 is caused by GPC exon deletions and the presence of Ls[a] is caused by exon

rearrangements. The absence of the high frequent antigens GEPL, GEAT and GETI, and the expression of the low frequent antigens Wb, An[a], Dh[a] and GEIS are caused by point mutations in the GYPC gene. The genotyping of the gene rearrangements (Ls[a]+ or Ge-2 of Ge-2-3 phenotype) can be more difficult, whereas genotyping of the other antigens is much easier. Antibodies against Ge2 and Ge3 have been described as clinical significant in some patients, while in other patients no adverse reactions have been seen in case of incompatible transfusions. Anti-Ge2 and Ge3 can be responsible for a positive DAT in newborns. Where anti-Ge2 has not been correlated with severe HDFN, anti-Ge3 has been reported to be able to suppress erythroid progenitor cell growth (as seen with Kell antibodies). Beside a role for GPC and GPD in the structural make-up of the red blood cell, recently also a role as regulator for the function of the adhesion protein BCAM, carrying the Lutheran antigens has been proposed.

2C-05-02

AND NOW THERE ARE 49: UPDATE ON THE MNS BLOOD GROUP SYSTEM

C Gassner

Molecular Diagnostics and Research & Development, Blood Transfusion Service Zurich, SRC, Zurich-Schlieren, Switzerland

MN was the second blood group system to be discovered in 1927 (Landsteiner, Levine, ProcSocExpBiol NY, 1927). The first anti-S and anti-s antibodies were described 20 years later (Walsh, Nature, 1947; Levine, ProcSocExpBiol NY, 1951) defining the basic two couples of the antithetical «public antigens» M and N, and S and s of the MNS blood group system. MN and Ss are encoded by their lead-alleles GYPA*01/GYPA*02 of GYPA, and GYPB*03/GYPB*04 of GYPB, respectively. GYPE completes this tandemly organized locus on chromosome 4q31.21. Despite their homology, gene specific point mutations, especially when affecting splice-sites, account for the pronounced difference in length between the single-pass transmembrane peptides GPA and GPB, and contribute to the barely detectable expression of GPE.

With respect to additional antigens, MNS is probably 2nd only to Rh in its complexity. Any approach to understand, or systematically group its antigens, needs (a) their distinction into dominant «Low» and recessive «High Frequency Antigens» (LFA, HFA), (b) consideration of their genetic origin (GYP/A/B/E), and (c) description of the molecular event, causal of the variation. For instance, MNS10 (Mur), most likely originated from an ectopic (unequal) gene conversion event in between GYPB as the recipient and GYPA as a donor. Due to its hybrid character, the allele lacks «A» and «B» in its name, GYP*501 (GYP*Mur). The resulting GYP(B-A-B) hybrid gene has a hybrid-exon 3, with an active splice-site coming from GYPA. The expressed Mur antigen has LFA prevalence in Caucasians and Black Africans, but is a HFA in certain East Asian populations. Of course, such molecular events are rare, happened in time-frames, relevant for evolution, and might originally have affected only single individuals.

Originally identified in Swiss, two new LFA MNS15 (St[a]) alleles, GYP*501 type G and type H, were the first to be described with repeated observations among Caucasians. Both were duplicated GYP(B-A) hybrid genes, and clearly distinguishable from formerly known types A to F, according to their «fusion-points» within intron 3. They became apparent due to their N-like seropositivity, while genotyping GYPA*02 (N) negative (Meyer, Brit J Hematol, 2016). Also recently, and observed in individuals from Australia and Canada LFA MNS47 (SARA), has been described as a GYPA variant with a c.240G>T missense point mutation and was termed GYPA*47 on the allele level (McBean, Transfusion, 2014). In Australians and Germans, LFA MNS48 (KIPP, encoded by allele GYP*506), apparently originated from a mechanism comparable to GYP*Mur, though involving smaller parts of GYPA (Lopez, Transfusion, 2016; Scharberg, Gassner, unpublished observation). HFA MNS49 (JENU) is the «newest» MNS antigen, having obtained an ISBT number yet. It is antithetical to Mur. In other words, only GYP*501 (Mur) homozygous individuals are negative for JENU. Anti-JENU antibodies may therefore most likely be expected in people from East Asia, with highest probabilities for GYP*501 (Mur) homozygosity (Lopez, Transfusion, 2017).

In Black Africans, recent reports on the detailed molecular nature and prevalence of GYPB deletional haplotypes and their contribution to a reduced risk for Malaria invasion (Leffler, Science, 2017), plus independent research and development of genotyping assays for such deletions underlying the resulting S–s–U– phenotype, may soon allow for targeted and unambiguous molecular approaches towards this last(?) "MNS frontier" of molecular MNS5/antigen U negative detection (Gassner, this conference, 2018).

2C-05-03

KIDD BLOOD GROUP SYSTEM: OUTWARDLY SIMPLE WITH HIDDEN COMPLEXITY

J Hamilton

Immunohematology Reference Laboratory, American Red Cross-Southeastern Michigan Region, Detroit, MI, United States

The Kidd blood group system was originally described as a three antigen system, Jk[a], Jk[b], and Jk3, defined by two codominant autosomal alleles. The complexity of the system has expanded through molecular analysis of the JK protein.

Kidd system antigens are products of the urea transport gene SLC14A1 on chromosome 18. The glycoprotein has 10 transmembrane domains with intracellular N- and C- termini. Jk[a] (JK1) and Jk[b] (JK2) antigens result from a G838A change in exon 9 resulting in an Asp280Asn substitution in the fourth external loop.

The two antithetical alleles result in three common phenotypes: Jk(a+b-), Jk(a+b+), Jk(a-b+). Red cells of these phenotypes express the high prevalence Jk3 antigen. Red cells of 50% Caucasians or Asians are Jk(a+b+) while Jk(a+b-) and Jk(a-b+) phenotypes each occur in 25% of these populations. Individuals of African descent are largely Jk(a+): more than 50% are Jk(a+b-). Only 8% lack Jk[a]. The red cell antigens are unaffected by proteolytic enzymes or sulfhydryl compounds.

SNPs in JK*01 or JK*02 alleles encode weak or partial Jk[a] or Jk[b] antigens. The most common is JK*01W.01 (c.130G>A, p.Glu44Lys) identified in Caucasians, Asians, and Chinese. A very weak Jk[a] antigen is produced. Several alleles produce partial antigens as determined by the production of an apparent JKa/Jk[b] alloantibody in an immunized antigen-positive person. Five JK*01W and two JK*02W are currently recognized. Other than JK*01W.01, most are found in persons of African descent.

Lack of Jk3 antigen identifies the Jk(a-b-) phenotype. This rare phenotype generally results from inheritance of two recessive silencing alleles. It has greater frequency in Polynesian or Finnish populations. In 0.1–1.4% Polynesians, JK*02N.01 allele (c.342-1G>A) causes a splice-site mutation and deletion of exon 6. In Finns, the JK*02N.06 allele encodes a Ser291Pro substitution. Twenty-three null alleles are recognized and are found in individuals from multiple ethnic backgrounds. A very rare Jk(a-b-) phenotype is associated with a dominant inheritance pattern [In(Jk)]. The molecular basis was recently reported as the deletion of a C2H2 zinc finger-encoding domain in ZNF850 gene on chromosome 19.

The Kidd glycoprotein is a UT-B1 urea transport molecule in both kidneys and red cells. In renal function, it is important in regulating urea as part of urine concentration; erythrocyte JK protein insures structural stability as red cells pass through the kidney. Jk(a-b-) individuals have decreased urine concentrating ability but little other clinical sequelae. The resistance of Jk(a-b-) red cells to lysis by 2 M urea has been exploited as a simple test to identify this rare phenotype.

Kidd system antibodies are immune antibodies causing both immediate and delayed clearance of JK+ red cells. Anti-Jk3 produced by immunized Jk(a-b-) individuals is clinically significant. Kidd antigens are detectable on fetal red cells by 7–11 weeks gestation; however, hemolytic disease of the fetus and newborn due to JK antibodies, including anti-Jk3, is generally mild.

JK antigens may have a role in renal transplant. Acute graft rejection simultaneous with appearance of a JK antibody several years after transplant has been reported, especially when donor specific HLA antibodies are present.

In routine practice, red cell phenotyping for Jk[a] and Jk[b] antigens and identification of anti-Jk[a] and anti-Jk[b] is straightforward. The presence of weak or partial antigens and silenced alleles can add complexity to interpretation of the routine tests.

Academy Day – Clinical Transfusion Practice

2C-06-01

IS IT TACO, TRALI OR SOMETHING ELSE?

MR Looney

Medicine, University of California, San Francisco, San Francisco, United States

Blood transfusions are not uncommonly associated with the development of respiratory complications including transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO). TRALI is the leading cause of transfusion-related mortality in many countries and is associated with longer stays in the intensive care unit and in the hospital. TACO is the more common complication and is also associated with substantial hospital morbidity. Adjudicating cases of TRALI and TACO can be challenging as both are pulmonary edema states and

diagnostic tests that distinguish hydrostatic from permeability pulmonary edema are generally not available. Additionally, TRALI and TACO may co-exist in some cases. Another challenge is the diagnosis of TRALI in cases where major risk factors for the acute respiratory distress syndrome (ARDS) are present ("possible TRALI"). In this presentation, a case-based format will be used to highlight key features TRALI, possible TRALI, and TACO that can be used by transfusion medicine professionals to adjudicate cases of transfusion-related hypoxemia.

2C-06-02

NONE TOO SMALL: THE GLOBAL CHALLENGE OF SEVERE MALARIAL ANEMIA AND ITS TRANSFUSION SUPPORT

C Cserti-Gazdewich

Blood Transfusion Laboratory & Division of Hematology, University Health Network/ University of Toronto, Toronto, Canada

In endemic areas, the global burden of malaria and anemia converge together upon children, with severe malarial anemia (SMA) accounting disproportionately for demands on limited red blood cell (RBC) supplies. The attributable morbidity and mortality from this manifestation of severe malaria remain high, and improved outcomes hinge in part on the timeliness, sufficiency, and safety of transfusion support. The pathogenesis of SMA is complex, and depreciation kinetics (towards syndrome-defining hemoglobin levels of <50 g/L) occur acutely or insidiously, and in relation to the parasite burden and host response. Beyond mere hemolysis of parasitized erythrocytes, mechanisms of bystander erythrocyte loss (broadened erythrophagocytosis, toxic dyserythropoiesis, and ineffective erythropoiesis) figure prominently, lending insight to the parallel of non-infectious hyperhemolysis syndrome. Involuntarily undertransfused children with SMA in low-income countries (LIC) differ in numerous ways from those adults in high-income countries (HIC) who deliberately renounce transfusion. Despite youth-related advantages in the physiologic power to adapt to anemia, critical reductions in oxygen carrying capacity illustrate the hierarchical impacts of organ anoxia, be it in terminal cardiorespiratory events to irreversible neurocognitive impairments in survivors. When resources permit, the dynamics of restored oxygen delivery by transfusion are particularly observable in SMA, as the triggers to transfuse are so much lower (and the odds of corresponding lactic acidosis so much higher) than in HICs. Questions on the best hemotherapy approaches to SMA (or other severe anemias in LICs) remain, be these in dosage, pace of administration, component preparation, or matching options; these fundamental concerns now transcend those related to storage duration. In SMA, the problem of RBC breakdown from a persisting global scourge ultimately drives and faces the mandate to bank and deliver a life-preserving RBC supply for those with the most to gain (or otherwise lose).

2C-06-03

WHAT IS ECMO, AND WHY DO WE USE IT IN CRITICAL ILLNESS?

E Fan

No abstract available

Academy Day – Immunohaematology

2D-07-01

AFTER 70 YEARS, SEROLOGICAL RHD DETERMINATION IS STILL CHALLENGING: DNA TO THE RESCUE

M Pisacka

Reference Laboratory for Immunohaematology, Institute of Haematology and Blood Transfusion, Prague 2, Czech Republic

RhD antigen is, after the ABO system antigens, the most clinically significant blood group antigen. This reflect its high immunogenicity and potential to cause haemolytic transfusion reactions (HTR) and severe haemolytic disease of the newborn (HDN).

Thus the correct determination of D antigen is essential for safe transfusion strategy and adequate indications of anti-D immunoglobulin prophylactic administration. RhD determination challenge started in 1939 with a case history of fatal HDN and HTR in the mother after transfusion with blood of her husband. Subsequent finding of an antibody reacting with 80% ABO compatible RBCs in serum of afflicted woman lead to a hypothesis, that mother was lacking an antigen present on father's and fetal RBCs and her production od corresponding antibody was responsible for both HDN and HTR, which was proven to be correct. The effort describe the origin of causal antigen coincided next year with an animal immunization experiment developing a similarly reacting antibody by injecting Rhesus monkey RBCs into rabbits and guinea pigs, and also with another publication of HTRs after ABO compatible blood transfusions in patients with antibodies of apparently identical specificity. This first challenge in "pre-DNA" era has named a bit erroneously the human antibody defined antigen as Rhesus and 20 years later the animal antibody got a name LW. Meanwhile the complexity of Rh group of antigens increased and aiming to explain it several genetic models were suggested: Rh-Hr single gene, three genes C, D and E and finally two locus model (which was few years later disclosed by molecular analysis as the accurate one).

At the beginning the serological determination of RhD was done with human anti-D, first by direct agglutination (IgM), later also by Coombs test (IgG). Challenge at that times were weak D antigens, the term D^U (now obsolete) was used for those antigens negative in direct agglutination and positive in the Coombs test. Weakening of D antigen could be caused indirectly by the "position effect C in Trans") or directly (mutations in RHD gene, usually point mutations coding for amino acids in transmembranous and intracellular parts of the polypeptide, to date 161 alleles). Extremely weakened D antigens are called Del, these are serologically detected only by adsorption/elution tests (to date 45 alleles, multiple genetic mechanisms).

Next challenge was revealed in sixties by observation of qualitative D variants – partial D antigens. First cases were detected after development of allo-anti-D in D positive individuals – immunized against that part of D protein missed in their D epitope mosaic. Mutual reactivity of anti-D from these individuals with different partial D antigens established the basis for the classification. The increase of characterized partial D accelerated dramatically after the development of the mouse hybridoma technique and production of numerous different monoclonal anti-Ds. According to patterns of reactivity of different partial Ds after two international workshops the number of D epitopes reached 30. DNA techniques subsequently allowed refine the discrimination between partial D types (to date 115).

The number of described variants of D antigen will be sure higher after this ISBT congress and Working Party meeting. A further increase could be anticipated after NGS will bring new information and more data will come from large Asian and African populations and the polymorphic complexity of RhD and the whole Rh system will grow.

2D-07-02

GETTING COMFORTABLE WITH RH BLOOD GROUP SYSTEM TERMINOLOGIES AND DATABASES

FF Wagner[1,2]

[1]Laboratory department, Red Cross Blood Service NSTOB [2]MVZ am Clementinenhaus, Springe, Germany

Background: The number of known RH alleles is steadily increasing. Information on the alleles is dispersed among many publications and nucleotide database entries. As a result, description of known alleles as "novel" occurred due to a failure of identifying the prior description.

Aims: This overview aims to exemplify possible pitfalls in allele description, to give an overview on publicly accessible allele listings and to present the Human RhesusBase as possible information source for RHD.

Methods: Pitfalls in allele description were exemplified by incidents identified during data-entry into Human RhesusBase. Descriptive statistical analysis was based on the statistics module of Human RhesusBase.

Results: Automatic data extraction is limited by nucleotide database entries which contain errors included during submission and artefacts produced by high throughput sequencing efforts. Possible secondary information resources include the allele lists of ISBT, Erythrogene (www.erythrogene.com), Blood group mutation database (regrettably shutdown in Oct 2017) covering all blood group systems and the Human RhesusBase focused on RHD. Currently (20 Feb 2018), 573 RHD alleles are listed in Human RhesusBase, 453 in Erythrogene and 409 listed by ISBT. ISBT allele names are numerical or a combination of numbers and name and indicate weakened, non-expressed or DEL alleles. For example, weak D type 1 is denoted as RHD*01W.01 or RHD*weak D type 1. The Human RhesusBase is a web resource trying to collate

molecular and serologic information. Data are based on 141 publications and 543 nucleotide sequence database entries scanned and on the ISBT allele lists. On data entry nucleotide database sequences are checked versus a standard sequence to identify errors and to ensure a high quality of entered records. Still, data quality is limited by the primary information: No serologic information was available for 120 alleles, 221 were described as weak, 115 as partial, 87 as D negative and 45 as DEL (multiple assignments possible). The most prevalent mechanism was a single missense mutation (n = 272) followed by multiple missense mutations (78) and hybrid alleles (62). The number of alleles described per year was <10 prior to 1999, 13–22 (median 20) from 1999 to 2011, culminated with 66 alleles in 2012 and remains 25–47 (median 35) thereafter.

Summary/Conclusions: Web resources are an important aid to quickly find information on RH alleles. High quality data cannot be maintained without a manual check during data entry which may present a bottleneck. For RHD, the Human RhesusBase tries to collate data on molecular structure and serologic information. The number of alleles described per year remains almost constant indicating that there is more allelic diversity left to discover yet.

2D-07-03

DECISION MAKING IN COMPLEX OBSTETRIC CASES: HOW TO END UP WITH A HEALTHY BABY IN HDFN

M Delaney[1,2]

[1]*Pathology & Laboratory Medicine Division, Children's National Health System*
[2]*Pathology & Pediatrics Departments, George Washington University, Washington DC, United States*

In pregnant patients, the impact of blood type and the presence of red blood cell antibodies influences the course of the pregnancy and the health of the fetus and newborn infant. Throughout history, hemolytic disease of the fetus and newborn (HDFN) has played a fundamental role in the discovery of the blood group antibodies and their cognate antigens. The mid-1900's were noted for the advent of Rh immunoglobulin. Now, the technological advancements in diagnosis and treatment of HDFN have provided the critical tools needed to support mothers with affected pregnancies. The knowledge of blood typing has been further refined with the explosion of understanding about blood group genes, particularly in the RH blood group. Genomic blood group typing, improvements in ultrasound technology and transfusion medicine progress have advanced the field. The care of women with potentially affected pregnancies has never been more robust. Despite this, the risk to the fetus is significant, and prevention strategies for maternal alloimmunization deserve continued attention.

Academy Day – Cellular Therapies and Haemovigilance

2D-08-01

MICROBIAL SAFETY OF CELLULAR THERAPEUTICS – LESSONS FROM OVER TEN YEARS' EXPERIENCE IN MICROBIAL SAFETY OF PLATELET CONCENTRATES

M Störmer[1], E Wood[2] and B Gathof[1]

[1]*Transfusion Medicine, University Hospital of Cologne, Cologne, Germany*
[2]*Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia*

Bacterial safety of cellular preparations including blood products and stem cell preparations still present challenges for physicians, manufacturers and regulators. Although there have been many new approaches to enhance the microbial safety of cellular products during the last decade, established methods for microbiological control still need to be fully adapted to the special circumstances of cellular preparations. The experience from transfusion medicine regarding microbial safety of blood components has already demonstrated the variety of problems and risk factors for the development of new strategies for microbial safety.

Special attention has been given to strategies and recommendations for the prevention and detection of bacterial contamination of platelet concentrates. But so far

none of the targeted strategies for rapid detection or pathogen reduction have become routinely implemented worldwide, in part at least because development and requirements of new technologies and their implementation into the routine laboratory setting is a whole different problem. As a result, the classical microbiological control methods still represent the gold standard. But factors including the short shelf-life and nontraditional lot sizes for cellular and gene-therapy products are driving the need for rapid microbiological methods.

Significant changes in regulatory requirements have been made recently by revising chapters of the European Pharmacopeia or by the FDA making changes to the requirements to address the needs of next-generation therapies. The other side of the coin is that standardized conditions will require extensive validation based on the conception of the corresponding authorities.

In conclusion, lessons from the microbial safety of platelet concentrates enable us to understand that the detection or reduction of bacteria represents a more difficult challenge in comparison to viruses and that cellular products with different formulations and shelf-lives may present different challenges. Recent regulatory changes demonstrate that we are getting closer to the goal of a shift from the traditional view of sterility evaluation (identify and inactivate anything and everything) to a new thinking about microbiological control.

2D-08-02

ADVERSE OUTCOMES AND SUBSTANCES OF HUMAN ORIGIN: CASES FROM THE NOTIFY LIBRARY

E Petrisli[1], B Whitaker[2,3], M Gandhi[4], E Muñiz-Diaz[5], J Menitove[6], A Navarro[7,8], C Carella[1], D Strong[9] and A Nanni Costa[1]

[1]*Italian National Transplant Centre (CNT), Italian National Institute of Health, Rome, Italy* [2]*AABB, Bethesda, MD* [3]*FDA, Silver Spring, MD* [4]*Division of Transfusion Medicine, Mayo Clinic, Rochester, MN, United States* [5]*Immunohematology Reference Laboratory, Banc de Sang i Teixits (BST), Barcelona, Spain* [6]*Retired, United States* [7]*Banc de Sang i Teixits (BST)* [8]*Catalan Transplant Organization (OCATT), Barcelona, Spain* [9]*Department of Orthopaedics and Sports Medicine, University of Washington, School of Medicine, Seattle, WA, United States*

Background: Blood components, corneas, hematopoietic progenitor cells (HPC), kidneys and gametes can improve, and often, save lives. They can be grouped under the term "Medical Products of Human Origin" (MPHO), since they require a human donor and share exposure to risk from breaches of ethical and safety standards, for example the risk of disease transmission. Lessons learned from the adverse occurrences (AO) associated with such human-derived products should be shared as widely as possible in order to maximize donor and recipient safety.

Aims: The Notify Library (www.notifylibrary.org) is a joint global initiative, cosponsored by the World Health Organization (WHO) and the Italian National Transplant Centre (CNT), that supports the sharing of published vigilance information for teaching purposes and for greater public transparency on the clinical use of MPHO in the settings of transplantation, transfusion and assisted reproduction

Methods: Since 2012, AO identified primarily by literature review and associated with MPHO are collected and analyzed by dedicated editorial groups of international experts in the Notify Library. Categories of occurrences that are analyzed include transmitted infections, malignancies, donor reactions, clinical complications and process-related incidents. In order to facilitate a structured database search, all cases have been classified according to an AO type (Harm to a recipient, Harm to a donor, Harm to a fetus or offspring, Risk of harm) and an MPHO type (Organs, Blood, Cells, Tissues, etc.) taxonomy. The experts have reviewed cases to identify alerting signals, latency, frequency and methods of confirmation of imputability. Blood experts joined the editorial groups in 2015 and since then haemovigilance records are also incorporated in the database.

Results: The Notify Library contains 2,457 references linked to 1,558 didactic cases: 596 organs, 331 blood/blood products, 290 cells, 259 tissues, 69 reproductive tissues and cells, 9 derived medicinal products, 4 other. Of the 331 reports of AO associated with blood/blood products, 57% are related to red blood cell transfusion, 21% to platelets, 11% to plasma, 7% to whole blood, 1% to granulocytes, and the remainder are not specified. Of the 88% of blood reports that have been classified under Harm to recipient, 49% of reports are immunological in nature, including delayed hemolytic transfusion reactions (DHTR, 33%), acute hemolytic transfusion reactions (AHTR, 28%), delayed serologic transfusion reaction (DSTR, 15%), transfusion related acute lung injury (TRALI, 13%), allergic reactions (7%) and other (4%) (Whitaker, Immunohematology, 2017). Of the 91 cases of infection transmission, 49% are bacterial, 35% viral, 12% parasitic, 2% fungal and 2% prion. Of the 283 records of AO associated with HPC (46% marrow, 44% apheresis, 8% cord blood, 2% source not

specified), 42% have been classified under Harm to a recipient, 50% under Harm to a donor and 8% under Risk of harm.

Summary/Conclusions: In conclusion, the NOTIFY Library is an important resource for the collection and description of AO in transplantation, transfusion and assisted reproduction. The Library aims to support clinicians, competent authorities, potential donors and recipients to better understand and reduce the risks associated with the donation and clinical application of MPHO.

2D-08-03
SAFETY AND SURVEILLANCE ISSUES IN STEM CELL MARKETING

D Sipp

No abstract available

Donors and Donation – Clinical Effect of Iron Deficiency

3A-S01-01
THE EFFECT OF IRON ON FETAL AND NEONATAL BRAIN DEVELOPMENT

M Georgieff

Pediatrics/Neonatology, University of Minnesota Medical Center, St. Paul, United States

The brain undergoes rapid growth and development during late fetal and neonatal life. During this development, the brain consumes 60% of the body's total oxygen consumption much of it for the purpose of neuronal growth, differentiation and synaptogenesis. The fetal brain is thus highly dependent on substrates that support that rate of oxygen consumption and ATP generation. Among these substrates, iron is critical for incorporation into cytochromes that mediate electron transport. Iron is not only necessary for neuronal energy demands but also for synthesis of neurotransmitters (eg, dopamine, serotonin) and myelin. Recent data show that iron also regulates fetal and neonatal neuronal gene expression through epigenetic modification of chromatin.

Multiple gestational and early postnatal conditions place the newborn at risk for total body and brain iron deficiency. These include severe maternal iron deficiency, hypertension (pre-eclampsia), diabetes mellitus and smoking. Postnatal conditions include premature birth, phlebotomy induced anemia, restrictive transfusion practices and rapid growth. Under conditions of negative iron balance, the fetus and neonate prioritize iron to red cells for hemoglobin synthesis at the expense of all other organs including the brain. A 33–40% reduction of brain iron concentration has been measured in the iron deficient neonate. Iron deficient neonates demonstrate poor recognition memory, a finding that continues through the pre-school years and is accompanied by planning difficulties in late childhood.

Pre-clinical models of this degree of iron deficiency demonstrate profound effects on myelination, dopaminergic neurotransmission and neuronal structure and function. The structural and functional deficits include altered cerebral metabolism including reduction in glutamatergic neurotransmission and altered cerebral phospholipids indicative of abnormal myelination. The structural abnormalities include reduced dendritic arborization and smaller synaptic spine heads. These are accompanied by a loss of electrical potential in the hippocampus, the area of the brain the serves recognition memory processing. Genetic models of neuronal specific iron deficiency in mice demonstrate a critical period for iron in hippocampal neuronal development in late fetal and early neonatal life. Failure to provide adequate neuronal iron during the critical period results in large scale alterations to synaptic plasticity gene expression that persist into adulthood in spite of iron repletion after the critical period. It is important to define that critical period in humans.

This talk will discuss the role of iron in brain development and early life brain function and will review the clinical conditions that lead to compromised fetal and neonatal iron status and its neurodevelopmental consequences across the lifespan.

3A-S01-02
THE EFFECT OF BLOOD DONATION OF WOMEN ON THE BIRTHWEIGHT OF THEIR OFFSPRING

H Ullum[1], A Rigas[1], O Pedersen[2], E Sørensen[1], L Thørner[1], K Nielsen[3], K Titlestad[4], M Larsen[1], G Edgren[5], K Rostgaard[6], C Erikstrup[7] and H Hjalgrim[6]

[1]*Department of Clinical Immunology, Copenhagen University Hospital, Copenhagen* [2]*Department of Clinical Immunology, Næstved Hospital, Næsteved* [3]*Department of Clinical Immunology, Aalborg University Hospital, Aalborg* [4]*Department of Clinical Immunology, Odense University Hospital, Odense, Denmark* [5]*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden* [6]*Department of Epidemiology Research, Statens Serum Institut, Copenhagen* [7]*Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark*

Background: The prevalence of iron depletion is high among pre-menopausal women, who donate blood frequently. Little is known about possible health-related consequences of iron depletion, but studies in non-donor populations indicate that iron deficiency anemia is associated with an increased risk of low birth weight as well as other adverse pregnancy outcomes. This prompts concerns that iron deficiency induced by frequent blood donation might impair subsequent fetal growth. So far this has been addressed only in a recent Canadian study reporting no association between pre-pregnancy donation intensity and risk of low birth weight (<2500 g) in offspring.

Aims: To validate and expand the Canadian observations, we used the Scandinavian Donation and Transfusion Database (SCANDAT) and national registers to assess whether pre-pregnancy donation intensity affects birth weight of singletons born at term (gestational week 38 or later) to nulliparous female donors in Denmark.

Methods: We identified 293,897 first live singleton births to Danish women between 1997 and 2012 with complete information on: gestational age, birth weight, child sex, parental ages, maternal smoking status during pregnancy, and parental education length and annual income. Linear regression analysis was applied with birth weight as outcome, number of donations 3 years prior to pregnancy as explanatory variable, and confounding variables as described. Similar analyses were performed comparing the following groups: high intensity donors (≥6 donations 3 years prior to pregnancy), low intensity donors (1–5 donations 3 years prior to pregnancy), and non-donors (no donation history before pregnancy). Lastly, in sub-analyses paternal donation intensity was used to evaluate whether an internal healthy donor effect affected the observed associations (women in these analyses were non-donors).

Results: Of the identified women, 91.3%, 7.5%, and 1.2% were non-donors, low intensity donors, and high intensity donors, respectively. Generally, female blood donors were older, less likely to smoke during pregnancy, and had longer educations than female non-donors. Low intensity donors gave birth to larger babies (3538 g) than both non-donors (3508 g; P < 0.001) and high intensity donors (3512 g; P = 0.002). In adjusted linear regression analysis considering donation intensity 3 years before the pregnancy, offspring birth weight decreased by 10.5 g (95% confidence interval (CI): 3.3–17.7 g) per donation per year. Similar estimates were observed for donation intensity time-windows of 5 and 7 years. Correspondingly, in adjusted analyses high donation activity resulted in a 20.2 g (95% CI: 5.1–35.3 g) lower birth weight compared with low intensity activity. In similar adjusted linear regression analysis high intensity paternal donors (≥6 donations 3 years prior to pregnancy) had no effect on subsequent birth weight compared with low intensity paternal donors (1–5 donations 3 years prior to pregnancy, regression coefficient: −2.3 g; 95% CI: −19.8 to 15.1; P = 0.79; n = 12,310).

Conclusions: High pre-pregnancy donation intensity is inversely associated with birth weight of singletons born at term to nulliparous women. We recommend that pre-menopausal female blood donors should be screened for iron deficiency. Moreover, it is of paramount importance that these findings are confirmed in other cohorts.

3A-S01-03
EXAMINING THE RELATIONSHIP BETWEEN REPEATED BLOOD DONATIONS IN FEMALE DONORS ON MATERNAL AND NEONATAL OUTCOMES: A COHORT STUDY

M Chassé[1], D Fergusson[2], M Murphy[2], G Smith[3], M Goldman[4], S O'Brien[4], M Walker[2], A Sprague[5], C van Walraven[2], K Wilson[2] and A Tinmouth[2]

[1]*Centre Hospitalier de l'Université de Montréal, Montreal* [2]*Ottawa Hospital Research Institute* [3]*Institute for Clinical Evaluative Sciences* [4]*Canadian Blood Services* [5]*Better Outcomes Registry & Network, Ottawa, Canada*

Background: Iron deficiency is a common problem in women of child bearing age and is known to be associated with adverse maternal and newborn outcomes. Repeated blood donations deplete iron stores and decrease hemoglobin levels.

However, the clinical impact of iatrogenic iron deficiency due to blood donation is unknown. Additional investigations into adverse outcomes associated with blood donation are required.

Aims: The objective of this study was to assess the association between repeated blood donations in female donors of child-bearing age and the associated risk of maternal and neonatal outcomes.

Methods: We undertook a longitudinal cohort study of all females who delivered a live or stillbirth infant in Ontario, Canada between 1 January 2010 and 31 March 2012 using data from the Better Outcomes Registry & Network, Canadian Blood Services and the Institute of Clinical Evaluative Science. Only a woman's first pregnancy within the study time frame was included for analysis. Women <18 years or >50 years of age at the time of delivery were excluded, as were multiple birth pregnancies. Records on all female donors who made whole blood donations between 1 January 2007 and 30 September 2013 were obtained from Canadian Blood Services. Data from the various sources were combined using probabilistic linkage. The primary outcome was diagnosis of a small for gestational age neonate. Secondary outcomes were preterm birth, stillbirth, APGAR <4 at 5 min, cord pH <7, neonatal death, maternal transfusion, infection, pre-eclampsia, gestational hypertension, gestational diabetes, placental abruption and maternal death. Regression models evaluated the effect of repeated donation and the time interval between donations on outcome development. Models were adjusted for maternal age at delivery, maternal BMI, maternal alcoholism, drug use and smoking, maternal diabetes and hypertension, use of assisted reproduction technologies, maternal deprivation quintile, ethnic concentration quintile, parity, and time since previous delivery.

Results: 260,048 women delivered live or stillbirth infants between 1 January 2010 and 31 March 2012. 8,831 (3.4%) women were whole blood donors, with a mean of 2.58 ± 2.34 donations during the study period. Mean maternal age at the time of delivery for non-donors and donors were 30.30 ± 5.38 yrs and 29.72 ± 4.92 yrs, respectively. Small for gestational age occurred in 23.646 (9.4%) of neonates born to non-donors, and 589 (6.7%) born to donors. The preterm birth rate was 6.0% and 5.5% among non-donors and donors, respectively. The adjusted odds ratio for risk of a small-for-gestational age neonate was 0.915 (95% CI 0.890, 0.941) with each additional donation. Proximity of donation to conception had no effect on risk of SGA. Secondary analyses are ongoing.

Summary/Conclusions: While there is evidence that repeated blood donations may result in anemia in female donors, our preliminary data suggest that there is no association between repeated blood donations prior to pregnancy and risk of a small for gestational age neonate, and confirm findings in other jurisdictions. Although possibly a result of a healthy donor effect, our findings are reassuring to female donors as well as clinical and blood organization stakeholders seeking to inform policy decisions.

3A-S01-04

IRON DEFICIENCY AND DEPRESSIVE SYMPTOMS AMONG FEMALE BLOOD DONORS – RESULTS FROM THE DANISH BLOOD DONOR STUDY

M Didriksen[1], C Mikkelsen[1], AS Rigas[1], E Sørensen[1], MH Larsen[1], KR Nielsen[2], KS Burgdorf[1], OB Pedersen[3], HM Paarup[4], C Erikstrup[5], H Hjalgrim[6,7], LW Thørner[1] and H Ullum[1]

[1]Clinical Immunology, Copenhagen University Hospital, Rigshospitalet, Copenhagen [2]Clinical Immunology, Aalborg University Hospital, Aalborg [3]Clinical Immunology, Nastved Sygehust, Nastved [4]Clinical Immunology, Odense University Hospital, Odense [5]Clinical Immunology, Aarhus University Hospital, Aarhus [6]Epidemiology Research, Statens Serum Institute [7]Hematology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

Background: Recent research suggests an association between levels of circulating ferritin and depression, and several studies have shown an increased prevalence of depressive disorder in patients with iron deficiency anemia. However, findings have been inconsistent and large population-based studies of the possible association are needed. Because blood donors are at increased risk of iron depletion it is imperative that potential links to depressive symptoms are explored.

Aims: To investigate the association between iron deficiency (ID) and depressive symptoms in blood donors. Further, to clarify if ID is associated with specific depressive symptoms.

Methods: A cross-sectional cohort study including 3262 women enrolled in the Danish Blood Donor Study. Depressive symptoms data were collected using the Major Depression Inventory (MDI), a self-report mood questionnaire, which assesses the presence of 10 depressive symptoms and has been validated in the general Danish population. Experience of depressive symptoms was defined as an MDI score ≥20

(range: 0–50). Data on antidepressant prescriptions, demographic and lifestyle factors were collected using a health-related questionnaire and from national population registers. ID was defined as a ferritin level <15 ng/ml. Further, the participants' mean corpuscular volume (MCV) was examined, where MCV≤83 fL indicated low iron. Ferritin levels were measured in thawed EDTA-anticoagulated plasma samples using a commercial assay on an automated system (Ortho Vitros 5600). MCV was measured in whole blood samples using Sheath flow Direct Current (Sysmex XN-1000). Descriptive statistics and multivariable linear, logistic, and cox regression analyses were performed. Analyses were adjusted for age, body mass index, smoking habits, and alcohol consumption. The Cox regression analyses were also adjusted for the number of blood donations since iron measurement.

Results: ID was found in 4.0% (n = 129) and 4.7% (n = 154) classified with depression. ID women had higher MDI scores (median: 6; interquartile range (IQR): 3–11) compared to women with normal ferritin levels (5; 2–8) (P = 0.002). Both ferritin and MCV were negatively correlated with MDI score (ferritin (ng/ml): regression coefficient (RC) = −0.51, P = 0.009; MCV (fL): RC = −0.06, P = 0.011). Further, ID women had increased odds for depressive symptoms compared with non-ID women (odds ratio (OR) = 2.32; 95% >confidence interval (CI): 1.29–4.20). Similar risk was found in women with low MCV (OR = 1.92; CI: 1.09–3.38). However, MCV was not an independent predictor of depressive symptoms with ferritin levels included in the model (P = 0.103). Among participants with depressive symptoms, the dominating symptom was "a feeling of lacking energy and strength", and ID women had increased odds for experiencing this particular symptom (OR = 2.11; CI: 1.03–4.31). ID was not statistically significantly associated with any other particular MDI-defined symptom. Finally, ID women had statistically insignificantly increased hazards for subsequent use of antidepressants (hazard ratio = 1.45; CI: 0.82–2.53).

Summary/Conclusions: A low ferritin level was associated with an increase in depressive symptoms in this large population of female blood donors. Because of the observed symptom pattern it is possible that the classification of depressive symptoms in this study mimics the natural effects of having a low ferritin level. Further studies are needed to clarify if ID is part of an underlying pathophysiological mechanism of depression.

Immunobiology – Red Cell Serology

3A-S02-01

DRUG-INDUCED HEMOLYTIC ANEMIA

DR Branch[1,2]

[1]Centre for Innovation, Canadian Blood Services [2]Medicine, University of Toronto, Toronto, Canada

It has been more than 50 years since the first reports of penicillin- and α-methyl-dopa-induced haemolytic anaemias emerged. Since these initial observations in 1966, that high-dose intravenous penicillin can result in a penicillin-antibody-dependent immune haemolytic anaemia and patients receiving α-methyldopa developed haemolytic anaemia similar to warm autoimmune haemolytic anaemia, cases of patients having a drug-induced haemolysis has expanded greatly to include a myriad of different drugs. Indeed, there are now well over 100 drugs that have been described as causing immune-mediated haemolysis. The history of drug-induced immune haemolytic anaemias can be subdivided into two different chapters: (1) The penicillin and methyldopa chapter and (2) the cephalothin and cefotetan chapter. In this review, these two chapters in the history of drug-induced immune haemolytic anaemias will be dissected, including the different mechanisms of haemolysis that have been proposed. These include so-called hapten, immune-complex, drug adsorption and autoimmune mechanisms. The biochemical and immunological mechanisms of drug-induced immune haemolytic anaemias will be discussed as well as important considerations in the approach to the laboratory investigation of these conditions in the blood bank and reference laboratories. An approach to the use of drug metabolites as well as a hypothesis as to how "nonspecific' drug adsorption occurs and how it can be prevented will be presented. The objective of this review will be to provide an up-to-date understanding of the types of drug-induced immune haemolytic anaemias, their differentiation in the laboratory and the biochemistry and immunology underlying these conditions.

3A-S02-02

DRUG–INDUCED HEMOLYSIS DUE TO IMATINIB AND IOMEPROF: TWO CASE REPORTS OF A RARE ADVERSE EVENT

TN Nguyen[1], E Maenulein[1], V Fihman[2] and J Moh Klaren[1]

[1]Medical Biology Laboratory, French Establishment of Blood, Ile de France, Site Saint-Antoine Paris, France [2]Medical Biology Laboratory, French Establishment of Blood, Ile de France, Site Tenon, Paris, France

Background: Drug-induced immune hemolytic anemia (DIIHA) is a rare, underdiagnosed condition. Two patients were suspected of having immune hemolytic anemia (IHA) due to imatinib and iomeprol respectively. Patient 1, a thirty-year-old man with a gastrointestinal stromal tumor (GIST) metastatic to the liver was treated with imatinib 400mg twice daily (after an initial dose of 400mg daily) when he developed an anemia (Hb= 80g/L) with evidence of hemolysis. Imatinib is an inhibitor of tyrosine kinases indicated in the treatment of chronic myeloid leukemia (CML) and metastatic GISTs . A first case of imatinib-induced HA has been previously reported in a patient with CML. The antibody was immunoglobulin IgG detected solely by the "drug adsorption" method. Patient 2, a forty-one-year-old woman with a history of recurrent ovarian cancer, developed a hemorragic shock associated with a severe IHA (Hb =30g/L) when she underwent a computerized tomography scan of the abdomen after receiving an infusion of iomeprol. Iomeprol is a nonionic contrast medium (CM), widely used in diagnostic imaging procedures.
Aims: The aim of this study was to support a clinical diagnosis of DIIHA.
Methods: Laboratory studies included direct and indirect antiglobulin tests (DAT and IAT). Drug antibodies investigation was performed by incubating patient's serum (adsorbed serum) or eluate in the presence of drug against random normal donor red blood cells (RBCs) that had not been previously treated with the drug (i.e., by the so-called "immune complex" method). To determine the immunoglobulin class of the reactive antibody, the test was repeated after incubation of patient 2' s serum with 0.01 M dithiotreitol (DTT). Drugs tested included imatinib, iomeprol and iodixanol, another widely used nonionic CM.
Results: Patient 1 had a negative DAT and no unexpected RBCs antibodies were detected by IAT in patient 's serum without the in vitro addition of the drug. A weakly reactive (1+) antibody directed against enzyme-treated normal donor RBCs was demonstrated in patient 's serum both by the tube and gel test in the presence of imatinib. Patient 2 had a positive DAT(anti-IgG= 2,5+; anti-C3d=2+) and evidence of a warm autoantibody in the patient's serum. An IgG+IgM activating-complement antibody directed against untreated random normal donor RBCs in the presence of iomeprol was demonstrated in patient's adsorbed serum (titer 8) but not in eluate. There was no evidence of anti-iodixanol in patient's serum and eluate. The pool of normal sera did not react in the presence of drug in the two cases.
Summary/Conclusions: Two patients with HA were demonstrated to have drug-dependent antibodies. We describe an example of a DAT negative HA associated with imatinib and report for the first time that imatinib-dependent antibody could be detected by the "immune complex" method in a patient with metastatic GIST (Patient 1). Patient 2 appeared to have iomeprol-dependent IgG+IgM antibody which did not show cross-reactions with iodixanol. As iomeprol is commonly used in diagnostic imaging, anti-iomeprol should be considered whenever patients undergoing various radiographic procedures develop hemolytic anemia and/or positive DAT.

3A-S02-03

NEW APPROACHES TO ELIMINATE CD38 MONOCLONAL ANTIBODIES RELATED INTERFERENCE IN PRE-TRANSFUSION TESTING

T Tremblay[1], N Baillargeon[2], M Chevrier[2] and L Loubaki[1]

[1]Affaires Médicales et Innovation [2]Laboratoire de référence et des cellules souches, Héma-Québec, Québec, Canada

Background: Immunotherapeutic strategies are emerging as novel therapeutic approaches in multiple myeloma, with several monoclonal antibodies (mAbs) being in advanced stages of clinical development. Of these, Daratumumab (Dara), an anti-CD38 mAb currently used in the treatment of patients with refractory multiple myeloma, is very promising. Blood samples from patients being treated with Dara demonstrated panreactivity in red blood cell (RBC) panel testing due to the expression of CD38 on RBCs, complicating the identification of clinically significant alloantibodies. It has been shown that the treatment of RBCs with dithiothreitol (DTT) allows the elimination of CD38 however, this treatment also eliminates other antigens, some of which being of clinical importance. Thus, treatment with DTT is an imperfect solution to a problem whose incidence is increasing.

Aims: To find adaptable methods, applicable to most therapeutic antibodies, to counter the interference in pre-transfusion testing without affecting the detection of other antibody of interest.
Methods: Two approaches were evaluated: 1) pre-treatment of panel RBC with a mouse anti-human CD38 neutralizing antibody prior to serological testing; 2) depletion of Dara from the plasma samples by adsorption on CD38-expressing Daudi cells prior to serological testing. Both methods outcomes were evaluated by flow cytometry and by gel card.
Results: Flow cytometry analysis revealed that pre-treatment of RBC panel with a monoclonal mouse anti-human CD38 resulted in a significant reduction of Dara binding signal (8 fold reduction of the mean fluorescence intensity (MFI)). However, gel LISS result showed no significant reduction of the interference. Pre-incubation of plasma from Dara patients with Daudi cells resulted in a significant reduction of the Dara binding signal (22 fold reduction of the MFI) in flow cytometry which was associated to the absence of interference in gel LISS assay.
Summary/Conclusions: Incubation of plasma from Dara-treated patients with Daudi cells can efficiently overcome the interference induced by this latter in serological testing.

3A-S02-04

BLOOD TRANSFUSION MANAGEMENT IN THE NEW ERA OF IMMUNE THERAPY: EXPERIENCE FROM THE BELGIAN RED CROSS BLOOD SERVICES

E Lazarova, V Pede, M Emonds, A Muylaert, P Vandekerckhove and V Compernolle
Blood Services, Belgian Red Cross-Flanders, Mechelen, Belgium

Background: Daratumumab (anti-CD38), already in use as monotherapy for adult patients with relapsed and refractory multiple myeloma, recently received the extended approval as a second line therapy in EU. This medication, however, interferes with routine blood bank tests by direct binding to CD38 expressed on reagent red blood cells (RBCs) or on cross-matched RBCs. A number of different methods exists to eliminate or bypass the anti-CD38 effects: dithiothreitol- or trypsin-treated reagent RBCs, cord RBCs, antigen-matched RBC transfusions guided by patient phenotyping or genotyping, and anti-CD38 neutralization. Unfortunately, there is no consensus on the best method or combination of methods to be used. The following transfusion policy was implemented by the Belgian Red Cross in Flanders region: RBC genotyping for clinically significant antigens was provided to patients before starting anti-CD38. Afterwards, on demand, blood was selected on the basis of extended donor phenotype and patient's genetically predicted phenotype.
Aims: We aimed to analyze 1 year after implementation if our transfusion policy was efficient, safe and adequate to the increasing demand of transfusions in immune therapy settings.
Methods: The study period was from November 2016 till November 2017. Patient molecular RBC typings were performed by RBC-FluoGene vERYfy PCR-SSP kit (Inno-Train). In the Rh system, C, c, E, e and Cw alleles are detected. Furthermore, blood groups Kell (KEL1/KEL2), Kidd (JK1/JK2), Duffy with the alleles FY1(A), FY2 (B), FYX and Fynull (GATA-box mutation), and MNS with the alleles MNS1(M), MNS2(N), MNS3(S), MNS4(s), U+var (P2) and U+var (NY) are tested. Regular blood group O and A donors are continuously phenotyped in Kell (K, k), Duffy (Fya, Fyb); Kidd (Jka, Jkb); MNS (S,s) systems.
Results: A total of 425 patient RBC molecular typings were performed. Over 130 patients enrolled in anti-CD38 treatment were genotyped (32.8% of all RBC genotypings). With an average of 24% of phenotyped active donors, resulting in 25.640 phenotyped blood group O RBCs and 13.653 phenotyped blood group A RBCs available for distribution, we were able to address the actual blood transfusion need for these patients. A total of 195 antigen-matched units were selected at our blood bank laboratories and were transfused to a total of 27 patients. No adverse transfusion events were reported. One of the patient presented a rare blood group antigen combination (O positive ccEE, K- k+ Fya- Fyb+ Jka+ Jkb+ M- N+ S+ s-) resulting in a complete phenotype with a combined incidence of 0.009%. A total of 22 pheno-identical donations were successfully transfused to this patient for a 3 month-period.
Summary/Conclusions: The selection of antigen-matched RBCs to support transfusion decisions is already common practice in complex clinical situations with panreactivity (e.g. auto-immune hemolytic anemia). Patients receiving Daratumumab could be successfully managed in the same manner. This approach avoids time and labor consuming pre-transfusion serologic techniques for CD38 elimination. Delay in issuing of RBC units is prevented too. If in the future Daratumumab becomes more widely used, the availability of convenient laboratory tests to cross match RBCs may become critical for adequate blood supply.

3A-S02-05

SUMMARY OF 2017 UK BENCHMARKING DATA FOR TRAINING ASSESSMENT AND COMPETENCY TOOL (TACT) – EVALUATION OF ERRORS AND USE FOR EDUCATIONAL REVIEW

CL Whitham, J White and M Rowley

UK National External Quality Assessment Service, (UK NEQAS BTLP), Watford, United Kingdom

Background: In the UK, Transfusion Laboratory Managers (TLMs) must comply with legislation, ISO 15189 accreditation standards, and UK Transfusion Laboratory Collaborative (UK TLC) standards to deliver comprehensive training and competency assessment for staff in transfusion laboratories. Increasing workload and retiring experienced staff add resource-related pressure to this task. Additionally, changing pathology service delivery models necessitate training and assessment of staff from other areas of blood sciences with little background in transfusion. These resource restraints contribute to the laboratory errors reported to Serious Hazards of Transfusion (SHOT) and errors in EQA. TACT was introduced in 2014 to support TLMs by providing resource-saving, continual, 'real-time' monitoring of knowledge based competency.
TACT is available 24/7 and complements existing practical competency schemes and EQA. Multiple variations on a standard pre-transfusion testing scenario are generated using controlled randomisation; logic rules for the automatic assessment of sample acceptance, ABO/D, antibody screen (ABS) and identification (ABID), and component issue are based on BSH guidance. TLMs can re-run participations with staff as an educational process to identify training needs, and can amend results to accommodate local policy or for other (locally auditable) reasons e.g. unfamiliarity with TACT, typographical error.
Aims: The aims were to determine areas where BMS training may be required, how TACT participation is being monitored by TLMs and to compare TACT, EQA and SHOT data.
Methods: TACT data from 01/01/2017 to 31/12/2017 was examined to determine error rate by complexity, and the extent of managerial review. Complex assessed elements are uninterpretable ABO and/or D groups, and situations where ABO specific blood is inappropriate or there are additional 'specific requirements' for red cells.
Results: Overall, 3377/88883 (3.8%) assessed elements were incorrect before review. 2189/3377 (66%) underwent TLM review and 1115/3377 (33.0%) were amended, reducing the overall error rate to 2.5%. 172/601 (28.6%) incorrect participation scores for ABO were amended by TLMs to correct, for D 180/512 (35.2%), for request acceptance 86/199 (43.2%), 239/770 (31.0%) for ABID, 134/180 (74.4%) for ABS and for component selection 304/1115 (27.3%). Error rates pre-review for 58852 assessed elements categorised as 'complex' or 'simple' were: ABO grouping 53/481 (11.0%) complex cf. 133/6503 (2.0%) simple, D typing 45/481 (9.4%) cf. 117/6503 (1.8%) and red cell component selection 153/358 (42.7%) cf. 608/4637 (13.1%).
Summary/Conclusions: Complex elements generated a higher error rate; the greatest being for complex component selection, supporting SHOT and EQA findings. In 2016, SHOT data included 253/331 incorrect blood component cases when specific requirements were not met; 49% originated in the laboratory. In a 2017 EQA exercise 22.8% of laboratories issued ABO specific blood in an emergency before completing all BSH recommended testing. The TLM error review rate is encouraging, demonstrating TACT's potential for education and training, as well as for monitoring competency. TACT has been updated to accommodate misspelling of 'positive' and 'negative' influencing the amendment rate for ABS. Amended sample acceptance errors may reflect local policy differing from national guidance. We plan to investigate all reasons for amendment and continue to develop TACT to monitor and address issues highlighted in EQA and SHOT data.

Cellular Therapies – ATMP

3A-S03-01

CORD BLOOD EXPANSION WITH NOVEL SMALL MOLECULE

G Sauvageau[1,2,3]

[1]IRIC, Université de Montreal [2]Division of Hematology, Maisonneuve-Rosemont Hospital [3]Department of medicine, University of Montreal, Montreal, Canada

Hematopoietic stem and progenitor cell (HSPC) transplantation is the most commonly used stem cell-based curative therapy in the medicine, but a considerable fraction of patients will not find a suitable unrelated matched donor. For these patients the umbilical cord blood (CB) represents a highly promising source of HSPCs. Broader availability of CB transplants is mostly limited by low cell numbers associated with high transplant related mortality (TRM). We identified a small molecule UM171 that enables ex vivo expansion of HSPCs with short- and long- term repopulating ability. The associated fed-batch culture system allows for small culture volumes, reduces the cost and labor, and has been approved for clinical applications. In the phase I/II clinical trial we are testing the safety and efficacy of expanded CB (eCB). Between 6/16-7/17, 16 adults were transplanted with a single eCB (13 pts) or with an eCB and a neCB (3 pts). Median 1st days of 100 and 500 neutrophils were day+10 and day+19, respectively. eCB recipients were fever-free on day+7 compared to day+15 determined for recipients of peripheral blood- or bone marrow-derived HSPSc, and hospitalization was reduced by 11 days compared to non-expanded CD transplants. Full donor chimerism was achieved in all cell subsets. This expansion protocol enabled utilization of smaller, but better matched CB for 11/16 patients, and 2 received a single CB instead of a double CB. With a median follow up of 4 months (range 1–13), there has been no TRM, 1 grade 3–4 acute GVHD and 2 mild chronic GVHD. Preliminary data thus suggested that a 7-day UM171 eCB provides clinical benefit beyond faster engraftment, better HLA matching and low TRM. Transcriptome analyses indicated that CB CD34^{+} cells respond to UM171 with enhanced of genes implicated in immunomodulatory activity such as antigen presentation, T cell activation and cytolytic effector response. Phenotypical analyses of eCB uncovered a noticeable expansion of CD34^{+}CD86^{+} dendritic cell progenitors. These cells can be selectively differentiated into either functional myeloid or plasmacytoid dendritic cells capable of stimulating allogeneic T cell proliferation and cytotoxicity of natural killer (NK) cells against leukemic blasts. Glucocorticoids suppress not only UM171-mediated expansion of dendritic cell but also compromise its capacity to expand HSPCs, suggesting that the immunomodulatory effect of UM171 is critical for immune effector cells and for HSPC activity. Preliminary observations therefore suggest that UM171 eCB enables a rapid and sustained engraftment of HSPCs and innate immune cells, and might provide an approach to immunotherapies of refractory leukemias.

3A-S03-02

THE USE OF CORD BLOOD IN METABOLIC DISORDERS AND HYPOXIC BRAIN INJURIES

J Kurtzberg

Carolinas Cord Blood Bank, Durham, United States

Cord blood cells can work through paracrine and trophic mechanisms to help endogenous cells heal brain tissue damaged by disease or injury. Learning from observations made using unrelated donor umbilical cord blood transplantation after myeloablative chemotherapy to treat children with certain inherited metabolic diseases, cord blood therapies have been developed to treat children with acquired brain injuries, like hypoxic ischemic encephalopathy, cerebral palsy, and autism. Results of preclinical and IND enabling studies will be presented to provide information about safety and potential mechanisms of action of cord blood cells in this setting. Data from early phase human clinical trials for safety and efficacy in these diseases will be presented by the speaker in this session.

3A-S03-03

NEUROPEPTIDE Y: A POTENT PROLIFERATIVE AGENT IN HEMATOPOIETIC STEM CELLS EX-VIVO CULTURE

S Moradinasab[1], K Atarodi[2] and A Pourfatholah[3]

[1]High Institute for research and education in Transfusion Medicine, Tehran, Islamic Republic of Iran [2]Hematology, High Institute for research and education in Transfusion Medicine [3]Immunology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran, Islamic Republic of Iran

Background: NPY has been recognized as a potent growth factor, causing cell proliferation in human embryonic stem cells and in mature lymphoid cells; however, its possible proliferative effects in hematopoietic stem cells (HSCs) remains unknown. Many previous studies has shown the role of sympathetic nervous system in regulation of BM microenvironment. Innervation of NPY releasing fibers in HSC microenvironments, suggests the evidence for direct link between nervous and hematopoietic system and involvement of NPY in hematopoiesis.
Aims: The aim of this study was to evaluate supportive role of neuropeptide Y on expansion of cord blood hematopoietic stem cells (CB-HSCs) with cytokine supplementation in addition to retaining the ability of multi-lineage differentiation.

Methods: CD34 + cells were isolated from mononuclear cells (MNC) of each cord blood. Expression of Y 1 receptor on cord blood CD34 + cells was studied by PCR. Ex vivo culture of CB-HSCs were performed in two conditions: One with cytokines as a control group and the other with different concentration of NPY (0.001, 0.01, 0.1 and 1 μm) in addition to cytokines. Proliferation responses following NPY treatment were studied by flow cytometry and with MNC, CD34 + cell and CD34 + CD38- cells calculation. The ability of expanded cells in formation of colonies during short term and long term culture were examined via CFU assay and LTC-IC. Statistical analysis performed by Paired sample t-test using IBM SPSS 23.0. P-values < 0.05 were considered statistically significant.

Results: We detected the expression of the Y1R transcripts in CD34 + cells with PCR, which had not been described in HSCs so far. Ex vivo expansion of CB-HSCs after 7 days resulted in significant increase in the number of MNCs, CD34 + cells and CD34 + CD38- cells treated with 0.1 and 1 μm of NPY. A dose-dependent effect was observed with the highest expansion fold change at 1 μM of NPY. The concentration of 1 μM NPY elevated not only the number of MNCs by 20.5 ± 1.3–fold, but expand also CD34 + cells and CD34 + CD38-, 18.74 ± 1.14-fold and 18.8 ± 1.4-fold, respectively. After the 7-day culture, NPY-treated hematopoietic stem cells retained their ability to differentiate into various blood cells and formulate colonies in both short term and long term culture. The CFU assay showed that the number of colonies in NPY-treated CD34 + cells, control group and freshly UCB-derived CD34 + cells per 10^3 seeded cells was 81.66 ± 8.62, 64 ± 11.53 and 127 ± 12.1, respectively. The expansion fold of CFCs was significantly higher in NPY-treated group in comparison to control group. Our result from LTC-IC assay has shown that the capacity of multi-lineage differentiation in the long-term culture was preserved in expanded cells

Summary/Conclusions: This study highlights the supportive role of neuropeptide Y on expansion of CD34 + hematopoietic stem cells with retaining their potential of differentiate into various cell lineages after 7-day culture period with cytokine supplementation.

3A-S03-04

SYSTEMIC IMMUNOMODULATION VIA BIOREACTOR PRODUCED LYMPHOCYTE–DERIVED MIRNA: EFFICACY IN AUTOIMMUNE DISEASE AND CANCER

MD Scott[1,2], X Yang[2], W Toyofuku[1] and N Kang[1]

[1]Centre for Innovation, Canadian Blood Services [2]Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada

Background: T lymphocytes occupy a central role in the cellular immune response to non-self donor tissues, the pathogenesis of autoimmune diseases and in the effective killing cancer cells. Consequently, significant, and often expensive, pharmacological tools have been developed to either suppress or enhance the T cell response. Previous work from our laboratory demonstrated polymer-bioengineered allogeneic leukocytes could be used to induce a tolerogenic state both in vitro and in vivo. Surprisingly these polymer grafted cells also exerted a potent, and persistent, systemic immunomodulation. Subsequent studies identified that the absence/presence of polymer generated unique patterns of extracellular microRNA (miRNA) that could be purified and used to achieve the same effects both in vitro and in vivo.

Aims: Using a bioreactor manufacturing approach, our laboratory has developed two miRNA based therapeutic cocktails to either induce tolerance (TA1; Tolerance Agent 1) or enhance inflammation (IA1; Inflammatory Agent 1). Mechanistically, these miRNA-based agents significantly alter the ratio of Regulatory T cells (Treg) to proinflammatory Effector T cells (Teff).

Methods: The immunomodulatory activity of both TA1 and IA1 were examined in the mouse and human context using a in vitro mixed lymphocyte reaction (MLR) model. TA1 was further assessed in vivo using the NOD mouse model of Type 1 diabetes; a T cell dependent autoimmune disease model. The proinflammatory effects of IA1 was experimentally examined using an in vitro T cell-mediated cancer killing model.

Results: In vitro, TA1 dramatically INCREASED the Treg: Teff ratio and prevented CD4^{+} and CD8^{+} alloproliferation. In immunologically normal mice, in vivo studies demonstrated that TA1 gives rise to a highly persistent (>270 days for a single dose) tolerogenic state and prevents inflammatory response to transferred allogeneic leukocytes. Of more clinical relevance, a single TA1 treatment of NOD mice (an autoimmune murine model giving rise to Type 1 diabetes) resulted in significantly decreased levels of multiple Teff subsets with corresponding increases in multiple tolerogenic T cell subsets leading to a dramatic increase in the Treg:Teff ratio in mice treated mice relative to untreated animals. Consequent to the TA1-mediated immunomodulation, the incidence of T1D was decreased by >60% and islet histology was better maintained. The efficacy of TA1 has been further examined relative to

etanercept, a soluble TNF-α receptor, and was found to be equal or superior to etanercept modulating both CD4^{+} and CD8^{+} T cell proliferation subsequent to allogeneic challenge. In contrast, IA1 dramatically DECREASED the Treg:Teff ratio (i.e., proinflammatory) in the MLR model. Moreover, naïve human PBMC pretreated (24 Hrs) with IA1 demonstrated a significant increase in their anti-cancer effect as measured by cancer cell proliferation assays.

Summary/Conclusions: These studies provide significant new insights into the potential utility of bioreactor-derived miRNA-based therapeutics as an approach to modulate the systemic immune response creating either a tolerogenic or proinflammatory environment. This cost effective therapeutic miRNA approach may have broad clinical relevance in treating diseases as diverse as graft rejection, autoimmune disorders and cancer therapy.

Clinical – Patient Blood Management

3A-S04-01

PATIENT BLOOD MANAGEMENT BUNDLES

P Meybohm and K Zacharowski

University Hospital Frankfurt, Frankfurt am Main, Germany

More than 30% of the world's population are anemic with serious medical and economic consequences. Red blood cell transfusion is the mainstay to correct anemia, but it is also one of the top five overused procedures and
carries its own risk and cost burden.

Patient blood management (PBM) is a patient-centered and multidisciplinary approach to manage anemia, minimize iatrogenic blood loss, and harness tolerance to anemia in an effort to improve patient outcome. Despite resolution 63.12 of the World Health Organization in 2010 endorsing PBM and current guidelines which include evidence-based recommendations on the use of diagnostic/therapeutic resources to provide better health care, many hospitals have yet to implement PBM in routine clinical practice.

Here we propose simple, cost-effective measures enabling any hospital to reduce both anemia and red blood cell transfusions in surgical and medical patients. Comprehensive bundles of PBM components encompassing 107 different PBM measures will be provided, divided in 6 bundle blocks acting as a working template to develop institutions' individual PBM practices for hospitals beginning a program or trying to improve an already existing program. A stepwise selection of the most feasible measures will facilitate the implementation of PBM. In this manner, PBM represents a new quality and safety standard (Ref: Meybohm P et al. Transfusion Medicine Reviews 31 (2017) 62–71).

3A-S04-02

QUESTIONING THE BENEFIT OF RESTRICTIVE TRANSFUSION PRACTICE IN OLDER ADULTS

G Simon[1], A Craswell[2], O Thom[3] and L Fung[1]

[1]School of Sport and Health Sciences [2]School of Nursing, Midwifery and Paramedicine, USC Australia, Sippy Downs [3]Department of Emergency Medicine, Sunshine Coast Hospital and Health Service, Birtinya, Australia

Background: In recent years, randomised controlled trials (RCTs) have published findings comparing patient outcomes associated with liberal versus restrictive transfusion strategies. RCT evidence has challenged some assumptions generated by earlier observational studies. Guidelines based on RCTs promote restrictive transfusion practice, except for specific patient groups where there is insufficient evidence to make recommendations. Most adult studies enrol patients across a broad age range, with very few studies focussed on patients aged 65 years and above. Patients aged 65 years and above are the highest consumers of red cells.

Aims: To examine evidence regarding restrictive and liberal transfusion strategies in older adults; and to examine pathophysiological changes associated with ageing that may impact tolerance of anaemia and transfusion outcomes.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used. We first identified RCTs that focussed on transfusion evidence in adults aged 65 years and above. As only three RCTs met this condition, inclusion criteria were widened to incorporate additional studies that had a mean

patient age of at least 64 years. The identified RCTs comparing liberal versus restrictive transfusion strategies were subjected to meta-analysis. Literature related to the pathophysiology of aging was examined for factors that impact circulation and oxygen transport.

Results: A total of nine RCTs, with mean patient ages ranging from 64 to 87 years, were included. Meta-analysis of evidence from the RCTs supported liberal transfusion strategies for older adults with respect to mortality and cardiac outcomes. Infection risk and hospital length of stay were equivocal between restrictive and liberal transfusion strategies. After publication of these findings, the Transfusion Requirements in Cardiac Surgery (TRICS III) study report, including analysis of older patient sub-groups, was released. It found that a restrictive strategy in moderate-to-high risk patients was non-inferior to a liberal strategy, including in older sub-groups of patients. Differences in Hb thresholds were noted between the studies. In our meta-analysis, liberal Hb thresholds for the RCTs restricted to patients aged 65 and above ranged from 100 to 113 g/l. TRICS III, however, applied lower liberal thresholds of 85 g/l for non-ICU and 90 g/l for ICU patients. Pathophysiological changes of ageing occur at cellular and systemic levels, negatively impacting the rate of oxygen delivery relative to haemoglobin level.

Summary/Conclusions: Recent RCTs have provided valuable new information and challenged some observational study evidence regarding associations between blood transfusion, infections and length of stay. However, findings from RCT and meta-analysis regarding transfusion outcomes in older adults are conflicted. Differences in RCT Hb triggers complicate interpretation, and consequently the inference of the terms 'liberal' and 'restrictive' transfusion. This paper will critically analyse differences in study approaches and outcomes, with the intent of highlighting challenges that need to be considered and addressed. Age-related pathophysiological changes may explain differences in outcome associated with the various Hb triggers used in RCTs. Avenues for further research will be discussed, particularly in the context of informing PBM guideline development for older adults, the largest cohort of blood recipients.

3A-S04-03
INTERNATIONAL CONSENSUS CONFERENCE TOWARDS EVIDENCE-BASED PATIENT BLOOD MANAGEMENT IN FRANKFURT/MAIN, GERMANY, APRIL 2018

MM Mueller[1], H Van Remoortel[2], P Meybohm[3], K Aranko[4] and E Seifried[1,4]

[1]German Red Cross Blood Transfusion Service Baden-Wuerttemberg – Hessen, Frankfurt, Germany [2]Centre for Evidence-Based Practice, Belgian Red Cross, Mechelen, Belgium [3]Department of Anaesthesiology, Intensive Care Medicine and Pain Therapy, University Hospital, Frankfurt, Germany [4]European Blood Alliance, Amsterdam, Netherlands

Background: Patient Blood Management (PBM) is a comprehensive initiative in quality management focussing on improving patients outcome by diagnosing and treating preoperative anaemia, implementing blood saving measures throughout the courses of diagnosis and treatment, and transfusing patients following accepted and evidence-based transfusion triggers.

Aim: The international consensus conference (ICC) on PBM was initiated in order to evaluate current evidence regarding three different topics in PBM. Firstly, red blood cell concentrate (RBC) transfusion triggers are available for different perioperative and clinical settings, but the evidence quality in different indications is variable ranging from no or very low-quality evidence available to high-quality evidence. Secondly, pre- and perioperative anaemia is not uniformly accepted as a perioperative risk factor, while definition, diagnosis and treatment are still a matter of debate. Thirdly, PBM measures are not uniformly implemented in different countries and not even within one single country. The ICC PBM took place in Frankfurt/Main, Germany on April, 24 and 25, 2018. Together with partners from Australia, Canada and further international scientific groups, the European Blood Alliance (EBA), the AABB, formerly known as the Association of American Blood Banks, the International Society of Blood Transfusion (ISBT) and the French (SFTS), Italian (SIMTI) and German (DGTI) scientific Societies of Blood Transfusion co-sponsored these activities.

Methodology: PBM for the ICC was defined according to the World Health Organization (WHO) definition. PBM is a patient-focused, evidence-based and systematic approach to optimize the management of patients and transfusion of blood products for quality and effective patient care. To identify the available scientific evidence, the Scientific Committee (SC) phrased different PICO (Population, Intervention, Comparison, Outcome) questions according to the three chosen topics: 1) preoperative anaemia, 2) RBC transfusion triggers and 3) implementation of PBM. The Centre for Evidence-Based Practice (CEBaP) carried out a systematic literature review and developed search strategies in four different biomedical databases (Pubmed, Embase, Cochrane Library and Transfusion Evidence Library). CEBaP screened approx. 18,000 papers and included more than 140 relevant papers within the three PBM topics. The

evidence-based conclusions as well as the quality of the evidence using the GRADE methodology was presented at the Frankfurt consensus conference by the SC. A transparent evidence-to-decision framework according to the GRADE approach was used by three multidisciplinary expert panels to formulate recommendations and compile consensus statements.

Results: Consensus statements with the supporting evidence will be presented during the lectures. A comprehensive summary of all consensus statements will be published later.

Conclusion: This first International Consensus Conference on the three chosen PBM topics was performed using an internationally accepted, systematic and rigorously evidence-based methodology. It is of utmost importance to all clinicians performing haemotherapy to follow updated evidence as closely as possible in order to perform the most effective medical treatment.

Working Party Session on TTID

3A-S05-01
OVERVIEW OF TTID WORKING PARTY MISSION, MEMBERSHIP AND ACTIVITIES

CR Seed[1] and M Busch[2]

[1]Donor and Product Safety Policy Unit, Australian Red Cross Blood Service, Perth, Australia [2]Executive Director, Blood Systems Research Institute, San Francisco, United States

The Working Party on Transfusion Transmitted Infectious Disease (WP-TTID) is responsible for evaluation and advocacy of ways to increase blood safety in the world in order to reduce the frequency of TTIDs. This is accomplished by: I) reviewing, gathering and analyzing relevant data; 2) developing and coordinating international studies; 3) publishing scientific reports; 4) proposing guidance, procedures and advocating for blood safety technologies in all regions, taking into account differences in regional epidemiology and resources.

The WP membership brings together scientific experts, company representatives and members from leading institutions in the fields of blood safety and infectious diseases. The WP-TTID members will be categorized into the following groups: Individual Members; Institutional Liaisons; Corporate Members; Honorary Members and Observers. Invited guests can attend at the discretion of the organising committee (OC). The WP-TTID has 134 full members (including 43 corporate members) from 44 countries.

The WP-TTID activities are coordinated by the OC and Sub-Group coordinators. The OC is comprised of five (5) individuals who are active members of the WP-TTID, elected from the membership (currently 4 year terms) comprising of the WP-Chair, Vice-Chair, Individual and Corporate Member representatives and Treasurer/Secretary. The OC meets on a quarterly basis considering financial, membership and functional issues, partly with Sub-Group coordinator participation. The full WP meets annually during ISBT congresses, the last meeting occurring during the 2017 Regional Congress in Copenhagen.

Presently there are five sub-groups (SG); Bacteria; Parasites; Surveillance, Risk Assessment and Policy (SRAP); Transmissible Spongiform Encephalopathies (TSE) and Virology. Sub-groups have one or more coordinators appointed by the OC to coordinate activities including; convening regular teleconferences to progress SG specific projects, publishing findings and developing content for the annual meetings. Current SG projects include; an international survey of the impact of parasitic infections; optimising HIV risk modelling for MSM deferral criteria; reviewing HBV vaccine breakthrough, developing a frozen panel of bacterial strains for RBCs, and studying the effects of room temperature exposure on the quality and safety of thawed plasma.

3A-S05-02
SURVEILLANCE, RISK ASSESSMENT AND POLICY (SRAP) – UPDATE ON CURRENT ACTIVITIES

S O'Brien[1] and B Custer[2]

[1]Epidemiology & Surveillance, Canadian Blood Services, Ottawa, Canada
[2]Epidemiology and Health Policy Science, Blood Systems Research Institute, San Francisco, United States

Background: The SRAP sub-group of the ISBT Transfusion Transmitted Infectious Disease (TTID) Working Party focuses on research methodology using surveillance and population data to assess infectious disease risks and implications for policy.

Aims: To describe surveillance and risk assessment in relation to policy and to describe current work of the SRAP subgroup.

Methods: There are currently 16 members in the subgroup. SRAP meet by teleconference at least 4 times per year as well as at the annual TTID working party meeting. SRAP members also participate in project specific teams that communicate by teleconference and email.

Results: Surveillance data (donor, patient and general population) are fundamental to quantitative risk assessment and evidence-based policy formulation. Quantitative risk assessment aims to estimate as accurately as possible the probability of an event occurring (such as releasing an infectious unit of blood into inventory). A SRAP team is currently evaluating mathematical models to predict HIV risk after reducing the deferral period for male-to-male sex to 1 year. Uncertainty predicting consequences is related to assumptions required to construct the model, as well as the quality of data on which the model is based. As the deferral period was changed in England and Canada with more than a year observation, the model can be validated by comparing predicted incidence with actual incidence. Furthermore, the team is modifying the model to predict risk for shorter deferral periods, and for other strategies such as alternative risk questioning (e.g. not asking about male-to-male [MSM] history) or removing the MSM criteria with plasma product quarantine and retest or with use of pathogen reduction technology. Another SRAP team is collecting data to better assess the duration of transient hepatitis B virus (HBV) antigenemia. Data from symptomatic patients is available, but as donors are generally asymptomatic the course of infection may be different. With HBV infection, there is a period of time during which hepatitis B surface antigen assays or NAT would identify an infection, but once resolved these indicators would be negative. To estimate risk from hepatitis B in blood donors, it is important to estimate how many of these transient antigenemia cases occur, otherwise risk will be underestimated. A third team is collaborating with the TTID Parasitology sub-group to evaluate the decision making processes in five developed countries relating to blood donor policies intended to reduce the malaria risk. To gain insight into the potential benefit of using the ABO Risk-Based Decision Making Framework the assessments carried out in each country are compared with those that the Framework would require. A fourth team collaborating with the TTID Transmissible Spongiform Encephalopathy sub-group has formed to evaluate vCJD policy in different countries.

Summary: The SRAP sub-group covers a range of infectious disease risks and works collaboratively with other sub-groups. The focus of SRAP is methodology for mathematical modelling of risk, and application of surveillance and risk assessment to policy formulation.

3A-S05-03

ACTIVITIES OF THE ISBT WORKING PARTY FOR TRANSFUSION TRANSMITTED INFECTIOUS DISEASES – BACTERIAL SUBGROUP

S Ramirez-Arcos[1] and C McDonald[2]

[1]Canadian Blood Services, Ottawa, Canada [2]NHSBT, London, United Kingdom

The Bacteria Subgroup (BS) of The ISBT Working Party on Transfusion Transmitted Infectious Disease (WP-TTID) undertakes activities focused on the enhancement of blood safety and dissemination of knowledge on new developments (e.g., bacterial testing and pathogen inactivation technologies). The BS has two coordinators and 19 active members who meet in a quarterly basis to discuss projects led by the group, activities of the individual members, potential publications, and participation in ISBT congresses. Since March 2017, members of the BS have met 14 times to discuss different ongoing activities.

Currently, the BS is coordinating a study aimed at generating a repository of bacterial strains for Red Blood Cells (RBCs), to be endorsed by the World Health Organization (WHO). These standardized bacterial strains will be used for growth kinetic studies and the validation of detection and pathogen inactivation technologies in RBCs. Frozen stocks of six candidate bacteria, which have shown ability to proliferate in RBCs, have been prepared at the Paul-Ehrlich Institute and shipped to 19 participant laboratories throughout the globe. This study will be performed in 2018.

A second study being coordinated by the BS focuses on determining the effect on the safety of thawed plasma upon room temperature excursions. This initiative involves three organizations, Canadian Blood Services and Héma-Québec in Canada, and NHSBT in England. The study aims at providing evidence to support individual exposures of thawed plasma to room temperature for up to 60 min during 5-day storage at 1–6 °C. In-vitro quality and bacterial growth experiments will be undertaken by the three organizations in 2018.

Publications of the Bacteria Subgroup in 2017 included a survey on bacterial testing of platelet concentrates in Latin America and the enlargement of the WHO repository bacterial strains for platelet components, both published in ISBT journals.

At present, there are two ongoing publication initiatives: a Conference Proceeding summary of the presentations given at the 2017 ISBT Copenhagen Congress at the TTID Meeting to be published in the ISBT Sciences Series and three sequential reviews on the key bacterial issues of bacterial culture detection methods, rapid testing techniques, and pathogen inactivation to be published in Vox Sanguinis.

The BS will meet in person at ISBT 2018 Toronto during the WP-TTID Meeting. Presentations in this session will include updates on current studies: repository strains for RBCs and the effects of room temperature exposures on thawed plasma. Other presentations under consideration for this session include: 1) proposals to increase platelet safety by the Food and Drug Administration in the US; 2) a review of culture methods for detection of bacterial contamination in platelet products, 3) an update on pathogen inactivation technologies, and 4) rapid methods for bacterial detection.

3A-S05-04

ACTIVITIES OF THE ISBT WORKING PARTY FOR TRANSFUSION TRANSMITTED INFECTIOUS DISEASES – BACTERIAL SUBGROUP

E Bloch[1], S Wendel[2] and D Leiby[3]

[1]Pathology, Johns Hopkins University School of Medicine, Baltimore, United States [2]Sírio Libanês Hospital Blood Bank, Sao Paulo, Brazil [3]Office of Blood Research and Review, U.S. Food and Drug Administration, Silver Spring, MD, United States

Background: Transfusion transmitted parasites remain neglected. Despite low perception of risk, their impact exceeds that of many of the major transfusion transmitted viruses, particularly in high-income countries where robust measures to contend with viral risk are already in place. Published data on transfusion transmitted parasites (TTPs) such as Babesia (babesiosis), Plasmodium (malaria), Trypanosoma cruzi (Chagas disease) and Leishmania (leishmaniasis) are limited compared to transfusion transmitted viruses and bacteria, but we are actively striving to fill this void.

Aims: The Parasite Subgroup of the International Society of Blood Transfusion (ISBT) Working Party on Transfusion-Transmitted Infectious Diseases (TTID) is comprised of approximately 12 members and is overseen by three co-chairs. The Subgroup strives to further research related to TTPs, conducts reviews of current practices and policies with regular updates of any innovation or development to mitigate risk of TTPs. The Subgroup conducts quarterly calls to review progress and brainstorm new ideas. More frequent communication is guided by the individual members related to ongoing projects. In addition, updating of the Subgroup's activities is conducted annually or biannually at ISBT congresses.

Methods: Projects that have been conducted over the past 2 years include (1) a pilot serosurvey of Babesia microti in Chinese blood donors (2) completion of an international parasite survey to compares practice for the major TTPs and (3) an evaluation of T. cruzi mitigation in non-endemic countries. Occasionally Subgroup members collaborate with other subgroups on projects of shared interest (e.g., investigation of malaria policy formulation in non-endemic countries with the SRAP Subgroup).

Results: Progress to date on individual projects is as follows: (1) A total of 1000 blood donors from Heilongjiang province were screened for antibodies against B. microti by indirect fluorescent antibody testing (IFAT); 13 (1.3%) of the donors were IFAT positive of which 8 were at a titer of 64 and 5 were positive at a titer of 128. The findings suggest that B. microti is present and merits further investigation. Molecular surveillance and donor-recipient linkage will be important to future research endeavors. A manuscript that details the findings from this collaborative, multi-institutional effort is under review at Vox Sanguinis (2) A global survey was completed of TTPs; 28 countries participated (14 from Europe, 7 from the Americas, 4 from Africa and 3 from Asia Pacific). A manuscript detailing the findings is under review at Vox Sanguinis. The results highlight the challenges surrounding mitigation of TTPs and wide, regional variation in practices that is informed –in part- by the epidemiology of the individual TTPs. (3) a survey of mitigation practices to contend with transfusion transmitted T. cruzi in non-endemic countries has been piloted and will be distributed in 2018 to selected ISBT member countries. In addition to research activities, there has been continued administrative oversight of the Subgroup coupled with growing membership.

Summary: The Parasite Subgroup continues to be active with ongoing projects and growing interest. "This work reflects the views of the authors and should not be construed to represent FDA's views or policies."

Working Party Session on IT

3A-S06-01

ELECTRONIC IDENTITY CONTROL, REPLACEMENT IDENTIFICATION, AND MULTIPLE TRANSFUSIONS MADE EASY IN THE OR/ER

J Georgsen and L Espensen

Department of Clinical Immunology, South Danish Transfusion Service and Tissue Center, Odense C, Denmark

Background: Correct identity control of donors and patients is pivotal at collection and for transfusion respectively. For more than half a century the unique national person identification number (PIN) has been used for identification of donors and patients in the Nordic countries. During the last decade the identification process has become electronic. However, for some patients their PIN is either not available or does not exist and consequently a replacement PIN is needed. In the OR/ER the wristband is often covered and the barcode with the PIN thus not available for scanning.
Aims: To describe the use of the PIN and the replacement PIN and the pros and cons regarding a national replacement PIN. To describe a newly implemented system for electronic identity control for transfusion in the OR/ER environment where the patient's wristband is covered.
Methods: All procedures regarding collection and transfusion are registered using the Blood Establishment Computer System (BECS) ProSang® (Databyrån AB, Stockholm). The national PIN is a unique ten digit number allocated few minutes after birth by the National Population Register and kept unchanged "forever". The first six digits shows the DOB, the last four holds information regarding century of birth, gender and a modulus 11 check digit. Together with an electronic image of the fingerprint the PIN identifies the donor at collection. The PIN is connected to the ISBT 128 Donation Information Number (DIN).
Before transfusion a Datamatrix bar code is scanned from the wrist band with the PIN embedded in ISBT 128 data structure 025. Thereafter the DIN and the product code are scanned from bar codes on the label of the blood component. Online checking with the BECS gives the clinician a go or a stop message regarding the transfusion.
Patients brought in unconscious or who for other reasons are incapable (small children, psychiatric patients, retarded persons) and foreigners need a replacement PIN for the hospitals IT systems. When the DOB is known it appears in the first six digits, whereas information regarding century of birth and gender is embedded in the last four alphanumeric characters. Two of these characters will be letters to distinguish it from a normal PIN. When DOB is not known, the number will be automatically generated but still with two letters and information about gender in the last four characters.
In the OR/ER the wristband will often be covered and thus not available for scanning. By allocating a unique identifier to all ORs/ERs and "scanning the patient into the room" at the start of the procedure it is possible to transfuse multiple components by scanning only the DIN and the component code from each unit assuming that the will be only one patient per OR/ER. At the end of the procedure the patient is "scanned out of the room".
Results and Conclusions: The unique national PIN and a regional system for replacement PINs has made the implementation of electronic identification easy. This development has further increased the safety level and saved considerable resources in the transfusion chain.

3A-S06-02

FINDING BLOOD PRODUCTS VIA RFID AND COMPLEMENTARY TECHNOLOGIES

L Briggs

Information Services, Versiti/Blood Center of Wisconsin, Milwaukee, United States

Background: The ability to locate and provide needed blood products remains a critical pillar in patient care world-wide. Further, the need to more precisely match rare or uncommon blood products to critically ill or frequently transfused patients calls for technologies to better enable the gathering, storage and ready access to blood product location and key attributes (HLA or antigen typings)
Aims: Describe how the use of RFID technologies using the ISBT data standards, coupled with Internet of Things (IoT) cloud services, and emerging data sharing/transmission standards can better enable our industry in finding and getting the right product to the right patient at the right time.
Methods: ISBT has established data standards which have proven to be a solid foundation in ensuring all blood banks can understand what blood products they have and key information about them. Coupling this standard with RFID and other

higher density data storage and transmission technologies, and relatively low cost cloud and Internet of Things (IoT) options, we are no longer limited by eye readable labels, barcode limitations, and system to system data exchanges to find blood products. A new world of blood product tracking, tracing can be opened up. This ease of data gathering and sharing also enables greater data analytics about what products are needed where, as well as potential for faster transfer and movement of blood products across a wider geography.
Results: Better visibility and transparency of information to not only locate, but predict where blood products will be needed – better ensuring we can get the right product to the right patient at the right time.
Summary/Conclusions: Better visibility and transparency of information to not only locate, but predict where blood products will be needed – better ensuring we can get the right product to the right patient at the right time.

3A-S06-03

PRACTICAL CONSIDERATIONS IN IMPLEMENTING RFID FOR THE BLOOD SUPPLY

S Lam

Blood Services Group, Health Sciences Authority, Singapore, Singapore

Background: The technology development and cost reduction of RFID over the years have make it possible to harness its use more cost-effectively on the fragile blood products for managing the fluid inventory movement and to secure blood and patient safety. The possible application and potential benefits to the blood supply chain has been widely studied in the blood transfusion industry but adaptation of use nationwide has been slow. Singapore intend to implement use of RFID for real-time management of the national blood inventory and to enhance blood transfusion safety.
Aims: To outline the potential application and objectives of RFID in Blood Supply Chain. To explain the use of gap analysis and value stream mapping tools for identification of areas of improvement that RFID can address. To highlight various practical point of concerns to address in the use of RFID for Blood Supply Chain based using Singapore's experience.
Methods: RFID for the national blood programme was one of the key IT initiative towards smart healthcare in Singapore, harnessing technology to increase blood and patient safety, effective management of national blood supply and increase staff productivity. In order to ensure effective use of RFID to complement the existing blood bank computer system and hospitals' laboratory and patient medical record information systems, a gap analysis and value stream mapping study was conducted to identify areas of improvements from existing processes and workflows. A business proposal with funding requirements was put up to various stalk-holders for acceptance.
Results: Many practical considerations were raised during this process that delays the project actualisation. This includes the impact on current processes and equipment, the extend of use of RFID; the funding needed and cost allocation; the type of RFID hardware to be use; the type of network infrastructure; the scope of RFID tagging; the data to be capture; mode of data exchange between RFID and existing systems; RFID system security and integrity and scope of application software. The most critical concern is to ensure buy-in from various stalk-holders which includes leadership and operational personnel from both the blood service and the hospitals.
Summary/Conclusions: From our experience, a good change management plan of the RFID project communicated in the early stage of planning and continual updates of progress will be instrumental in the smooth implementation to achieve the full benefits of RFID in blood supply chain.

Plenary Session – Arthropod Borne Infections

PL1-01

INSECT DISEASE VECTORS AND THEIR IMPACT ON HUMAN HEALTH

LC Harrington

Entomology, Cornell University, Ithaca, United States

Insect-borne pathogens pose a considerable risk to the global safety of blood products. An overview of the biology, exposure risk and transmission dynamics for vector borne pathogens that are of greatest risk to the supply of blood products will be

presented. These agents include mosquito-borne viruses such as dengue, chikungunya, yellow fever and zika as well as parasites of public health importance such as malaria, babesia and bacterial pathogens. The role of vectors in a recent spread of viral diseases that impact transfusion and why this may have happened will be presented, in addition to future strategies that entomologists are considering for vector borne disease control.

PL1-02
HUMAN GENETIC RESISTANCE TO MALARIA

E Leftler[1,2]

[1]Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford [2]Wellcome Trust Sanger Institute, Hinxton, United Kingdom

The Plasmodium parasites that cause malaria have been widespread in tropical regions for thousands of years and still lead to a large number of cases and deaths today. Due to its severity and historical prevalence, malarial disease has driven the spread of genetic resistance variants in human populations, and characterization of these resistance mutations offers a distinctive window into pathogenic mechanisms of disease, host-parasite interactions, and the nature of evolutionary selection. Because the clinical symptoms of malaria occur during the blood stage of infection, polymorphisms affecting red blood cell structure or function are strong candidates for malaria resistance, and indeed several have been shown to play a role in malaria susceptibility. However, most have been identified through candidate gene studies that rely heavily on such prior expectation and knowledge. Genome-wide association studies (GWAS) in large numbers of individuals provide an alternative avenue to search the human genome for variation associated with susceptibility to malaria, enabling novel discovery as well as elucidation of the protective effects of previously reported loci.

Here I will present results from a multi-site GWAS carried out by the Malaria Genomic Epidemiology Network (MalariaGEN) involving over 10,000 severe malaria cases and population controls from malaria-endemic countries in Africa. Analysis of this data replicates associations at several loci including the sickle cell variant at HBB and the O blood group variant at ABO, and also identifies novel associations. In particular, we identify variation associated with protection from severe malaria near the glycophorin gene cluster encoding the red blood cell proteins GYPA and GYPB, which serve as receptors for parasite invasion and also determine the MNS blood group system. By investigating copy number variation at this locus, we find that the association is explained by a complex structural variant involving the loss of GYPB and gain of two GYPB-A hybrid genes. We further show that this structural variant corresponds to the Dantu (NE) blood group variant and is primarily present in some east African populations, where it reaches much higher frequencies than have previously been reported in surveys of Dantu. Moreover, frequency variation across populations and haplotype structure suggest this variant has been under recent selection. In contrast, the more frequent GYPB deletion variants show no evidence of association with severe malaria. Follow up functional work to understand how the hybrid receptors contribute to protection from malaria, but absence of receptors apparently does not, may yield new insight into the process of parasite invasion.

The GWAS conducted by MalariaGEN is the largest such study for an infectious disease to date, and has revealed a new association between a Dantu blood group variant and malaria susceptibility. This finding reinforces the importance of the red blood cell and blood group polymorphism more specifically in resistance to severe malaria. Intriguingly, both ABO and GYPA/GYPB also show signals of long-term diversifying selection, and this raises further questions about how current resistance to malaria may relate to long-term selection patterns and the drivers of genetic diversity at these loci.

PL1-03
IMMUNE ROLE OF PLATELETS IN MALARIA

B McMorran

The John Curtin School of Medical Research, Australian National University, Canberra, Australia

Malaria is an infectious disease caused by the protozoan parasite, Plasmodium. It threatens the lives of over 3 billion people from more than ninety countries, and despite control efforts spanning several decades there are still more than 400,000 fatalities annually. Survival to malarial infection has been a major driver in the evolutionary history of humans, but many of the host response mechanisms that determine an individual's ability to survive infection remain poorly understood. My laboratory discovered a novel protective mechanism in malaria involving platelets.

These seemingly innocuous agents of the bloodstream, well-known for their functions in hemostasis, are now understood to mediate a range of immunological functions and are important determinants in the host's response to many types of infections.

In malaria platelets appear to have different and opposing roles depending on the context and severity of the infection. On the one hand, platelets have been implicated adversely in cerebral malaria, which is a severe disease manifestation where microvascular occlusions develop in the brain, leading to inflammatory foci and brain swelling, and causing coma and often death. Platelets adhere to the cerebral endothelium and mediate the accumulation of infected erythrocytes in the brain, with the postulated outcome of increasing severity or of even mediating this disease. Clinically, one of the earliest signs of infection is an induced thrombocytopenia, which is considered as an adverse prognostic marker in malaria. However, the underlying causes of thrombocytopenia are not well-understood and have been variously attributed to systemic platelet activation, immune-mediated clearance and vascular pooling. Recent observations from my laboratory indicate a significant role for platelet-binding to red blood cells, which have been observed in animal models of malaria and clinical infections.

On the other hand, platelets bind to infected red cells in the periphery, and activate and release the cytokine PF4. This, in turn, binds to the Duffy antigen on the red cell and is then internalized and enters the parasite food vacuole which it then destroys, killing the parasites. The platelet-dependent and PF4-directed killing of malarial parasites has been observed in in vitro parasite culture systems and mouse models of the disease. More recently, studies in my laboratory have observed the occurrence of platelet and PF4-directed parasite killing in human malaria, and evidence of their significant contribution to the host's ability to control the infection.

Our understanding of the interactions of platelets in malaria and in many other infectious diseases has improved immensely in the past decade and continues to accelerate. This knowledge is certain to lead to exciting insights into host responses and mechanisms of infectious disease, and provide novel interventions and therapeutic tools.

Management and Organisation – Management of Blood Components in Different Settings

3C-S07-01
EMERGENCY PREPAREDNESS FOR MASS CASUALTY EVENTS

HA Doughty

Medical Department, NHS Blood and Transplant, Birmingham, United Kingdom

Emergency transfusion preparedness is increasingly being recognised as an important element in the healthcare response to Mass Casualty Events (MCE). Planning should be designed to support an integrated response between the Blood Services and hospitals. Both should be alerted early following such events. The lessons identified from Manchester and other recent incidents are being incorporated into wider UK planning and revised transfusion guidance for hospitals. The guidance has been informed by the global experience of civilian MCEs and the changing trends in trauma care. Planning assumes that pre-hospital and trauma care will be optimised across trauma networks where these exist. Trauma networks provide a valuable forum for policy, planning, education and exercising. Transfusion teams and services should be encouraged to participate in exercises at all levels from local to cross border events.

Current evidence suggests that only a modest number of the patients hospitalised following MCEs require transfusion. Past experience suggests this may be approximately 20%. The mean demand has been consistently calculated at 2–3 red cell units within the first 6 hr. However, a small number of critically injured with multi-trauma may require access to massive transfusion and haemostatic resuscitation. Most blood is used on day one but there may be ongoing requirements due to revision surgery. Demand planning is only one aspect of transfusion emergency preparedness. Communications and the logistic response are key enablers. Equal efforts must address patient identification, organisation of transfusion staff and laboratory management. Facilities receiving large numbers of patients may consider pre-positioning of transfusion staff with red cells and thawed plasma within the Emergency Department. Forward transfusion triage enables the best use of components and laboratory resources.

Many blood services have reported meeting initial demand for blood from existing stock. However, careful communication with donor communities is essential to manage a controlled replenishment of stocks. Stock management for MCEs should consider both component type and blood group. Similar principles may be applied when proactively building stock as part of planning for mass gatherings such as sporting or entertainment events. Preparation should be informed by sound Business Continuity principles and operational systems should be sufficiently resilient to accommodate a surge in both clinical demand and donations. Transfusion has not traditionally been an important element for major incident planning. However, the transfusion community is encouraged to plan for MCEs, share their operational experience and work together for mutual support.

3C-S07-02

LONDON 2017: A YEAR TO REMEMBER FOR ALL THE WRONG REASONS!

D Mckeown[1], F Chowdhury[1,2] and F Regan[1]

[1]Haematology, Imperial College Healthcare NHS Trust [2]Clinical, NHS Blood and Transplant, London, United Kingdom

Background: St Marys Hospital opened its doors as a Major Trauma Centre in 2010 and in October 2014 it was ranked the best in the country by NHS England who assessed the service. Our Major Trauma Centre covers North-West London and is one of London's four Major Trauma Centers. In 2017 our hospital was stood up for all 4 major incidents. The first on Westminster Bridge involved a vehicle attack and stabbing by a single perpetrator, the second incident involved a vehicle attack on London Bridge & Borough Market and stabbings by multiple attackers. The third incident involved a fire in a residential tower block "Grenfell Tower" and the fourth involved a bomb on a train at Parsons Green tube station.
Aims: To share our experience and learning's from coping with very different types of major incidents over a short period of time and to describe our coping strategies from a transfusion and trauma centre perspective.
Methods: Review experience and reports from debriefings from in each major incident.
Results: Despite being a Major Trauma Centre which is well prepared and trained to cope with different types of major incidents we identified different shortcomings in each incident. In the first incident, security of patients and the perpetrator were identified as an issue at debriefing. The London Bridge incident occurred on a Saturday night and was co-ordinated by many managers off site with limited staff. The Grenfell Tower fire incident highlighted the importance of safeguarding paediatric patients (as family missing) and the difficulty in identifying family members. We also discovered that patients were sent inappropriately to other hospitals by London Ambulance Service during this incident, which resulted in patients being treated by non-trauma centres leading to delays in correct management of patients. Additionally we experienced problems with sample labelling in more than one incident despite training. For the fourth incident we were stood up early but the injuries sustained were minor. For all the incidents we ordered in extra blood components as we were expecting significant numbers of victims but this did not materialise and impacted on our wastage figures. Redistribution across sites proved difficult due to road closures in some of the incidents, and also our other sister sites were stood up to receive patients. The physiological and psychological impact of four major incidents over a short period on different clinical and non-clinical teams could not be overestimated.
Summary/Conclusions: No matter how much preparation and training that is carried out, each incident highlights different shortcomings and needs depending on the type and time of day this occurs. Subsequently wastage of blood and components will be inevitable as under ordering to minimise wastage would not be acceptable.

3C-S07-03

GROUP O RHD NEGATIVE RED BLOOD CELL UNITS: WHEN ENOUGH IS ENOUGH

L Bielby[1], C Flores[1], C Akers[1], J van Diemen[1], B Glazebrook[1], P Beard[1] and J Daly[2]

[1]Blood Matters, Australian Red Cross Blood Service, West Melbourne [2]Clinical Services and Research, Australian Red Cross Blood Service, Brisbane, Australia

Background: In Victoria, Australia, there has been a 21% reduction in demand for red blood cell (RBC) units since 2011. This reflects both national and international decline in demand for RBC. In contrast, the demand for group O RhD negative RBC

has increased by 19%, an increase of approximately 4,500 units between 2011 (24,500 units) and 2017 (29,000 units). This accounts for 16% of all RBC O neg issues in contrast to the Australian donor population of 9%. During this time period, wastage of O RhD negative units has declined from 10% to 3%, partly due to the National Blood and Blood Product Wastage Reduction Strategy 2013–17.
In order to conserve stocks and ensure availability of O RhD negative units for patients for whom there is no alternative, the Australian Red Cross Blood Service developed guidelines for when it is appropriate to use group O RhD negative RBC units, endorsed by the National Blood Transfusion Committee in 2008. To help understand the increased demand of O RhD negative, Blood Matters audited their use compared to the 2008 Guidelines.
Aims: To document the use of O RhD negative RBC units issued to health services and compare against the 2008 Guidelines.
Methods: Audits circulated to all Victorian, and participating health services in Tasmania, Australian Capital Territory, and Northern Territory. The audit included questions to determine the alignment of O RhD negative use against the 2008 Guidelines. Questions included patient gender and age, ABO and RhD group (and if known at time of issue), specific antibody or phenotype requirements, and transfusion urgency. The health service identified the primary reason an O RhD negative unit was selected for each patient. Algorithms were developed to determine alignment of O RhD negative unit to 2008 Guidelines as mandatory, recommended, or acceptable indications for use.
Results: Preliminary data shows of O RhD negative units transfused, there was a large variance from 2008 Guidelines (range 24–100%, mean 58%). Similarly, the numbers of O RhD negative units transfused to avoid time-expiry varied widely (range 0–48%, mean 15%). Discard rate is consistently low across the reporting health services (range 0–14%, mean 3%). Data highlighted issues resulting in non-compliance are often unique to individual health services. For example, regional "hubs" receiving large numbers of rotational stock from satellite sites with short expiry results in high "used to avoid time-expiry"; and routine transfusions of O RhD negative units to patients with known non O blood group as a result of not holding a full ABO inventory as a strategy to reduce wastage.
Summary/Conclusions: Initial data shows more improvements are required to meet the 2008 Guidelines. With an increased understanding of how O RhD negative units are used; and identifying themes of noncompliance, strategies can be implemented to reduce inappropriate demand to better reflect the true need, and ensure availability for patients whom there is no alternative. Blood Matters will provide individual report cards to health services, including recommendations for improved practice.

3C-S07-04

USING THE AB PLASMA APPROPRIATENESS INDEX AS A BENCHMARKING TOOL IMPROVED AB PLASMA TRANSFUSION PRACTICE THROUGH QUALITY IMPROVEMENT INITIATIVES

A Orzińska[3], S Al Khan[1,2], K Rosinski[3], L Sham[3], T Petraszko[2,4], K Roland[5], M Hudoba[5] and A Shih[5]

[1]Central Blood Bank, Ministry of Health, Muscat, Oman [2]University of British Columbia [3]Vancouver Coastal Health Authority [4]Canadian Blood Services [5]Vancouver Coastal Health Authority, University of British Columbia, Vancouver, Canada

Background: Group AB plasma is scarce as approximately 4% of North American donors are group AB. Its growing use, in part due to massive transfusion protocols (MTPs) in bleeding patients, poses challenges. A key quality indicator (KQI) for its appropriate usage currently does not exist to aid in benchmarking and quality improvement.
Aims: We hypothesized that 1) our institution transfused a disproportionately high amount of AB plasma to non-AB patients as assessed by the AB plasma appropriateness index (ABAI); and 2) we could mitigate inappropriate non-AB matched plasma transfusion through quality improvement initiatives in our MTP processes.
Methods: Data on all AB plasma units was collected retrospectively for the period of January 2016 to February 2017 for hospitals in British Columbia (BC), Canada through the BC Provincial Blood Coordinating Office. AB plasma utilized was analyzed by disposition status (transfused, expired, discarded) and transfused units by recipient blood group.
The ABAI was calculated as a KQI of AB plasma utilization, defined as: the ratio of AB plasma transfused to AB patients (and those with unknown blood groups) compared to all AB plasma utilized including expired/discarded units. ABAIs closest to 1 are ideal.
In our institution, data on all AB plasma units was collected retrospectively for the same period. The data collected included the disposition of AB plasma units

including specific indications for AB plasma transfusion, including usage in MTPs, usage to prevent expiry, and plasmapheresis.

Results: The total number of transfused, discarded, and expired AB plasma units in BC during the study period were 3847 units, 255 units, and 318 units respectively. The overall ABAI for the province of BC was 0.42 (1856/4401). The ABAI for our institution was 0.49 (915/1838), which placed it below the median of assessed BC hospitals (range 0.18–0.65).

In our institution during the audit period, 30% of AB plasma units were transfused to non-AB patients to prevent expiry and 8% for 28 MTP activations. Thus, we implemented a 4-unit thawed A-plasma bank for the first MTP cooler instead of an AB bank, beginning in July 2017. Based on retrospective assessment, we projected a 48% decrease in AB plasma utilization with this change.

From July 2017-January 2018, after excluding units used for plasmapheresis, 132 units of AB plasma were used compared to 416 units in the same 6-month period of the previous year. Plasmapheresis was excluded as appropriate use accounted for 86% (804/936 units) in the change period. Observed usage of AB plasma to non-AB patients were 14 (10.6%), 23 (17.4%), and 6 (4.5%) units to prevent expiry due to thawing for another patient, stat use with unknown ABO groups, and incorrect use. Excluding plasmapheresis, the ABAI over the 6-month period in the previous year was 0.36 and 0.63 during the change period.

Summary/Conclusions: The ABAI is a novel KQI which can indicate inappropriate AB plasma usage as a target for quality improvement. This led to the use of a thawed A plasma for MTPs which was effective for reducing inappropriate AB plasma usage.

3C-S07-05

DEVELOPMENT OF SCENARIOS FOR THE FUTURE DEMAND OF BLOOD PRODUCTS IN THE NETHERLANDS: AN OVERVIEW

P Langi Sasongko[1], M van Kraaij[2], K van den Hurk[3] and M Janssen[4]

[1]Transfusion Technology Assessment, Donor Studies [2]Unit Medical Affairs [3]Donor Studies [4]Transfusion Technology Assessment, Sanquin, Amsterdam, Netherlands

Background: Western blood transfusion practices are currently changing due to various drivers such as adoption of blood management policies, ongoing technological developments, and new therapeutic options. In the Netherlands, these have resulted in a diminishing trend of red blood cells and fresh frozen plasma, yet an increased use of plasma proteins for medicinal purposes and a steady trend for platelets. It is uncertain of how these trends will continue into the future. Therefore, it is important for blood bank management to anticipate the future demand of blood products for the sake of medium and long term decision making. To support this decision making, we employ scenario development, which is used in many other sectors (such as finance and transportation) and can also be applied to blood transfusion. Therefore, a mixed qualitative and quantitative methods approach is applied in order to explore this topic in a systematic yet exploratory manner.

Aims: This study aims to prepare a list of highly probable medium and long term scenarios with detailed specifications of organizational implications of the medium term scenarios for the Dutch national blood bank, Sanquin, using a mixed qualitative and quantitative approach.

Methods: Literature was searched and discussions were held regarding the selection of methods that could support or be adapted for scenario development in blood transfusion in the Netherlands.

Results: Combining qualitative and quantitative methods, an integrated four step approach was developed: 1) to interview various experts in blood transfusion in the Netherlands in a semi-structured manner simultaneously to an extensive literature review of a database and gray literature. Within the literature review, the historical developments of blood usage and various innovations that would impact the future demand of blood products for the Dutch context are explored; 2) to conduct a quantification of historical blood use in the Netherlands using prior data with estimates per patient group; 3) to organize expert elicitation workshops to estimate changes of blood use per patient group and construct various medium and long term scenarios; 4) to develop an organizational model to be tested with sensitivity analyses and applied with probabilistic mappings.

Summary/Conclusions: The first step of this ongoing research is nearly complete. It is expected that the aforementioned approach will ultimately result in the creation of medium and long term scenarios and the organizational implications therein. This approach will contribute towards adaptive policy recommendations to support the Dutch national blood bank, Sanquin, for the (un)foreseeable future.

Donors and Donation – Donors Vasovagal Reactions

3C-S08-01

DONOR VASOVAGAL REACTIONS, HOW CAN WE REDUCE THEM?

J Castrén

Finnish Red Cross Blood Service, Helsinki, Finland

Vasovagal reactions (VVR) represent the majority of reported donor adverse reactions among whole blood and apheresis donors. Rates of VVRs with loss of consciousness for whole blood donors variate in international donor hemovigilance reports from 0.1 to 0.5%, and the VVRs without loss of consciousness from 1.0 to 7.0%. Reported VVR rates for apheresis donors are remarkable lower than among whole blood donors. Incidence of VVRs is strongly associated with donor characters. Young age, female sex, small estimated blood volume, and donating at first time are risk factors for all types of VVRs. Besides unpleasant experience, harm, and risk for trauma occurred VVR induce reduced donor returning rates and extra work to collection staff.

There are three main categories of methods effective in preventing or reducing VVRs: physiologic interventions, psychologic approaches, and donor selection.

Physiologic interventions and donor selection has their base in blood establishment environment familiar theories and methods, and are medical based, clinical interventions. Their theoretical models cover changes in blood volume, changes in fluid balance, and nervous mechanisms active in stabilizing effects of blood loss. Physiologic interventions having effectivity in preventing or reducing VVRs: pre-donation water or isotonic drink loading, applied muscle tension during donation, and pre-donation caffeine consumption.

Psychologic approaches having effects on preventing or reducing donor VVRs have a shorter history and a smaller number of donor research publications than physiologic interventions. Approaches having scientific evidence in preventing or reducing VVRs: fear or anxiety assessment and reduction, active donor participation in the donation process, audio-visual distraction, and social support. Even applied muscle tension was discovered and studied as a physiologic method it has also been shown to have effects as a psychological approach.

Donor selection criteria taking account the risks for VVR include limits for donor weight, age, and estimated blood volume as well as taking to account donors previous donation experiences, especially adverse reactions.

The importance of donor care and well-being of the donors has been comprehended in blood establishments for years ago, but there are still challenges to implement all the data with scientific evidence of VVR prevention and reduction into the daily life in collection centers and at each donor contact. There is a need of practical, easy to use models and tools of combined physiological and psychologic preventive methods feasible to implement to daily donor contacts. There is also need for more research with the focus of the active role of the collection staff in preventing VRRs as part of donor care. Reflecting the general trends of personal, individual demands in every custom service situation, the most effective new approaches reducing VVRs might be discovered in the context of genuine donor-staff encountering and might include targeted and evidence based methods easy to implement.

3C-S08-02

BLOOD DONATION IN INDIVIDUALS OVER AGE 70: A BEST COLLABORATIVE GROUP STUDY

M Goldman[1], M Germain[2], Y Grégoire[2], H Kamel[3], M Bravo[3], R Vassallo[3] and S O'Brien[1]

[1]Canadian Blood Services, Ottawa [2]Héma-Québec, Québec City, Canada [3]Blood Systems, Inc., Scottsdale, Arizona, United States

Background: Both the general and donor population are aging in many countries. The upper age limit for whole blood (WB) donation is variable, and few recent studies have evaluated the safety of donation in older individuals.

Aims: To assess the contribution older donors make to the blood supply in 5 countries that permit donation by individuals aged 71 + , and compare deferral and vasovagal reaction rates in donors aged 71 + vs 24–70 years.

Methods: BEST members with no upper age limit for WB donation in Canada (Héma-Québec and Canadian Blood Services), New Zealand (New Zealand Blood Services), England/Northern Wales (National Health Service Blood and Transplant) and

USA (American Red Cross, Blood Systems Inc., Carter Blood Care, Bloodworks Northwest, UCLA, Memorial Blood Center) or an upper age limit of 80 (Australian Red Cross Blood Service) provided 2016 data on donors and donations, deferral rates, and vasovagal reactions by donor age. Donors <24 were not included in deferral and reaction rates, since they have different characteristics and comprise variable proportions of each country's donor base. All comparisons were between age groups within countries thus controlling for variable deferral and donor reaction definitions and data capturing between countries.

Results: Donors 71 + accounted for from 1.0% (New Zealand) to 4.3% (USA) of WB donors, and from 1.5% (New Zealand) to 5.8% (USA) of all WB donations. Donation frequency was higher in 71+ than in 24–70 years old (2.4 vs 1.9 donations per donor, P < 0.001) in all countries. In all countries, the deferral rate in males 71 + was higher than males 24–70 years old for hemoglobin, vital signs (if performed), and donor history (10.9% vs 6.6%, P < 0.001), but very similar in female donors 71 + and 24–70 (16.4% vs 15.8%, P < 0.001). Males and females in all countries had lower vasovagal reaction rates among 71+ year old donors: Odds ratios (OR) for 71 + vs 24–70 year olds (ranging from 0.2, England/Northern Wales to 0.8, USA) all had 95% upper Confidence Intervals (CI) <1. Vasovagal reactions with loss of consciousness (LOC) were rare in all countries (<3 per 1,000 females, <1.5 per 1,000 males) and OR for 71 + vs 24–70 year olds (ranging from 0.4, Canada to 0.7, USA) all had 95% upper CIs <1. Numbers were too small for meaningful analysis in New Zealand (only 3 LOC reactions in all older donors), with an OR of 1.5 and 95% CI between 0.5 and 4.8.

Summary/Conclusions: Data on over 470,000 donations from close to 200,000 donors aged 71 + demonstrate that these donors donate more frequently, have similar (females) or slightly higher (males) deferral rates and lower vasovagal reaction rates compared to 24–70 year olds. LOC reactions are rare in all donors in all countries, but are lower in donors 71 + compared with 24–70 year olds. Healthy older individuals may continue to safely donate and make a substantial contribution to the blood supply past arbitrary age limits.

3C-S08-03

RISK FACTORS FOR ON-SITE OR DELAYED FAINTING REACTIONS IN MALE AND FEMALE BLOOD DONORS: RESULTS FROM THE EVASION STUDY

C Morand[1], C Rolland[2], N Coudurier[3], S Thoret[2], C Vermorel[2], P Tiberghien[4] and J Bosson[2]

[1]Etablissement Français du Sang Rhone Alpe Auvergne [2]Université Grenoble Alpes, Grenoble [3]Etablissement Français du Sang Rhone Alpe Auvergne, Lyon [4]Etablissement Français du Sang, La Plaine St-Denis, France

Background: Prevention of fainting reactions (FR) associated with whole blood donation is an important issue for donor safety and donor retention. The Evasion study, a prospective randomized trial involving 4576 blood donors, demonstrated that muscle tensing at time of donation could reduce the incidence of early FR during donation while drinking 500 ml of an isotonic solution could reduce the incidence of delayed FR as well as tiredness (Morand, Transfusion, 2016).

Aims: As part of the Evasion study, an analysis of risks factors for on-site and delayed FR in male and female blood donors was performed.

Methods: Data pertaining to putative FR risk factors were prospectively collected. Odd ratios were determined by univariate analysis, followed by a multivariate analysis by means of a backward stepwise elimination in a conditional logistic regression model.

Results: Fainting reactions occurred in 2.9% (n = 66) and 8.1% (n = 187) of male and female donors, respectively. As expected, a female versus male gender was associated an increased FR [univariate analysis, odds ratio (OR) = 2.96, P < 0.01].

In female donors, multivariate analysis revealed that being a student (a risk factor closely linked to age) [OR = 2.9, P < 0.001], a donation before or during working hours, or being without professional activity (versus donation after working hours) [OR = 1.9, P = 0.030; OR = 1.6, P = 0.050; OR = 1.8, P = 0.039 respectively], donation-related stress [OR = 1.85, P = 0.008], a high hemoglobin (Hg) level [OR = 1.3 per g/100 ml Hb increase, P = 0.005], reduced physical status [OR = 1.20 per reduced grade on a scale of 1 to 10, P = 0.012] were FR risk factors.

In male donors, a first donation [odds ratio (OR) = 3.8, P < 0.001], donation-related stress [OR = 2.57, P = 0.010], a donation on a mobile site (vs fixed site) [OR = 2.25, P = 0.013], a high hemoglobin (Hb) level [OR = 1.6 per g/100 ml Hb increase, P = 0.001], pain at time of venipuncture [OR = 1.21, P = 0.005] or during donation [OR = 1.23, P = 0.033] were independent FR risk factors.

Risk factors associated with on-site versus delayed FR were examined in female donors (3.7%, n = 86 and 5.1%, n = 117, respectively). The low number of delayed

FR (0.9%, n = 20) prevented a similar analysis in male donors. Physical status, donation-related stress, pain during donation, donation on a mobile site were risks factors associated with on-site FR, while a high hemoglobin level, blood donation before or during working hours, or being without professional activity were risk factors associated with delayed fainting reactions. Being a student was a risk factor for both on-site and delayed fainting reactions. Lastly, on-site FR occurrence was associated with a higher frequency of delayed FR (delayed FR among female donors with an on-site FR: 18.6%, IC 95 [11.0%; 28.4%]; delayed FR among male donors with an on-site FR: 8.0%, IC 95 [2.2%; 19.2%].

Summary/Conclusions: These results confirm previously identified risk factors such as female gender, young age (strongly associated in our model to a student status), stress and pain at donation, while highlighting less know risk factors such as a high hemoglobin level. Risk factors can differ significantly depending on the donor gender as well as to when the fainting reaction occurs. Such findings could pave the way to the implementation of personalized risk prevention strategies.

3C-S08-04

BRADYCARDIA AND TACHYCARDIA ASSOCIATED WITH SYNCOPAL/PRE-SYNCOPAL ADVERSE EVENTS IN BLOOD DONORS

H Kamel, M Bravo and M Townsend

Medical Affairs, Blood Systems, Scottsdale, United States

Background: The mechanisms underlying syncopal/pre-syncopal adverse events (AEs) in blood donors are thought to include the psychological stress of instrumentation and giving blood (i.e., fear of needles, pain, and the sight of blood), the direct effects of removal of about 500 ml of whole blood, and the orthostatic effects superimposed on a hypovolemic state after the donation.

Aims: To determine the prevalence of bradycardia (pulse <50 bpm) and tachycardia (pulse >100 bpm) in syncopal/pre-syncopal AEs starting at various periods of the donation process.

Methods: Between 1/1/2010 to 8/31/2017, in donors presenting for WB donations at a multi-center US blood bank, we analyzed syncopal/pre-syncopal AEs for the presence of bradycardia or tachycardia recorded on donor AE forms during vital signs monitoring of donors experiencing AE. Rates of bradycardia or tachycardia were calculated based on the period of donation when the event occurred: Period 1 (P1) – screening/ registration; P2 - <=4 min after needle removal; P3A - >4 min after needle removal, onsite; P3B (P3B) - >4 min after needle removal, offsite. Other donor (estimated blood volume (EBV), sex, age, experience) and donation (with or without needle) characteristics were described for both groups.

Results: We identified 14,849 AEs (10,964 syncopal and 3,885 pre-syncopal events): 1.2, 39.8, 49.7 and 9.4 percent started in periods, 1, 2, 3A and 3B respectively. Bradycardia was reported in 6.3% and tachycardia was reported in 9.9% of the AEs. Bradycardia occurred mostly in P1 (7.6%) & P2 (8%), among Males (10%), those with No Needle (8.3%) or Incomplete Collections (9.2%), and among 23 and older donors (7.5 and 7.0%). Tachycardia occurred mostly in P3A (11.9%) and P3B (8.6), among females (11.7%), those with complete collections (10.7%), and among 16–22 y/o (14.3%).EBV was shown to be significantly lower among those observed to have tachycardia (4070 ml, 95% CI 4038–4103) compared to those with bradycardia (4471, 95% CI 4417–4524).

Summary/Conclusions: The findings support the hypothesis that syncopal/ pre-syncopal AEs occurring before or during the process of blood donation are neurally mediated reflex reactions, namely, sympathetic withdrawal and/or increased vagal tone (bradycardia); and those occurring after blood donation, either on-site or off-site, when donors are in the hypovolemic state and ambulating are driven primarily by orthostatic central hypovolemia (tachycardia). Varying strategies to mitigate vasovagal events throughout the course of donation such as distraction and fluid replacement should be continually promoted.

3C-S08-05

TO STUDY THE EFFECT OF PRE-DONATION SALT LOADING ON VASOVAGAL REACTIONS IN COLLEGE-GOING STUDENTS

K Kumar, N Marwaha and S Sachdev

Transfusion Medicine, PGIMER, Chandigarh, India

Background: There have been studies conducted on association of VVRs (Vasovagal reactions) with various factors like age, gender, weight, blood pressure and

predonation water intake on the effect of orthostatic hypotension post donation. But there is paucity of data comparing the effect of salt loading on immediate and delayed VVRs separately and also to compare the distribution of immediate and delayed VVRs in various groups based on the gender, age, weight, BMI, donation status and percentage blood volume withdrawn.

Aims: To study the effect of pre-donation salt loading on VVRs in college going students who came for voluntary blood donation.

Methods: 3060 young (18–25 years) voluntary blood donors were randomized into control group (1515) and test group (1545). Donors in the control group were given 300 ml sweetened limewater and donors in the test group were given 2.5 gm salt with the above mixture. The donors were observed for immediate VVRs (IVVRs) at the campsite and were telephonically followed up after 72 h for delayed VVRs (DVVRs).

Results: There were 90 VVRs in the present study out of which 57 were IVVRs and 33 were DVVRs. The reaction rate of VVRs was less in the test group (1 in 42), as compared to the control group (1 in 29). The decrease in DVVRs was statistically significant (P-0.020), but the decrease in IVVRs was not significant (0.063). In both the groups, female gender was a significant risk factor, however in the test group females, there was a significant decrease in both the IVVR (0.016) and DVVR (0.010) when compared to control group females. First time donors (FTDs) tended to have higher reaction than repeat donors (RDs). Salt loading did not affect the incidence of VVRs in FTDs, as first time donation in itself was an independent risk factor. In the test group, RDs had significant reduction in DVVRs (0.005) and mild decrease in IVVRs (0.67).Overall, donors in the weight range of 50–60 kg had more reaction as compared to higher weighing donors, but difference was not seen in test vs. control group when analyzed for weight. A trend of decrease in occurrence of VVRs was observed as the BMI of the donors increased, but there was an increase in the percentage of VVRs in obese donors (BMI>=30 kg/sq m) when compared to donors with a BMI range of 25.99–29.99 kg/sq m. Donors from whom a higher blood volume withdrawn had more VVRs, but there was a decreasing trend in the test group but did not reach statistical significance.

Summary/Conclusions: The overall reaction rate of VVRs was less in the salt loaded young whole blood donors. The decrease in DVVRs was statistically significant.

Young Investigators Session

3C-S09-01
RE-EVALUATING THE SHELF-LIFE OF WHOLE BLOOD FOR CIVILIAN USE

S Huish[1], L Green[2,3,4], L Bower[1], C Cavagnetto[1], E Curnow[5], S Garner[1], L George[1], J Jolley[1], M McAndrew[1], A Pullen[1], F Seeney[5], P Smethurst[1], M Wiltshire[1] and R Cardigan[1,6]

[1]Component Development Laboratory, NHS Blood and Transplant, Cambridge [2]NHS Blood and Transplant [3]Barts Health NHS Trust UK [4]Blizzard Institute, Queen Mary University of London, London [5]NHS Blood and Transplant, Bristol [6]Department of Haematology, University of Cambridge, Cambridge, United Kingdom

Background: Early resuscitation of trauma patients with blood components is becoming increasingly widespread. Whole blood (WB) was used routinely by the military between 1940 and 1960, but by 1965 its use reduced significantly due to the introduction of blood components. There is renewed interest in administering whole blood (WB) for the resuscitation of bleeding trauma patients, owing to evidence from studies such as the PROPPR trial which suggest 1:1:1 red cell: plasma: platelets may improve patient outcomes.

Aims: The shelf-life of WB (21–35 days depending on jurisdiction) was established decades ago, based on the viability of red cells. However, plasma quality during WB storage is not established and was examined in this study.

Methods: Leucocyte- and platelet-depleted WB (WB-PLT) was prepared using standard UK processes and compared to WB processed using a platelet-sparing leucocyte depletion filter (WB+PLT). WB was held at 2 – 6 °C for 35 days alongside standard red cells in SAGM (RBC-SAGM) and never frozen liquid plasma (LP). Thrombin generation and coagulation factor assays were used to assess the plasma from WB-PLT and WB+PLT compared to LP, to understand the effect of storing plasma alongside red cells ±platelets. Thromboelastography was performed on WB-PLT and WB+PLT, as well as the plasma separated from each, and LP. Contact activation was assessed with S-2302. Statistical post-tests compared coagulation factor levels on subsequent days to day 1, and WB-PLT and WB+PLT to LP on days 9 and 14.

Results: Whilst certain coagulation factors remained unaffected by storage with platelets and/or red cells (e.g. fibrinogen and a_2-antiplasmin), others varied depending on the type of cell it was stored with, or time at 2–6°C. Most notably, FV activity was lost significantly during storage of WB+PLT, and statistically different from LP (day 14: 0.59 ± 0.14 IU/ml vs. 0.75 ± 0.1 IU/ml, respectively). Free protein S antigen was also reduced in WB-PLT and WB+PLT, and significantly different from LP. Free protein S activity decreased dramatically in all three arms, and by day 35 was below the level of detection (<10%) in WB-PLT and WB+PLT, and only marginally higher in LP (16 ± 8.7%), with WB-PLT being significantly different to LP at day 9. FVIII activity in WB-PLT and APTT results for WB+PLT were significantly higher than LP at day 14. Levels of FVIII, FV and FVII remained on average >0.50 IU/ml at day 14 in WB-PLT and WB+PLT. Thrombin generating potential of plasma remained relatively stable to day 28 in all groups. Contact activation was demonstrated in 25% of LP units after day 14 and 12.5% of WB-PLT units, but not in WB+PLT.

Summary/Conclusions: These data suggest that in terms of plasma quality, a shelf life of 14 days or less may be more appropriate than 21–35 days for WB. These data will be used to propose a shelf-life of WB-PLT in the UK for trial use in the treatment of major haemorrhage. Further data on platelet function in WB+PLT is needed to inform its shelf-life.

3C-S09-02
RED BLOOD CELL UTILIZATION AND TRANSFUSION TRIGGERS IN PATIENTS DIAGNOSED WITH CHRONIC LYMPHOCYTIC LEUKEMIA IN ICELAND 2003–2016

HH Thorvaldsson[1], S Sveinsdottir[1,2] and A Halldorsdottir[1,3]

[1]Faculty of Medicine, University of Iceland [2]Hematology [3]Blood Bank, Landspitali National University Hospital of Iceland, Reykjavik, Iceland

Background: Revised guidelines on patient blood management (PBM) were published in Iceland in 2012, proposing a restrictive red blood cell (RBC) transfusion threshold of 70 g/l for patients with chronic anemia and 100 g/l for patients with bone marrow suppression. Anemia is a frequent complication of chronic lymphocytic leukemia (CLL) and RBC transfusions are commonly used as supportive treatment. In Iceland, all blood components are provided by a single blood bank, facilitating nation-wide studies of blood component utilization.

Aims: To investigate transfusion practices in CLL over a 14 year period with emphasis on hemoglobin transfusion triggers.

Methods: This retrospective investigation utilized a registry of Icelandic CLL patients, including all CLL patients diagnosed in Iceland during the period 2003–2016. Medical records were reviewed for information on symptoms, laboratory tests and treatment. Survival data were obtained from national registries and transfusion data were retrieved from the Blood Bank information system. For comparison of transfusion triggers, the period was split in two: A) 2003–2012 and B) 2013–2017.

Results: A total of 213 patients (143 males, 70 females) were diagnosed with CLL over the study period. A total of 77 (36.2%) patients had received RBC transfusion(s) (by March 2017) and the median time from CLL diagnosis to first transfusion was 2.2 years (range 0–9.9 years). The total number of RBC units transfused varied widely (range 1–115, median 6 units) as did the number of transfusion episodes (range 1–64, median 3) per patient. Most patients (n = 46) had <=3 transfusion episodes, and only 15 (7.0% of CLL cases) had >= 10 transfusion episodes. Higher age at diagnosis was associated with higher number of RBC transfusions (P < 0.01). Patients with Rai stage 3–4 at diagnosis were more likely to receive transfusions than patients with lower Rai stages (stage 0: P < 0.05, stage 1–2: P = 0.06) as well as patients who received chemotherapy (P < 0.001).

Data on hemoglobin (Hb) transfusion triggers for each patient′s first RBC transfusion were available for 65 cases (84.4%). The mean Hb trigger was 81.2 (95% CI: 75.9–86.5) in the latter period, which was significantly lower than the mean Hb threshold of 90.4 in the earlier period (95% CI 85.8–95.0, P = 0.011). When the group was stratified according to the presence or absence of confirmed bone marrow infiltration the difference in Hb trigger was only significant in the group without involvement, where Hb was 80.5 g/L in the latter period (95% CI: 75.2–85.8) compared to 93.5 g/L in the earlier period (95% CI: 86.7–95.6, P = 0.0041). The median time from CLL diagnosis to transfusion was significantly longer in the second period (2.9 years, 95% CI 1.9–5.0 years) compared to the first period (1.6 years, 95% CI 0.46–2.64 years, P = 0.01).

Summary/Conclusions: One-third of CLL patients required RBC transfusions during the course of the study. Older patients, those with higher Rai stage, and who needed chemotherapy were likelier to receive RBC transfusions. After the publication of PBM guidelines in 2012 the Hb transfusion trigger dropped significantly in patients without bone marrow infiltration while time to first RBC transfusion increased.

3C-S09-03

CD44 ANTIBODIES INHIBIT MACROPHAGE FC GAMMA RECEPTOR-MEDIATED PHAGOCYTOSIS OF PLATELETS AND ERYTHROCYTES IN AN IGG SUBTYPE AND FC-DEPENDENT MANNER: A POTENTIAL REPLACEMENT FOR IVIG?

PA Norris[1,2,3], G Zhu[1], G Fairn[1,2], H Ni[1,2,3] and A Lazarus[1,2,3]

[1]St. Michael's Hospital [2]University of Toronto [3]Canadian Blood Services, Toronto, Canada

Background: Immune thrombocytopenia (ITP) is an autoimmune disease characterized by immune-mediated reductions in platelet counts, leading to severe bleeding and potentially fatal intracranial hemorrhage. The majority of ITP patients possess anti-platelet autoantibodies that can mediate platelet destruction in the spleen through macrophage Fcγ receptor-mediated phagocytosis. Intravenous injection of pooled human serum immunoglobulin (IVIg) has been used as a first-line treatment in ITP for decades. However, IVIg replacement therapies are of significant interest due to IVIg's high cost, theoretical risk of disease transmission, and demand on blood donors. We have previously demonstrated that monoclonal antibodies to the hyaluronic acid receptor CD44 can successfully treat murine antibody-mediated ITP at three-log-fold lower doses than IVIg by an unknown mechanism. As CD44 is expressed on leukocytes including macrophages, we hypothesized that anti-CD44 increases platelet counts by interfering with macrophage phagocytosis.
Aims: Our study aimed to determine whether CD44 antibodies increase platelet counts in mice by inhibiting macrophage Fcγ receptor-mediated phagocytosis.
Methods: Three different CD44 antibodies were tested for inhibition of macrophage phagocytosis of platelets. Platelets were opsonized with one of five different anti-platelet antibodies of different IgG subtypes. The role of Fcγ receptor interactions with CD44 antibodies was evaluated by deglycosylation and F(ab')2 fragment generation of CD44 antibodies. Finally, the above methods were also tested using IgG-opsonized erythrocytes as phagocytic targets to determine whether anti-CD44 could inhibit phagocytosis of erythrocytes in a similar manner.
Results: Here we demonstrate that macrophage Fcγ receptor-mediated phagocytosis of platelets can be completely inhibited by anti-CD44 antibodies. Anti-CD44 inhibited phagocytosis in a dose-dependent manner, up to near complete (>90%) inhibition. Using monoclonal antibodies to murine platelets of mouse IgG2a, IgG2b, and IgG1 subtypes, we found anti-CD44 inhibited phagocytosis only when the opsonizing and therapeutic antibody subtype were matched for putative Fcγ receptor binding. These results suggest that anti-CD44 inhibits Fcγ receptor-mediated phagocytosis of platelets by Fc blocking. Removal of anti-CD44 Fc-Fcγ receptor interactions by Fc deglycosylation or generation of F(ab')2 fragments led to complete loss of anti-CD44 therapeutic activity. In addition, inhibition of macrophage Fcγ receptor-mediated phagocytosis of murine erythrocytes was also dependent upon IgG subtype and presence of anti-CD44 IgG Fc, suggesting that anti-CD44 antibodies inhibit phagocytosis of erythrocytes by the same mechanism.
Summary/Conclusions: CD44 antibodies constitute potent inhibitors of macrophage Fcγ receptor-mediated phagocytosis of both platelets and erythrocytes in a manner dependent upon the anti-CD44 Fc portion and IgG subtype. These results suggest important implications of IgG subtypes in monoclonal antibody therapeutic efficacy, and whether subtype may explain failure of some therapeutic antibodies remains to be explored.

3C-S09-04

NEUROPROTECTIVE EFFECTS OF A DEDICATED VIRALLY-INACTIVATED PLATELET LYSATE CONCENTRATED IN NEUROTROPHINS IN CELL-BASED AND ANIMAL MODELS OF PARKINSON'S DISEASE

M Chou[1,2,3], J Wu[3], F Gouel[2], A Jonneaux[2], K Timmerman[2], T Renn[1], C Laloux[2], H Chang[1], L Lin[1,4], J Devedjian[2], D Devos[2] and T Burnouf[3,5]

[1]Graduate Institute of Medical Sciences, College of Medicine, Taipei Medical University, Taipei, Taiwan, Republic of China [2]Service de Pharmacologie Clinique LICEND COEN Center Lille, University of Lille, INSERM UMR-S 1171, CHU de Lille, Lille, France [3]Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering, Taipei Medical University [4]Department of Microbiology and Immunology, School of Medicine, College of Medicine, Taipei Medical University [5]International PhD Program in Biomedical Engineering, College of Biomedical Engineering, Taipei Medical University, Taipei, Taiwan, Republic of China

Background: One of the most promising clinical developments of human platelet lysates (HPL) in regenerative medicine is their potential to be used as a disease

modifying treatment of neurological disorders. The scientific rational supporting this therapeutic approach is that platelets are rich in multiple neurotrophic molecules, including growth factors (PDGF, VEGF, BDNF, TGF-b, etc.) and neurotransmitters. The challenge created by this therapeutic strategy, as applied to a complex organ like the brain, lies in the need to ensure an optimal quality and safety profile for a safe administration by either the intracerebroventricular (ICV) or the intranasal (i.n.) routes. We have recently developed (Chou et al. Biomaterials, 2017) a tailor-made platelet lysate for brain administration; free of fibrinogen (to avoid fibrin deposition), devoid of thrombogenic, proteolytic, and inflammatory activity. When from allogeneic source, this HPPL should also be subjected to virus reduction treatments.
Aims: To develop a virus-free tailor-made neuroprotective HPL enriched in multiple neurotrophic growth factors, depleted of plasma proteins including fibrinogen, with a safety profile compatible with brain administration for a disease modifying strategy of Parkinson's disease (PD).
Methods: Apheresis platelet concentrates were centrifuged to eliminate plasma. The platelet pellet was then suspended in PBS and subjected to three freeze-thaw cycles (−80°/37°C). After centrifugation, the platelet lysate supernatant was subjected to heat-treatment (56°C for 30 min), solvent-detergent (S/D) treatment by TnBP/Triton X-45 or 20-nm-nanofiltration using Planova 20N. The in vitro thrombogenic, proteolytic, and inflammatory activity was assessed by thrombin generation assay, Zymuphen prothrombinase assay, procoagulant phospholipid-dependent clotting time assay and inflammatory markers accessed by BV2 microglia cell model. The neuroprotective effect was assessed (a) in vitro using a LUHMES cell model exposed to MPP$^+$ neurotoxin and (b) in vivo using C57BL/6 mice exposed to MPTP neurotoxin.
Results: The heat-treatment resulted in the decrease of the total protein content, a modification of the neurotrophic growth factor content, an elimination of the thrombogenic and proteolytic activity, and an inactivation of ≥ 2.5 log of HCV. Furthermore, the HPPL did not stimulate the release of inflammatory markers (e.g. COX-2, iNOS) by BV2 microglial cells in culture, could restrict COX-2 expression upon LPS exposure, and provided strong neuroprotective activity of LUHMES in vitro. Its i.n. administration in mice induced a diffusion of platelet derived growth factor (PDGF) in olfactory bulb, striatum and cortex brain areas), protected the expression of tyrosine hydroxylase (TH) by dopaminergic neurons in the substantia nigra pars compacta and striatum, and was not inflammatory based on Iba-1 expression my microglia. The S/D treatment and 20 nm-nanofiltration steps were shown to inactivate ≥ 2.5 Log of HCV in each step (more than 7.5 log HCV reduction after 3 different viral inactivation steps) and still preserved the neuroprotection in vitro.
Summary/Conclusions: It appears feasible to develop a virally-safe platelet lysate preparations as potential biotherapy for the treatment of neurodegenerative disorders of the central nervous system, such as PD.

3C-S09-05

COMBINED ORAL CONTRACEPTIVES ARE ASSOCIATED WITH HIGHER LEVELS OF BLOOD PLATELETS AMONG HEALTHY WOMEN: RESULTS FROM THE DANISH BLOOD DONOR STUDY (DBDS)

K Dinh[1], K Kaspersen[1], O Pedersen[2], M Petersen[1], S Mikkelsen[1], K Rostgaard[3], H Hjalgrim[3,4], H Ullum[5] and C Erikstrup[1]

[1]Department of Clinical Immunology, Aarhus University Hospital, Aarhus [2]Department of Clinical Immunology, Naestved Hospital, Naestved [3]Department of Epidemiology Research, Statens Serum Institut [4]Department of Haematology [5]Department of Clinical Immunology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

Background: Combined oral contraceptives (OC) are used by 27% of women aged 15–49 years in Denmark. OC offer convenient, effective and reversible fertility regulation. A fundamental side effect is the well-known venous thromboembolism including deep vein thrombosis and pulmonary embolism. Other potential serious side effects are myocardial infarction and ischemic stroke. Studies have investigated metabolic, proinflammatory, and haemostatic effects of estrogen and progestins contained in OC. Platelets play an important role in the pathogenesis of venous thromboembolism, however, the impact of OC on blood platelet levels remains unknown.
Aims: The aim of this study was to examine the impact of OC on the levels of blood platelets in a large cohort of blood donors.
Methods: Blood platelet levels in 28,950 women from The Danish Blood Donor Study giving blood in 2011–2016 in the Capital and Central Danish Regions were measured by automated haematology analysers at each donation. All participants completed a standard questionnaire on lifestyle factors and further stated their use of contraception, childbirth, and menopausal status. Type of OC and OC exposure period were identified by ATC codes in the Danish National Prescription Registry.

The association between OC and blood platelet levels was explored by repeated measures mixed model analysis. Analyses were adjustment for age and time since previous donation was performed. Results are presented as coefficients with 95% confidence intervals (CI).

Results: A total of 9,327 female participants (32.2%) filled an OC prescription in the study period, of whom 5,821 were intermittent OC users and 3,506 were continuous OC users. Among users, 559 (2.7%), 5,552 (26.8%), 12,447 (60.0%) and 2.172 (10.5%) were users of 1st, 2nd, 3rd, and 4th generation of OC, respectively. Blood platelet levels were higher among OC users compared to non-users (coefficient: 9.7 billion thrombocytes/L, CI: 9.2–10.2). The difference was increased when comparing OC continuous users vs. non-users (coefficient: 18.5, CI: 16.4–20.6) although the difference between OC intermittent users vs. non-users (coefficient: 10.2, CI: 8.5–11.9) was the same as for OC users vs. non-users. There was no difference between OC types in their effect on blood platelet levels.

Summary/Conclusions: OC users had higher levels of blood platelets than non-users. The findings are important to help the understanding of the effect of OC on risk of thromboembolism. The mechanism of OC on blood platelets needs further investigation. Our finding underscores that blood donor cohorts are feasible in studies of health properties in healthy persons.

3C-S09-06

UNDERLYING INFECTION CONTRIBUTES TO TRANSFUSION-RELATED IMMUNE MODULATION IN AN IN VITRO PLATELET TRANSFUSION MODEL

A Sultana[1,2,3], M Dean[1,3,4], M Reade[2,5], R Flower[1,2,4] and J Tung[1,2,3,4]

[1]*Research and Development, Australian Red Cross Blood Service, Kelvin Grove* [2]*Faculty of Medicine, The University of Queensland, Queensland* [3]*The Critical Care Research Group, The Prince Charles Hospital, Chermside* [4]*Faculty of Health, Queensland University of Technology, Brisbane* [5]*Joint Health Command, Australian Defence Force, Canberra, Australia*

Background: Platelet concentrates are required for the treatment of thrombotic and haemostatic disorders. Platelets maintain vascular integrity by mediating coagulation and, contribute to immune responses. Despite therapeutic benefits, platelet transfusions can induce transfusion-related immune modulation (TRIM) and subsequent immunosuppression. Changes in immune responses can increase the patient's risk of adverse events such as infection, multi-organ failure, tumour growth and mortality. While TRIM has been described clinically and in experimental models, no definitive mechanisms of immune modulation have been provided. Using an established in vitro transfusion model this project aims to characterise monocyte, dendritic cell and neutrophil immune profiles associated with underlying infection.

Aims: To use an established in vitro transfusion model of monocyte, dendritic cell and neutrophil immune responses to:

Aim 1 – investigate the response to platelet supernatants

Aim 2 – determine whether these responses are altered in the presence of lipopolysaccharide (LPS) as a model of underlying bacterial infection

Aim 3 – determine whether these responses are further altered by increasing the concentration of LPS

Aim 4 – investigate whether platelet storage duration impacts any of the immunomodulation observed.

Methods: Monocyte, dendritic cell and neutrophil cytokine production were investigated following exposure to platelet supernatants in an established in vitro model. Fresh whole blood was cultured with RPMI media and Day 2, Day 5 or Day 7 pooled platelet supernatants (30 units pooled for each time point) at a final dilution of 10%, modelling a one unit transfusion. To model different levels of underlying infection LPS was used at 0 μg/ml, 0.23 μg/ml or 1 μg/ml. Protein transport inhibitor (containing Brefeldin A) was added to facilitate detection of intracellular cytokines (IL-6, IL-8, IL-10, IL-12, IL-1α, TNF-α, MIP-1α, MIP-1β, MCP-1, IP-10) via flow cytometry. Statistical difference between matched controls or LPS was determined at $P < 0.05$ using a one-way analysis of variance (ANOVA) or a two-way ANOVA with a Tukey's post-test.

Results: In the absence of LPS stimulation, platelet supernatants did not significantly modulate monocyte, dendritic cell or neutrophil cytokine production (i.e., Aim 1). In the model of underlying infection (i.e., LPS) platelet supernatants suppressed monocyte (IL-6, IL-12, IL-1α and TNF-α) and dendritic cell (IL-6, IL-10, and IL-12) cytokine production (i.e., Aim 2). When comparing a higher level of underlying infection with a lower level of underlying infection (i.e., 1 μg/ml vs 0.23 μg/ml LPS), further modulation of monocyte (IL-1α and TNF-α) cytokine production was evident (i.e., Aim 3). Increased platelet storage duration did not significantly impact any of the monocyte or dendritic cell responses observed in this study

(i.e., Aim 4). Neutrophil cytokine production was below the limit of detection and differences were not observed in this in vitro transfusion model.

Summary/Conclusions: Together these data provide evidence that underlying infections can induce changes in patient monocyte and dendritic cell immune profiles, which are further modified in the presence of platelet supernatants. There is also evidence that the level of underlying infection further modulates immune profiles, which may contribute to poor patient outcomes including an increased risk of infection post-transfusion.

Blood Products – Platelets: Novel Products and Processes

3C-S10-01

NOVEL PLATELET PRODUCTS

R Cardigan

No abstract available

3C-S10-02

INSIGHT INTO THE OPTIMAL PLASMA CONTENT IN PLATELET STORAGE MEDIA TO ACCOMPLISH COLD STORAGE OF PLATELET CONCENTRATES

I Marini[1], K Aurich[2], R Jouni[3], A Greinacher[2], T Thiele[2] and T Bakchoul[4]

[1]*Transfusion Medicine, Medical Faculty Tübingen, Tübingen* [2]*Transfusion Medicine, University Medicine Greifswald, Greifswald* [3]*Transfusion Medicine, Medical Faculty of Tübingen, Tuebingen* [4]*Transfusion Medicine, Medical Faculty of Tübingen, Tübingen, Germany*

Background: Bacterial contamination is a major problem for platelet transfusion, since platelet concentrates (PCs) are routinely stored at room temperature (RT). Cold storage of PCs is a potential approach to overcome this risk, but chilled platelets have been shown to have poorer recovery and survival compared to RT stored platelets. We hypothesized that the residual plasma content in platelet storage media influences the storage lesion and recovery of cold stored platelets.

Aims: To evaluate the impact of different residual plasma proportions in platelet storage media during cold storage of PCs on platelet function and survival.

Methods: Apheresis PCs (APCs) were collected from healthy volunteers and resuspended in plasma or platelet additive solution (PAS, SSP+, Maco Pharma, France) at a final plasma concentration of 20%, 35% or 100%, respectively. APCs were stored either at RT or at 4 °C under constant agitation. Recovery and survival of transfused platelets were assessed applying the NOD/SCID mouse model 60, 120, 300 and 1440 min after injection. Adhesion and spreading ability was analysed over collagen and fibrinogen coated surfaces.

Results: Platelets stored at 4°C always showed impaired survival compared to those stored at RT. Comparable survival curves were found for a 35% plasma content compared to 100% plasma regardless of storage temperature. Platelets stored in PAS at very low plasma concentration (20%) were cleared from the mouse circulation faster compared to those stored at 100% plasma, especially when those were cold-stored at 4°C (mean±SEM of PLT survival after 2 h: 36%±5%, vs. 18%±4%, $P = 0.003$, plasma-APC vs. PAS-20-APC, respectively). On the other hand, platelet storage at 4°C preserves their hemostatic functionality better than current standard care. More cells adhered to both collagen and fibrinogen compared when platelets were stored at 4°C. However, this effect disappeared when plasma was reduced to 20% suggesting that excessive reduction of plasma volume lower than 35% impairs PLTs adhesive functions especially at 4°C.

Summary/Conclusions: Plasma factors do not seem to have major impact on cold lesions, although excessive reduction of plasma impairs platelet function and survival. Platelet concentrates stored in 65% PAS were not inferior to those stored in 100% plasma at room temperature as well as at 4°C.

3C-S10-03

PLATELET ADDITIVE SOLUTION (PAS): A STEP TOWARDS UNIVERSAL SINGLE DONOR PLATELETS (SDP)

M Chowdhry, M Patel and S Agrawal

Transfusion Medicine, Indraprastha Apollo Hospital, New Delhi, India

Background: During shortage of ABO-compatible SDP (Single Donor Platelets), alternate group SDP is used albeit a risk of acute haemolytic transfusion reactions (AHTR). This is more so in the 'high titred' O group donors (anti-A and/or anti-B are ≥128). Platelet Additive Solution (PAS) overcomes the risk of AHTR/allergic reactions and is proposed to prolong the shelf life of SDP to 7 days.

Aims: To compare various haematological and biochemical parameters of PAS stored SDP units with the SDPs stored in plasma over 7 days. To assess the feasibility of using PAS to obtain low titre SDP units which can be utilised across the group.

Methods: This prospective study was performed from June 2017 to January 2018 after clearance from the institutional ethical committee. The study group included donors of O, A and B group whose SDP was prepared in 70:30 ratio of PAS SSP+ (Macopharma) to plasma. The control group included donors of AB group whose SDP was stored in plasma. SDPs from both the groups were compared for visual appearance, swirling, Arterial blood Gas analysis (ABG) and platelet indices on day 1, 5 and 7. The sterility testing for both the groups was assessed on day 7. The Pearson test was used to analyse the correlation of pH with the platelet indices from day 1 to 7 in all group.

In O group SDP's, anti-A and anti-B titres were compared before and after modification of SDP with PAS and between 'high titre' and 'non-high titre group'.

Results: The study group comprised of 200 donors and control group consisted of 62 donors. Of all the parameters compared, bicarbonate level reached statistically significant higher levels in control group on day 1 & 5 (P < 0.05). Though the mean pH was higher in the study group compared to control group on day 5, (P > 0.05) it did not reach significance.

On day 7, pH was significantly well maintained in the study group compared to control group (P < 0.05). Mean increase in mean platelet volume (MPV) on day 7 compared to day 1 was significantly higher in control group (P < 0.05) as compared to the study group. Potassium was higher in control group compare to study group on day 7 but was statistically not significant. Mean decrease in mean platelet component concentration (MPC) from day 1 to day 7 was higher in control group compare to study group but was statistically not significant. None of the remaining parameters or Pearson's correlation reached statistical significance. No bacterial growth was seen in both the groups.

In the study group, the median antibody titres in O group SDP's (n = 100) was 128 prior to PAS addition and reduced significantly by 3-fold to 16, post-modification (P < 0.001). In both the 'high' (n = 48) and 'non-high' tittered (n = 52) group, significant titre reduction was noted (P < 0.001)

Summary/Conclusions: In vitro characteristics of platelets stored in PAS maintains its quality as per the standards till 7 days of storage. Use of PAS for SDPs eliminates the need for group-specific platelets and thereby helps in maintaining a better inventory.

3C-S10-04

A NOVEL FUNCTION FOR PLASMA CLOTTING FACTOR VA IN CLOT DISSOLUTION

E Pryzdial and F Lee

Department of Pathology and Laboratory Medicine, University Of British Columbia, Vancouver, Canada

Background: Cardiovascular disease is the leading cause of death worldwide. The major contributor is blood clots (i.e. thrombi) that block normal blood flow. Thrombi are comprised largely of fibrin, which provides structural support to the clot. Current clot-dissolving (i.e. thrombolytic) drugs were designed based on the naturally occurring protease tissue plasminogen activator (tPA), which activates plasminogen (Pg) to plasmin, the enzyme responsible for cleaving and dissolving fibrin. However, tPA is an active enzyme that must be given at a high dose to overcome its rapid clearance and therefore can work through the body, not just at the thrombus site. This causes life-threatening bleeding in up to 8% of patients. Treating thrombosis may be improved by instead accelerating intrinsic tPA using a non-enzymatic therapy localized to the clot itself. We have discovered that plasmin cleaves and converts the essential coagulation cofactor, factor Va (FVa), into a fibrinolysis cofactor capable of accelerating tPA-mediated Pg activation when associated with anionic phospholipid (aPL), which localizes to the clot. Complex sequential cleavages of FVa by

plasmin dissociate its heavy (FVaH) and light subunits (FVaL) causing loss of coagulant activity.

Aims: Our goal is to determine the simplest combination of plasmin-mediated FVa-derived fragments that accelerate tPA, providing a safer therapeutic alternative.

Methods: To correlate the fragmentation of FVa following plasmin cleavage to the acquisition of tPA cofactor activity, a chromogenic assay was used to measure plasmin production. Either intact or plasmin-cleaved FVa was incubated with tPA and Pg, and samples were taken over time to measure plasmin generation. FVaH- and L-derived fragments that remain bound to aPL were separated by differential centrifugation. Fragmentation of FVa-derived samples was concomitantly analyzed by polyacrylamide gel electrophoresis and Western blot to correlate fragmentation to tPA cofactor activity. Additionally, autoradiography was used to assess direct binding of FVa fragments to ^{125}I-radiolabelled Pg (^{125}I-Pg).

Results: Cleavage of FVa by plasmin prior to incubation with tPA and Pg significantly accelerated Pg activation, demonstrating that proteolytic modulation by plasmin confers tPA cofactor activity. This enhancement was observed only in the presence of anionic phospholipid (aPL). Interestingly, when separated, both aPL-binding FVaL-derived fragments and FVaH-derived fragments not bound to aL enhanced plasmin generation by tPA. However, only a ~50 kDa FVaH-derived fragment was shown to directly bind to ^{125}I-radiolabelled Pg, suggesting that the FVaL-derived fragment enhances tPA cofactor activity through an additional mechanism.

Summary/Conclusions: In addition to understanding physiological fibrinolysis, an extension of our work is in treatment of thrombotic disease such as stroke and heart attack where thrombolysis is required to restore blood flow. Since FVaL contains the high affinity-binding site for aPL, and aPL must be present for efficient conversion of FVa function, the nascent tPA cofactor function would be localized exclusively to the clot. We are now generating a recombinant fibrinolytic fragment of FVaL toward a non-enzymatic cofactor-based approach to dissolving clots, reducing the side effects associated with therapeutic tPA.

3C-S10-05

IMPROVING BLOOD MANAGEMENT: NON–DESTRUCTIVE QUALITY ASSESSMENT OF RED BLOOD CELL CONCENTRATES USING MINI-BAGS

P Schubert[1,2], B Culibrk[1], Z Chen[1], A Howell[3], D Devine[1,2] and K McTaggart[4]

[1]Centre for Innovation, Canadian Blood Services [2]Pathology and Laboratory Medicine, University of British Columbia, Vancouver [3]Centre for Innovation, Canadian Blood Services, Edmonton [4]Centre for Innovation, Canadian Blood Services, Ottawa, Canada

Background: As required by Canadian standards, 1% of red blood cell concentrates (RCCs) produced by Canadian Blood Services are held for destructive quality testing on day 43 of storage, one day after expiry, resulting in the loss of some 8,000 RCCs per year from inventory.

Aims: Here we present a pilot concept which would potentially eliminate the need to discard RCCs for quality control (QC) testing by using an aliquot removed from the RCC at the time of production and stored in a separate mini-bag until testing at expiry. This technique would also enable increased sample sizes to better understand donor variation without negatively impacting inventory.

Methods: Rectangular (R) shaped mini-bags with a capacity of 10 ml, 17 ml or 25 ml and comparable length to width ratios were designed and welded in-house as a modification of our standard RCC storage bag (MacoPharma, Lille, France). RCCs were produced using the buffy-coat method. The three sizes of mini-bags were filled by syringe with RCC volumes between 3 to 9 ml, 5 to 11 ml and 7 to 13 ml, respectively (n = 6 per arm). To test for potential impact of air in the mini-bags, air bubbles of 0, 1 or 2 ml size were added via syringe (n = 6 per arm). The mother units (MUs) and corresponding filled mini-bags were stored at 4°C to expiry. Assessment of red blood cell (RBC) quality at day 43 of storage included RBC count, hematocrit, hemoglobin, hemolysis (Harboe method), pH, glucose, lactate and supernatant potassium.

Results: The RBC counts, hematocrit and hemoglobin levels were not statistically different in R17 and R25, but were ~4-fold higher in R10 compared to the respective MU. Hemolysis development was lowest in the middle of the volume range tested for all three mini-bag sizes and had the smallest change of 0.02 + /- 0.03% to the MU in the R17 mini-bag with 9 ml RCC. This finding aligned with potassium levels showing a difference of 1.97 + /- 0.73 mM (~7%) compared to the MU. Metabolic activity measures also showed a similar trend with no effect on pH. Using the R17-9 ml configuration, the addition of a 1 or 2 ml air bubble had no significant effect on any measurements compared to no air. In order to challenge this system, RCCs (n = 6) were held at room temperature for 48 h prior to filling the mini-bags and subsequent 4°C storage of the MU and mini-bags. As expected, the quality was

markedly decreased with ~2-fold increased glucose consumption and 2- to 3-fold higher potassium release and hemolysis development; however, the R17-9 ml mini-bags reflected this lower quality in the same small margins as regular RCCs.

Summary/Conclusions: Here we present data presenting a mini-bag concept (shape and RCC fill volume) exhibiting a very similar storage feature compared to respective RCC MU. Once this concept is validated in a blood production setting, implementation of a separate mini-bag as a non-destructive sampling method would avoid the loss of RCCs for QC testing.

Blood Safety – Bacterial and Parasitic Infections

3C-S11-01

BACTERIAL CONTAMINATION OF 7-DAY PLATELETS: EXPERIENCE AT CANADIAN BLOOD SERVICES

S Ramirez-Arcos, S Evans, T McIntyre, C DiFranco and M Goldman

Canadian Blood Services, Ottawa, Canada

Background: Platelet concentrates (PCs) are routinely screened for bacterial contamination with the automated BacT/ALERT culture system. Since August 2017, the PC shelf-life was extended from 5 to 7 days with an improved bacterial testing algorithm, including: cultures performed at ≥36 h post collection vs 24 h; inoculation of one aerobic culture bottle and one anaerobic culture bottle for buffy coat (BC) pools and single apheresis units; screening of double apheresis with three aerobic bottles and one anaerobic bottle; and a 6-h post-sampling quarantine period. Contaminated PCs with negative screen results may be found through reporting of transfusion reactions or Quality Control (QC) testing of outdated PCs.

Aim: Summarize bacterial screening results for 7-day PCs obtained since August 2017.

Methods: From August to December 2017, 35,643 BC pools and 6,842 apheresis units were screened during routine testing. In addition, 908 outdated PCs, including apheresis units and BC pools, were QC-tested. Positive results were classified as: "confirmed positives" if the same bacterium was isolated in initial and confirmatory cultures or if the same bacterium was isolated in an initial PC culture and an associated co-component when the implicated PC was unavailable for re-culture; "false positive" if no bacteria were isolated in initial or confirmatory cultures; "unconfirmed positive" if bacteria were present in the initial culture but not in confirmatory testing, or if no PCs were available to confirm initial results and testing of co-components was negative. "False negatives" were those units missed in routine screening and captured during QC testing of outdated PCs or implicated in septic transfusion reactions.

Results: Twenty-eight (0.08%) and three (0.03%) culture results were categorized as confirmed positives during routine screening of BC pools and apheresis units, respectively. Bacteria isolated from BC pools included Propionibacterium acnes (17), Streptococcus spp (3), coagulase negative Staphylococcus (CoNS, 5), Staphylococcus aureus (2), and diphtheroid bacillus (1). Seven of the 28 confirmed positives (25%) involved an initial culture of a PC pool and confirmatory testing of an associated RBC unit, all contaminated with P. acnes. Confirmed positive cultures obtained from apheresis PCs were identified as P. acnes (1), Streptococcus viridans (1), and CoNS (1). False positive results accounted for 0.1% and 0.8% of BC pools and apheresis units tested, respectively, while unconfirmed positives yielded rates of 0.1% and 0.4%, correspondingly for BC and apheresis PCs. Out of the 908 outdated PCs that were QC-tested, one BC pool was confirmed to be contaminated with CoNS. One non-fatal septic transfusion reaction involving a 7-day BC pool contaminated with Staphylococcus epidermidis was reported for an approximate rate of 0.002% transfusion reactions.

Summary/Conclusion: Comparing results of confirmed positive cultures presented herein to those for 5-day PCs (prior to August 2017), screening of 7-day PCs demonstrates enhanced detection of contaminated products. Detection of contaminated PCs has increased approximately 3-fold for aerobic bacteria in both apheresis units and BC pools. When cultures of anaerobic organisms are included, the detection of contaminated pools and apheresis units has increased approximately 8-fold and 5-fold, respectively. These results indicate improved sensitivity of the current PC screening protocol. A longer observation period is necessary to quantify residual safety risk

3C-S11-02

IMPROVING THE SAFETY OF PLATELETS BY INCREASING THE SAMPLE VOLUME AND TIME FOR SAMPLING AND ISSUING – BACTERIOLOGICAL RESULTS

F Bernier[1] and G Delage[2]

[1]Product Qualification [2]Medical Affairs, Hema-Quebec, Saint-Laurent, Canada

Background: Bacterial detection in platelets (PLT) was introduced at Héma-Québec (HQ) in 2005 for all PLT products (PLT from whole blood and apheresis). Despite this, from 2005 to 2013, HQ received reports of 3 septic reactions (1 fatality) out of 276,866 products transfused (S. aureus – 2006 and 2011, S. pyogenes – 2013). Because of this, improvements to the process were needed.

Aims: To reduce the risk of adverse reactions due to contaminated PLT by improving the process for bacterial detection. This was achieved by increasing the time of sampling, increasing the volume sampled and delaying the issue of the PLT.

Methods: Between February 2005 and November 23, 2014, 4–10 ml were sampled 18–24 h after collection of the PLT, inoculated in an aerobic bottle (BPA) and incubated in the BacT/Alert® Classic (bioMérieux, Durham, NC). The PLT was issued once the incubation had been started.

From November 24, 2014 to October 25, 2015, 20 ml were taken at least 24 h after collection: 10 ml were inoculated in the BPA and 10 ml were placed in the newly introduced BPN. The platelet was issued once the incubation had been started.

Since October 26, 2015, the time of sampling was increased to 48 h and a 12 h incubation period in the BacT/Alert was added before issuing the PLT. We also extended the PLT shelf-life to 7 days with Health Canada approval.

Results: From 2005 to 2014 the true positive rate (TPR) was 0.013% (59/465,375). Only 2 PLT were transfused before the culture became positive: no adverse reaction was observed (coagulase-negative Staphylococcus and S. epidermidis).

In 2014–2015, the TPR was 0.037% (10/27,013). Eight of them were intercepted, and two were transfused (coagulase-negative Staphylococcus and Propionibacterium sp.) but gave no adverse reaction. Nine were positive with the anaerobic bottle only: 6 Propionibacterium sp., 2 coagulase-negative Staphylococcus, 1 Staphylococcus saccharolyticus (strict anaerobes). One breakthrough infection due to Bacillus was reported.

From October 2015 to December 2017 the TPR was 0.035% (22/62,531). Five were transfused (Propionibacterium sp.) with no adverse reaction (mean time of detection = 4.15 days and positive only with BPN). No breakthrough infection was reported (close to 90,000 products cultured).

Excluding the Propionibacterium cases, the TPR was 0.011% in 2005–14, 0.015% in 2014–15 and 0.019% in 2015–2017.

Using two bottles (aerobic and anaerobic) caused an increase in false positive rate (FPR) (false signal read by the instrument, culture negative). Using BPA only, the FPR was 0.031%, but using BPA and BPN increased the FPR to 0.229%.

Summary/Conclusions: Increasing the sample volume, time of sampling and time for issuing has increased the true positive rate of our cultures and consequently reduced the risk of adverse reaction due to bacterial contamination in PLT. Increasing the delay before sampling and issuing required the adoption of a longer shelf life.

3C-S11-03

RAPID BACTERIAL DETECTION SYSTEM PREVENTS SEVERE BACTERIAL INFECTION

M Schmidt[1], K Hourfar[2], K Gubbe[3], U Mayr-Wohlfart[4], A Karl[5], H Schrezenmeier[6] and E Seifried[7]

[1]Quality Management [2]Blood Donor Screening, German Red Cross, Frankfurt [3]Quality Management, German Red Cross, Plauen [4]Blood Donor Screening, German Red Cross, Ulm [5]Blood Donor Screening, German Red Cross, Plauen [6]Management, German Red Cross, Ulm [7]Management, German Red Cross, Frankfurt, Germany

Background: Bacterial contamination of blood components is still a major challenge in Transfusion Medicine especially for platelet concentrates which are stored at room temperature. To improve blood safety the maximum shelf life was reduced in Germany for platelets from 5 to 4 days. In addition rapid bacterial screening methods were developed (NAT and Bactiflow) to implement a generic bacteria screening 48 h to 72 h after blood donation.

Aims: We implemented a mini-pool bacteria screening system (Bactiflow) for platelets with a maximum pool size of 10 platelet components per pool. Platelet were released without bacterial testing on day 1–2. 48 h after blood donations samples from platelet concentrates were collected, pooled and tested for bacteria contaminations. Shelf life of all screened platelets with a negative test result will be extended to 5 days.

Methods: Platelets were released after production without any delay. All platelets which were not transfused 48 h after blood donations were tested for bacterial contaminations by the Bactiflow system. The analytical sensitivity of the method is app. 500 CFU. The bactiflow method is able to detect transfusion relevant bacteria strains spiked in platelets with a concentration of 10 CFU/bag after storage of 48 h at room temperature.

Results: Between May 2016 and January 2018 52,136 platelets were screened for bacterial contaminations. In Total 4 platelets were identified with bacterial contaminations (Klebsiella pneumoniae, Staphylococcus epidermidis, Escherichia coli and Staphylococcus aureus). Growth kinetics demonstrated rapid bacteria growing.

Summary/Conclusions: Compared to the culture methods, bacterial rapid detection methods like Bactiflow or NAT are characterized by a high clinical efficiency rate. Bacterially contaminated platelet concentrates could be identified and discarded before release of platelet components. Recalls as described by culture methods with the negative-to-date concept are not necessary. The introduction of rapid bacterial screening methods leads to an improvement to supply hospitals with platelet concentrates by extending the shelf life to 5 days, and in addition increases blood safety. Therefore, our blood donor service performs on a voluntary basis a test strategy to screen all available platelet concentrates from day 3 onwards on bacterial contaminations which is a major step to improve blood safety.

3C-S11-04

NATIONAL SEROPREVALENCE OF TRYPANOSOMA CRUZI IN MEXICAN BLOOD DONORS, 2007–2016

L Salazar[1], J Rojo Medina[2], G Estrada-García[1] and J Trejo[3]

[1]Director [2]Head Director [3]Blood Bank, National Blood Transfusion Center, Mexico, Mexico

Background: Chagas disease, or American trypanosomiasis is a life-threatening disease caused by the parasite Trypanosoma cruzi. It is found mainly in Latin America, where it is transmitted to humans principally through contact with infected insect feces, called vector transmission. [1]

Blood transfusion infection is the second transmission mechanism after the vector. This was due to the process of urbanization in Latin America, intensified in the second half of the twentieth century and the increase in population movements that have modified the epidemiological profile of this disease and have become a global risk, due in particular to the blood donation, by migration of people from endemic areas to non-endemic areas where triatomines do not exist.

Mexican Official Standard NOM-253-SSA1-2012 "For the Disposal of Human Blood and its Components for Therapeutic Purposes," states that infectious seroreactivity screening is mandatory for all donated whole blood units, including T. cruzi. However, transmission of infection can be prevented by selecting blood donors. Likewise, it is difficult to establish a confirmatory diagnosis during asymptomatic or mild clinical manifestations, so it is important to standardize the serological tests to demonstrate the antibodies against T. cruzi.

Aims: To determine the seroprevalence of reactivity against Trypanosoma cruzi by the detection of antibodies in blood donors in Mexico during a study period from 2007 to 2016.

Methods: The present work is an observational, multicenter, longitudinal, retrospective, prolective study that demonstrates the behavior of seroprevalence of reactivity against T. cruzi in blood donors in 516 different Blood Banks of the Health System in Mexico.

Monthly serology reports on blood donors were organized and analyzed by descriptive statistics, which were sent to the National Blood Transfusion Center (CNTS) by Blood Banks (n = 516). Health System in Mexico, these reports include: number of donors studied for T. cruzi, detection of sero reactivity against T. cruzi, as well as repeatedly reactive results of the same causal agent. The tests used were: reagent strip, immunoenzymatic assay, complement fixation, indirect hemagglutination, direct agglutination and indirect immunofluorescence.

Results: From 2007 to 2016 the CNTS received 15,853,840 serological reports for reactivity detection against T. cruzi, of which 61,536 serological studies were repeatedly reactive. An increase in the percentage of application of reactivity tests for T. cruzi in blood donors (2007: 54.1% to 2016: 100%) and decrease in reactivity seroprevalence in the study period (0.40 to 0.32) was observed, identifying the States of Michoacan, Colima, Guerrero, Nayarit and Tamaulipas as the five Federative Entities with the highest seroprevalence of reactivity against T. cruzi.

Summary/Conclusions: The transmission form of T. cruzi, called Urban Chagas (transfusional/transplants), is a challenge in our country, which conditions 100% screening coverage in blood donors. Transmission via the vector of T. cruzi remains in Mexico the most important, however, blood transfusion remains as a transmission

risk due to migration in our country, with emergence of cases in geographical areas where the vector before had not been detected; Therefore it is important to always consider the transfusion history and risk factors for the transmission of T. cruzi. Blood banks are an opportunity field to create and effective clinical care algorithm for reactive blood donors to T. cruzi, which can be implemented nationwide across all sectors.

3C-S11-05

A RETROSPECTIVE COMPARISON OF MALARIA POLICY FORMULATION IN 5 NON–ENDEMIC COUNTRIES

S O'Brien[1], S Ward[2], C Seed[3], A Kitchen[4], C Fabra[5], W Steele[6], G Delage[7] and D Leiby[8]

[1]Epidemiology & Surveillance [2]International Collaboration and Corporate Secretariat, Canadian Blood Services, Ottawa, Canada [3]Australian Red Cross Blood Service, Perth, Australia [4]National Transfusion Microbiology Reference Laboratory, National Health Service Blood and Transplant, London, United Kingdom [5]Laboratoire de Qualification Biologique des Dons, Etablissement Francais du Sang, Poitiers, France [6]Scientific Affairs, American Red Cross, Rockville, United States [7]Medical Affairs and Microbiology, Hema-Quebec, Saint-Laurent, Canada [8]Center for Biologics Evaluation and Research, Food and Drug Administration, Silver Spring, United States

Background: Malaria, a mosquito-borne parasitic infection causing cyclic fever, is endemic in Africa and many parts of the world. In non-endemic countries transfusion transmission risk is from blood donors born in or having spent time in an endemic area. Risk is addressed by selectively testing at-risk donors or by deferral. Policies vary between countries. The Alliance of Blood Operators Risk Based Decision Making Framework recommends a range of assessments be considered when determining policy.

Aims: To compare the types of assessments used to formulate malaria policies in England, France, Australia, Canada and the USA with those recommended by the Framework.

Methods: The key relevant elements of the Framework were identified: the intervention, safety threat, availability threat, donor impact, financial implications, risk communication, stakeholder relations and regulatory aspects. Decisions were analyzed in two key areas separately: decisions to implement selective testing, and selected donor criteria decisions. Details of assessments and information considered were compared against components of the Framework. The concern level for key considerations of the Framework were rated.

Results: Three countries implemented selective testing strategies: France, England and Australia. In France safety risk was key, whereas risk was already addressed by deferral or blood component restrictions in England and Australia. Sufficiency of the blood supply was assessed highly important in all 3 countries. Societal and donor concerns were considered. The main tradeoffs were to accept high operational impact and cost in exchange for reduced donor deferral/fresh component loss, and in France an increase in safety. The screening criteria decisions selected for analysis were: in France having been born in or lived in an endemic country during first 5 years of life, in England the criteria to accept donors if they returned from travel more than 12 months ago (in France and Australia these donors would be tested if travel was within the last 3 years), in Australia 3 year deferral of travelers to Papua New Guinea, in Canada permanent deferral of donors with malaria history, and in the USA 3 year deferral for donors with malaria history. The risk involved isolated transfusion transmission cases or near misses in Canada, Australia and France, 1 – 2 cases per year in the USA, and for England a shorter period over which travelers are tested than other countries. Social concerns were assessed to be high in France and Australia, political/regulatory influence was high is France, Australia and Canada, sufficiency was a key consideration in Canada, and in the USA, donor impact was important. Decision trade-offs varied by country, but generally involved accepting moderate operational impact to address perceived safety risk and political/regulatory concerns.

Summary/Conclusions: The assessments and information considered in each country were generally consistent with the objectives of the Framework. When data supported quantified risk assessment, safety and operational feasibility had the greatest weight in decisions. When risk was not well defined contextual factors such as social and political concern have greater weight. While stakeholder concerns and health economics carried proportionally less weight in these decisions, current expectations would require greater attention.

Working Party Session on Quality Management

3C-S12-01

PRINCIPLES OF DATA COLLECTION AND ANALYSIS IN ACHIEVING AN EFFECTIVE QUALITY MANAGEMENT SYSTEM IN BLOOD ESTABLISHMENTS

T Vuk

Quality Management, Croatian Institute of Transfusion Medicine, Zagreb, Croatia

Data management in healthcare system is increasingly important and challenging. Given the role of transfusion medicine in different areas of medical science and public health, the significance of data at its disposal goes beyond their use for managing transfusion services.

A huge amount of different data is generated in blood establishments (BE) on a daily base. These data differ according to their source, significance and purpose. The value of the data largely depends on how we use them.

Information technology has enabled the collection of large amounts of data from different sources. Nowadays, it is common for data from devices, analyzers and other sources to be transferred to the central system. In addition to automatic data transfer, some of them are only available after manual entry by the operator. It is therefore essential to ensure the accuracy and reliability of these procedures. Application of bar-code scanning technology, data entry verification, Optical Character Recognition (OCR), Intelligent Character Recognition (ICR) and redesigning data entry forms are examples of how to reduce the risk of errors. The additional benefit of using computer technology is its ability to combine individual data in order to increase their value.

Software in BE can be in-house developed or commercial. Their application can be on a local or national level. National blood bank software is an additional contribution to the integration of data and their comparison at the international level. It is extremely important that these systems are properly validated. In addition to the variety of specific requirements related to their quality, safety and cost-effectiveness, "vein to vein" traceability is of utmost importance.

Data serve as an important resource for staff training. Organizations increasingly perceive the need to document and retain knowledge to be used as an educational and decision-making tool. Efficient data management can also result in savings as a result of selecting optimal strategies and better allocation of resources.

Although quality is integrated into all activities, some data are of crucial importance to the quality management system (QMS). Examples include data related to audits and inspections, non-conformities, deviations, adverse events and reactions, product recall, complaint management, quality control of materials, equipment, products and services, data related to the process of product/service realization.

Quality improvement is one of the fundamental objectives of QMS. To what extent this objective will be achieved largely depends on the data available and the way we use them in selecting improvement strategies.

Collected data have an important role in benchmarking. By comparing data with other institutions, it is possible to detect comparative strengths and weaknesses as well as opportunities for improvement. Benchmarking is closely related to defining key performance indicators. The correct interpretation of the data is a prerequisite for making the right decisions. It is therefore important that the data are of high quality and comparable. The data related to the QMS, its functionality and effectiveness are part of the periodic reports used for the management review, but also for informing other employees in BE.

3C-S12-02

GMP IN THE COLLECTION PRACTICES OF BLOOD COMPONENTS AND SOURCE PLASMA FOR FRACTIONATION – THE IPFA EXPERIENCE

P Strengers

Executive Office, International Plasma and Fractionation Association, Amsterdam, Netherlands

For the production van plasma derived medicinal products (PDMPs) such as intravenous immunoglobulin, coagulation factors and albumin which are life-saving in a great number of hereditary and acquired diseases and disorders, human plasma is the source material for manufacturing. Human plasma is a rich biological substance and about 20–30 plasma proteins can be isolated from plasma into concentrated therapeutic plasma protein products. Because of the requirements of regulatory authorities that the production of medicinal products takes place under Good Manufacturing Practices (GMP) conditions, the starting or source material for the production of PDMPs should be obtained and processed under GMP conditions and the establishments responsible for the supply of the source material should have in place facilities and trained personnel subject to quality assurance (QA) programs that comply with the principles of GMP.GMP (and Good Practices (GP) for blood establishments as proposed by the Council of Europe and adopted by the European Union) are requirements on quality and safety which are the guidance for the QA system of a blood establishment. Requirements for a QA system are defined for the collection, processing and quality control of blood, blood components and PDMPs. These requirements imply the existence of a national structure that is independent of manufacturers, compliance with the process of quality assurance for biological products — i.e. control of starting material(s), production processes and final product(s) — and strict adherence to the principles of GMP or GP. Since the WHO has put blood components on its Model List of Essential Medicines, blood establishments need to comply with GMP or GP for the production of blood components. Their QA system should be based on GMP principles which implies active and operational quality assurance system covering all activities in the blood establishment. The quality of blood and plasma is dependent on collection, preparation, testing, storage and transport and the quality of plasma for manufacturing influences the range, quality and safety of PDMPs. If the blood establishment wishes to supply recovered or source plasma for manufacturing, a quality agreement according to agreed standards with a manufacturer should be signed for supplying plasma for manufacturing. This requirement is important since this has impact and cost of the organizing oversight, including authorization, vigilance, traceability and inspection. If a blood establishment wishes to start with the collection of source plasma for the manufacturing of PDMPs by means of plasmapheresis, the modes of operation are not different from the general GMP requirements also required for blood components. Unfortunately, in the 'Guide' of the Council of Europe, the general GMP requirements are defined, the collection of source plasma is not sufficiently addressed. It might be interesting to review in light of the possible introduction of less stringent Transfusion Transmitted Infection (TTI) testing criteria taking into account the safety measures being taken during the manufacturing process of PDMPs.

3C-S12-03

SELF-INSPECTION AND AUDITS BASED ON GMP AND GPG PREPARING FOR REGULATORY INSPECTIONS – THE EUBIS EXPERIENCE

C Seidl

German Red Cross Blood Donor Service Baden-Württemberg-Hessen, Frankfurt am Main, Germany

Background: Self-inspection or audit system is an important element of a quality management system. It should cover all parts of the operations of the blood establishment to verify compliance with the standards and regulatory requirements and serves as an ideal and valuable tool for evaluating the facility's quality and operational systems.

Aims: Self-inspection should include risk assessment, quality indicators for processes and products, the implementation of necessary corrective/preventive actions or measurements to assist in continuous quality improvement and to ensure the safety and quality of blood and blood components. EuBIS, the European blood inspection system, has been initiated by co-funding through the Public Health Programme (Directorate General Sante) of the European Commission bringing together regulators (competent authorities) and manufacturers (blood establishments) to jointly develop criteria and standards aimed to assist blood establishments in need to optimise their quality system and self-inspection process and to prepare for regulatory inspections by competent authorities.

Methods: Standards and criteria for the inspection of blood establishments have been published in a EuBIS manual and a EuBIS guide (www.eubis-europe.eu). The structure of the EuBIS guide follows critical aspects of quality management to be addressed in order to achieve good/best practice. For each of the quality related critical points, a criterion description, examples evidence and references to relevant international standards (Good Manufacturing Practice (GMP), standards by the Pharmaceutical Inspection Co-operation Scheme (PIC/S), Good Practice Guidelines (GPG) of the Council of Europe/EDQM CD-P-TS and related EU Directives). Based on this guide, a risk based approach for an audit trail including risk assessment and management can be easily developed in a systematic fashion covering all relevant activities of a blood establishment.

Results: A global survey carried out by the ISBT Working Party on Quality Management indicated that 73% of blood establishments will need to improve their system of self-inspections, audits and continuous improvements, with 46% of those needing substantial modifications to improve their self-inspection system. In addition, self-inspection is strongly regarded as a tool to prepare the quality system for the requirements of regulatory inspections. These comprise besides national legislation (including EU Directives), requirements set by GMP, PIC/S, WHO and Council of Europe. A considerable number (42%) of blood establishments will have also to comply with regulations covering tissue and cells. Two third of the blood establishments have in addition to comply with audits performed by 'third' party subcontractors or non-governmental institutions. During self-inspections particular focus should be addressed for improvements made in documentation, handling of non-conformances and organisation of personnel (job descriptions and organograms).

Summary/Conclusion: Self inspection and continuous improvements is an important element in establishing and maintaining a sufficient quality management system for blood establishments and to assess risk management and the implementation of regulatory requirements.

3C-S12-04
BUILDING QUALITY AWARENESS IN DEVELOPING COUNTRIES – THE AFSBT EXPERIENCE

LA Bust

Africa Society for Blood Transfusion (AfSBT), Cape Town, South Africa

Background: A global survey carried out by the ISBT Quality Working Party indicated that 78% of participating blood services do not have a fully integrated Quality Management System (QMS). Areas identified as requiring improvement were documentation, internal audits, handling of non-conformances and organisation of personnel (job descriptions and organograms). Quality awareness in developing countries is less advanced as many are in the initial stages of QMS implementation.

Discussion: Developing countries often have limited human resources (especially with regard to trained and skilled personnel), poor infrastructure and logistics, lack of essential equipment and regular supplies, and inadequate government support. The challenge is to achieve an effective quality system in spite of these obstacles.

The Africa Society for Blood Transfusion (AfSBT) has developed a Step-Wise Accreditation Programme which allows countries to be certified at a basic or intermediate level, Step 1 or 2, before attaining full accreditation at Step 3. Accreditation assessments are done against the AfSBT Standards which were developed in conjunction with the American Association of Blood Banks (AABB) and a team of international experts. These Standards were recently revised and updated.

The accreditation process begins with in-country training on the AfSBT Standards followed by a baseline assessment to identify what is in place and what still needs to be developed. An action plan is drawn up and completed prior to performance of a progress assessment. If all is in order a formal accreditation/ certification assessment will be carried out at Step 1, 2 or 3.

To assist countries in preparing for accreditation AfSBT conducts additional training on a range of quality-related topics as well as management issues. A team of over forty AfSBT educators and assessors have been trained to conduct training and assessments. In addition, a small group of mentors has been trained to provide in-country coaching and mentorship.

Through its website, the AfSBT provides information on quality to assist countries establishing a QMS. Generic SOPs have been posted on all aspects of the blood transfusion chain and countries can use these as examples when generating their own documentation. Guidelines are also provided on how to develop organograms and job descriptions and how to perform risk management and draft emergency plans. Further guidelines are in the process of being drafted.

Conclusion: The approach used by AfSBT can be extended to developing countries beyond Africa to enhance quality awareness and the establishment of an effective QMS. A step-wise accreditation programme enables countries to start at a basic level and progress at a rate that suits their circumstances, laying a strong foundation for future growth. The major challenges in assisting developing countries relate to sourcing adequate funding and enhancing human resource capacity.

Blood Products – Pathogen Inactivation

3D-S13-01
PATHOGEN INACTIVATION TECHNOLOGIES: PROGRESS, HURDLES AND THE FUTURE

D Devine[1,2]

[1]Canadian Blood Services [2]Pathology & Laboratory Medicine, Univ. of British Columbia, Vancouver, Canada

Pathogen inactivation technologies (PI) used on blood products for transfusion have been with us for some 2 decades. Many jurisdictions have adopted PI, either fully or in part for the treatment of some blood products. Although technologies are available for treatment of either platelet concentrates or plasma, we have not yet seen consistent, wide-spread adoption of this blood safety technology. This presentation will review the status of pathogen inactivation technologies, including the hurdles that they face to move into routine use, and discuss the gaps that exist in our understanding of how to overcome these hurdles.

Numerous studies support the effectiveness of PI at killing pathogens although some differences in killing efficiency exist among the different technologies developed to date. Because of the underlying mechanisms by which PI kill pathogens, the human blood cells and plasma proteins in treated products are also affected to some extent by the processes. The extent of the PI-induced damage varies by the exact process and by the type of cell. While PI-mediated damage to platelets is apparent in laboratory analyses, it is unclear whether this matters in routine clinical use of platelets. Studies conducted to support product licensure as well as more recent clinical trials show a shortening of intertransfusion intervals and a concomitant increase use of platelets over the course of treatment, but not increased risk of significant bleeding. This may simply reflect the tradeoff of some circulation residency time for increased safety from transmissible agents using these technologies as they are currently formulated.

The hurdles to adoption of PI relate either to the funding model or to details of the process itself as well as concerns over the impact of PI on clinical management of patients. In jurisdictions that have mandated PI treatment of plasma or platelets, funding is available; however, for others an effort to seek cost offsets to divert resources to PI treatment is necessary. These may include optimizing the number of platelet or plasma units treated together (e.g., treating double buffy coat pools), cessation of bacterial testing or certain donor screening tests, or other offsets.

The current configurations of PI technology systems limit the concentrations of cells and the maximum volume that is treated. Because there is no international standardization around, for example, platelet concentration in a finished product, the adaptation of PI for some jurisdictions has been complicated. For some blood operators, current guard bands around platelet concentration/volume mean that not all products can be treated. These kinds of issues will eventually get sorted out, but may further slow implementation and adoption of PI technologies in some jurisdictions.

Because the clinical trials assessing the safety and efficacy of PI-treated products are normally conducted in stable patients: hypoproliferative thrombocytopenia patients receiving prophylactic platelet transfusions, or thalassemia patients receiving chronic RBC support, there are some concerns remaining about the possible additive loss of efficacy if all types of components given to trauma patients are PI-treated. While some small or retrospective studies seem not to support this concern, rigorous studies remain to be conducted in the trauma patients receiving large amounts of blood products in a short time. PI remains an important addition to blood safety practices and additional research will bring more comfort with the general approach.

3D-S13-02

COMPARING CLINICAL USE, EFFECTIVENESS, AND RISKS ACROSS TRANSITION FROM FRESH FROZEN PLASMA TO SOLVENT/DETERGENT PLASMA IN THE NETHERLANDS

N Saadah[1,2], M Schipperus[3,4], J Wiersum-Osselton[3,5], M van Kraaij[5,6], C Caram-Deelder[1,2] and J van der Bom[1,2]

[1]Jon J van Rood Center for Clinical Transfusion Research, Sanquin Research [2]Department of Clinical Epidemiology, Leiden University Medical Center [3]Transfusion and transplantation reactions In Patients (TRIP), Hemovigilance and Biovigilance Office, Leiden [4]Department of Hematology, Haga Teaching Hospital, The Hague [5]Department of Donor Affairs, Sanquin Blood Bank [6]Department of Transfusion Medicine, Sanquin Blood Supply, Amsterdam, Netherlands

Background: In 2014 the Netherlands switched progressively from using fresh frozen plasma (FFP) to solvent/detergent treated pooled plasma (SD-plasma). The expected results of a national switch to SD-plasma were a reduction in the risk of TRALI, allergic reactions, as well as viral and prion transmission. Despite the smaller volume of SD-plasma units as compared to FFP units (200 ml vs. ~300 ml), the number of transfused plasma units was expected to remain consistent in patients transfused in surgical settings (where plasma is often ordered per unit), rising only in patients treated by plasma exchange (e.g. TTP/HUS) where a specific plasma volume is transfused.

Aims: We compared clinical use, effectiveness, and safety of plasma transfusion in the Netherlands in the period surrounding this transition (2011–2016).

Methods: We collected diagnostic data on transfusion episodes involving plasma transfusion in six Dutch hospitals, along with national blood bank data on units distributed to all Dutch hospitals and national hemovigilance data on transfusion reactions reported for each blood product transfused during the period 2011–2016. Stratifying patients by hospital type, ward, and diagnostic code, we compared use and plasma/RBC units ratio (f) for patients receiving FFP vs. SD-plasma, and calculated odds ratios (ORs) comparing SD-plasma to FFP for reported plasma transfusion reactions.

Results: From the six participating hospitals, we collected data on 21,269 transfusion episodes involving plasma transfusion. Together, these episodes involved transfusion of 89,606 plasma units (68,978 FFP; 20,628 SD-plasma), 7,002 RBC units, and 20,802 platelet units, and were coded by 1,216 unique diagnostic codes. Transfusion episodes were grouped by treating ward and analysis performed on three subcohorts: cardiothoracic surgery + cardiology (10,555 episodes); general surgery (7,545); gynecology (1,068). Transfusion episodes were further grouped by diagnosis and analysis performed on an additional three subcohorts: CABG, valve replacement, or MAZE procedure (6,040); non-elective aneurysm (1,642); partus (497). In cardiothoracic patients the mean plasma/RBC units ratio (f) was slightly higher for SD-plasma than FFP in cardiothoracic patients ($f_{SD} = 1.13$; $f_{FFP} = 1.01$; $f_{SD} - f_{FFP} = 0.12$ [95% confidence interval (CI): 0.07 to 0.17]). This change was not observed in other patient groups. National hemovigilance data suggested that SD-plasma was associated with reduced risk of allergic reactions (odds ratio [OR] = 0.19 [0.11 to 0.34; P < 0.01]) and Febrile Non-Hemolytic Transfusion Reactions (FNHTR) (OR = 0.38 [0.18 to 0.79; P < 0.01]) as compared to FFP.

Summary/Conclusions: The switch from FFP to SD-plasma in the Netherlands did not lead to substantial changes in clinical use or effectiveness, despite the difference in volume of the two products, though the plasma/RBC units ratio increased slightly in cardiothoracic patients. SD plasma is associated with fewer allergic reactions and FNHTR.

3D-S13-03

COMBINING UVC-PATHOGEN INACTIVATION AND COLD-STORAGE: A NOVEL APPROACH TO IMPROVE PLATELET SAFETY AND EXTEND THE SHELF-LIFE

M Cameron[1,2], L Waters[1,2], M Padula[2], D Marks[1,3] and L Johnson[1]

[1]Research and Development, Australian Red Cross Blood Service [2]Proteomics Core Facility, University of Technology Sydney [3]Sydney Medical School, Sydney, Australia

Background: Alternatives to room-temperature (RT) storage of platelets are of interest to increase the shelf-life and safety profile of these components. Cold-storage (2–6°C) may facilitate an extension of the shelf-life of platelets, while pathogen inactivation (PI) reduces the risk of pathogen transmission. Separate investigations into both cold-storage and ultraviolet C (UVC)-PI have shown that these two storage modalities differentially affect aspects of platelet quality.

Aims: The aim of this study was to determine the impact of combining UVC-PI and cold-storage (cold-PI) on in vitro platelet quality during platelet storage.

Methods: A pool and split design was used to generate platelets for four study arms: RT, cold, RT-PI and cold-PI (n = 8 in each arm). On day 1, platelets were left untreated or PI-treated using the THERAFLEX UV-Platelets System (MacoPharma). One unit from each pair was then stored at RT (20–24°C) or refrigerated (2–6°C). In vitro quality and function were tested over 9 days. Data was analysed using two-way ANOVA to assess the combined effect of treatment and storage, where P < 0.05 was considered significant.

Results: Combining UVC-PI treatment and cold-storage reduced platelet glycolytic metabolism. PI treatment (0.07 ± 0.01 mmol/10^{11}plts/day) accelerated glucose consumption compared to untreated RT platelets (0.05 ± 0.01 mmol/10^{11}plts/day), whilst cold storage (0.04 ± 0.01 mmol/10^{11}plts/day) had the opposite effect. Cold-PI platelets (0.04 ± 0.01 mmol/10^{11}plts/day) had a glucose consumption rate equivalent to cold platelets. Similar results were observed for lactate production. Whilst both RT-PI ($47 \pm 10\%$) and cold-storage ($35 \pm 3\%$) impaired the hypotonic shock response (HSR) compared to RT controls ($59 \pm 11\%$), combined PI treatment and cold-storage resulted in complete abrogation of this response by day 5. Combined PI treatment and cold-storage also led to increased externalisation of phosphatidylserine (annexin-V binding) and activation of the GPIIb/IIIa receptor (PAC-1 binding) above the levels seen with the individual treatments. Aggregation responses (ADP and collagen) were enhanced in the cold-PI platelets compared to both RT groups, but this was primarily mediated by cold-storage, rather than PI treatment.

Summary/Conclusions: Cold-storage of UVC-PI platelets reduced PI-induced acceleration of glycolytic metabolism. However, combining cold-storage and PI resulted in additional phenotypic and functional changes compared to each treatment individually. Further work is required to understand whether the impact of these changes would affect their clinical efficacy.

3D-S13-04

THREE YEARS ROUTINE EXPERIENCE OF MANUAL PRODUCTION OF DOUBLE-DOSE BUFFY COAT PLATELETS AND PATHOGEN INACTIVATION SYSTEM INTERCEPT: IMPACT ON ECONOMY, BLOOD SAFETY AND BLOOD COMPONENT QUALITY

H Ahlzén[1] and L Larsson[1,2]

[1]Clinical Immunology/Transfusion Medicine, Karolinska University Hospital [2]CLINTEC (Clinical Science, Intervention and Technology), Karolinska Institutet, Stockholm, Sweden

Background: Three years ago, Karolinska University Hospital switched from automated production of single-dose buffy coat platelets (BCPs) via OrbiSac production system (Terumo BCT), with enhanced Bacterial Detection System (eBDS, Pall)) in combination with irradiation as safety measure, to manual production of double-dose BCPs in combination with pathogen inactivation through Intercept blood system (Intercept, Cerus Corp.). This improved the safety of BCPs and cut costs. However, we saw potential for further improvement, since there were frequent production errors and fluctuating quality, wasting both time and money.

Aims: The aim was to evaluate the production process for 4 consecutive years, while it underwent different stages of development.

Methods: We compared blood component quality (yearly quality controls, N > 175), safety and production cost for year A: automated/eBDS, year B1: manual/Intercept implemented, year B2: manual/Intercept undergoing improvement and year B3: manual/Intercept post-improvement.

Results: Blood component quality: Implementation of the new production procedure decreased BCP volume by 48% (359 ± 13 ml to 189 ± 29 ml) when comparing year A to B1, while platelet count concomitantly decreased by 30% (3.4 ± 0.3 to $2.4 \pm 0.4 \times 10^{11}$/unit) due to more concentrated BCPs, allowing BCP double-doses to fit within the Intercept volume limits.

During the optimisation year (B2), platelet count increased to $2.7 \pm 0.4 \times 10^{11}$/unit, rendering a total platelet count decrease of only 20%. Mean count remained unchanged (2.7×10^{11}/unit) when optimisation was finished (B3) but SD decreased to $\pm 0.3 \times 10^{11}$/unit, demonstrating a more stable production. This was mirrored in volumes, which changed from 192 ± 19 to 191 ± 7 ml between B2 and B3.

The fluctuation in the manual, non-optimised procedure (B2) is reflected in 4.3% scrap rate. Year B3, after stabilisation of the procedure, scrap rate was reduced to 0.3%; even lower than year A (0.5%).

Quality of plasma and RBCs remained unaffected throughout the entire period.

Safety: Switching production system allowed the ratio of completed safety measures to increase from 55% (A: eBDS) to 98% (B: Intercept), which after optimisation reached 99% (B2 and B3). This was explained by shorter overall production time. Use of irradiation decreased correspondingly. Two cases of bacterial sepsis occurred

during the last 24 months preceding Intercept implementation, whereas no cases have been observed since (B1-B3).

Production cost: Changing production systems decreased total cost by 13% (year B1). After optimisation, cost was further reduced a total reduction of 21% (B3). The decrease during optimisation was mainly a consequence of reduced labour cost.

The stable production of year B3 also eliminated a previous need for extra quality controls implemented during B1, thereby contributing to reducing costs.

Summary/Conclusions: Intercept implementation greatly improves the safety of BCPs. In combination with manual BCP production, cost per unit is reduced. By optimising the production procedure, a standardised product is achieved, while further reducing cost. Quality of all blood components is still in agreement with EDQM guidelines, although, admittedly, platelet count is lower than before switching processes.

The benefit of a manual process is that details can be more meticulously controlled than in an automated process. We show that, with proper optimisation, a manual process gives BCPs with less fluctuating content than an automated process. We also show that this can cut costs further.

3D-S13-05

NO INTERCEPT (S-303/GLUTATHIONE)-SPECIFIC ANTIBODIES DETECTED IN A PHASE III, RANDOMIZED, CONTROLLED STUDY TO EVALUATE PATHOGEN-INACTIVATED RED BLOOD CELLS IN THALASSEMIA MAJOR PATIENTS (SPARC)

C Geisen[1], Y Aydinok[2], R Origa[3], A Piga[4], V Brixner[1], N Mufti[5], A Erickson[5], C Ernst[5], A North[5], L Corash[5] and R Benjamin[5]

[1]Institute of Transfusion Medicine and Immunohaematology, Goethe-University Frankfurt/Main, University of Frankfurt, Frankfurt, Germany [2]Ege University, Izmir, Turkey [3]University of Cagliari, Cagliari [4]University of Torino – San Luigi Gonzaga Hospital, Torino, Italy [5]Cerus Corporation, Concord, United States

Background: Thalassemia major outcomes are markedly improved with chronic Red Blood Cell (RBC) transfusion combined with iron chelation therapy, but treatment carries a high lifetime risk of transfusion transmitted infections. The INTERCEPT™ Blood System for RBCs (Cerus Corporation, Concord, CA) is an investigational device used ex vivo to prepare pathogen-inactivated RBC components for transfusion. INTERCEPT (S-303 [amustaline]/glutathione (GSH)) treatment results in broad spectrum inactivation of viruses, bacteria, protozoa and donor leukocytes. In a prior study using First Generation INTERCEPT RBC, low titer, non-hemolytic antibodies specific to surface-bound S-303 adducts were detected in two subjects after multiple study transfusions. The INTERCEPT process was reformulated to decrease RBC-bound treatment adducts and this current process is in late-stage development.

Aims: To assess the use of S-303/GSH-treated RBC as screening reagents in a gel column assay during a randomized controlled study to evaluate INTERCEPT RBC in Thalassemia major patients (the SPARC study).

Methods: A 3-cell RBC screening and a 6-cell confirmatory panel were generated with treatment of selected RBC concentrates using conditions similar to either the first generation INTERCEPT process (high S-303 adducts: 0.2 mM S-303 with 2 mM GSH) or the current process (low S-303 adducts: 0.2 mM S-303 with 20 mM GSH), or left untreated (Control). Surface-bound adducts were assessed by flow cytometry and by gel column agglutination (ID-Card IgG + C3d LISS/Coombs, BioRad) using plasma and RBC volumes according to the manufacturer's recommendations. The RBC screening panels had previously identified naturally occurring antibody to INTERCEPT RBC in general hospitalized and in chronically transfused patients. Subsequently, the screening panels and gel column assay were used prior to each transfusion episode during SPARC, a randomized, controlled, double-blind, non-inferiority, two-period, two-treatment, crossover study to evaluate INTERCEPT RBC in Thalassemia major subjects.

Results: Screening of 10,721 general hospitalized patients and 998 chronically transfused patients not previously exposed to INTERCEPT RBC, revealed 17 patients (0.1 and 0.5%, respectively) with naturally occurring low titer (1:2 – 1:32) IgM and/or IgG (non-IgG$_1$ or IgG$_3$ isotype) antibodies to INTERCEPT RBC with either acridine (14) or non-acridine (3) specificity. 11 of these sera reacted with low S-303 adduct RBC. In the SPARC study, 81 subjects were transfused with 1,007 INTERCEPT and 999 Control RBC study products at hospitals in Orbassano and Cagliari, Italy (n = 14) and Izmir, Turkey (N = 67). Mean subject age was 26.1 (±8.1) years, 37/81 (45.7%) were male and 15/81 (18.5%) were aged 11–18 years. 9/81 (11.1%) had pre-existing RBC alloantibodies. Subjects received means of 12.5 (range 3–18) units of Test and of Control RBC over 6 transfusion episodes in each period, with a mean transfusion interval of 19.4 (Test) and 19.5 (Control) days. No treatment emergent

RBC alloantibodies or INTERCEPT-specific antibodies were detected at any time during the study.

Summary/Conclusions: We describe RBC screening panels that are sensitive and specific reagents for detection of antibodies against INTERCEPT RBC. In Thalassemia major patients on a chronic transfusion regimen, multiple transfusions with INTERCEPT RBC did not evoke treatment-specific antibodies.

Clinical – Critical Care and Bleeding

3D-S14-01

PRELIMINARY EVIDENCE THAT INCREASED STORAGE DURATION OF TRANSFUSED PLATELET CONCENTRATES IS ASSOCIATED WITH REDUCED RESPIRATORY FUNCTION IN A SHEEP MODEL OF INFECTION

J Tung[1,2,3,4], G Simonova[1,2,3], S Engkilde-Pedersen[1,2,4], A Esguerra-Lallen[1,2], A Sultana[1,2,3], E Hewlett[1], N Obonyo[2] and J Fraser[2,3,4]

[1]Research and Development, Australian Red Cross Blood Service [2]Critical Care Research Group, The Prince Charles Hospital [3]School of Medicine, University of Queensland [4]Faculty of Health, Queensland University of Technology, Brisbane, Australia

Background: Transfusion of platelet concentrates (PCs) is a life-saving therapy used to control and prevent bleeding in cancer, haematological, surgical and trauma patients. However, transfusion of PCs is not risk-free, and can be associated with adverse outcomes such as transfusion related acute lung injury, infection and mortality. PCs are stored routinely at room temperature for up to either 5 or 7 days, depending on the country. During this period of routine storage a storage lesion (including soluble factors such as proteins, lipids and microparticles) develops in PCs that may contribute to adverse outcomes associated with their transfusion. In the absence of randomised control trial studies on this possible association, animal models are crucial to improve our understanding.

Aims: To investigate whether the storage duration of transfused PCs contributes to reduced respiratory function in a sheep infection model.

Methods: Standard buffy coat pooled PCs (n = 75) were obtained from the Australian Red Cross Blood Service. PCs were stored routinely for either 2 days (d), 5 d or 7 d (n = 25 for each time-period), after which supernatant (SN) was collected, pooled to form 3 pools (d2 pool, d5 pool and d7 pool), heat-treated (56°C for 30 min (min)), aliquoted and frozen at −80°C. Sheep (n = 21) were anaesthetized, mechanically ventilated (40% oxygen) and instrumented. After a 1 h baseline period, sheep were infused over a 3 h period with lipopolysaccharide (LPS; 11.25 µg/kg) to model a bacterial infection. After a further 1 h, sheep were then transfused (10% v/v) with either d2-PC-SN (n = 7), d5-PC-SN (n = 7) or d7-PC-SN (n = 7) over a 1 h period. Following PC-SN transfusion, sheep were monitored for 2 h, after which they were euthanised and underwent post-mortem. Throughout the experiment, arterial blood gas samples collected at 15 min intervals were used to measure arterial partial pressure of oxygen (PaO$_2$) by an automated blood-gas analyser. These PaO$_2$ results were used to calculate PaO$_2$/fraction of inspired O$_2$ (FiO$_2$) levels as a measure of respiratory function. PaO$_2$/FiO$_2$ ratios for each sheep were averaged across the baseline, LPS-infusion/post-LPS-infusion and PC transfusion/post-PC transfusion time periods. PaO$_2$/FiO$_2$ ratios across each of the three groups of sheep were analysed by one-way ANOVAs with Bonferroni post-tests for each group (P < 0.05).

Results: In each of the three groups of sheep, LPS-infusion resulted in a decreased PaO$_2$/FiO$_2$ ratio compared to baseline (P < 0.05, P < 0.01 and P < 0.05 for the d2, d5 and d7-PC-SN groups respectively). Further decrease in PaO$_2$/FiO$_2$ ratio post-PC-SN transfusion was dependent upon the storage duration of the PC as it was only evident in the d5-PC-SN and d7-PC-SN groups (P < 0.05 and P < 0.01 respectively).

Summary/Conclusions: These data suggest that increased storage duration of transfused PCs is associated with reduced respiratory function. Further analyses (e.g. post-mortem histology of lung sections) are required to demonstrate whether this decrease in PaO$_2$/FiO$_2$ ratios is associated with the development of lung injury. These data also implicate soluble factors present in the PCs as the causative agents, and subsequent studies are planned to identify these agents.

3D-S14-02

MEASUREMENT OF CELLULAR OXYGENATION IN CRITICALLY ILL PATIENTS RECEIVING RED BLOOD CELL TRANSFUSION

M Baysan[1,2], M Arbous[2], E Mik[3], N Juffermans[4] and J van der Bom[2,5]

[1]Clinical Transfusion Research, Sanquin Research [2]Leiden University Medical Center, Leiden [3]Erasmus MC- Universal Medical Centre Rotterdam, Rotterdam [4]Academic Medical Center, Amsterdam [5]Sanquin Research, Leiden, Netherlands

Background: One of the main goals of therapy in critical care medicine is to obtain adequate tissue oxygenation. Global oxygen delivery can be assessed through monitoring of cardiac output and arterial oxygen content, but cellular oxygenation cannot be clinically assessed yet. The protoporphyrin IX-triple state lifetime technique, measuring mitochondrial oxygenation tension (mitoPO$_2$) in vivo, may be an early indicator of oxygen demand in the cell and might be a promising, new monitor for the cellular compartment. The mitoPO$_2$ measurements are obtained through the oxygen-dependent optical properties of protoporphyrin IX, a technique that is validated in vivo in various tissues in animal models as well as in healthy volunteers. In healthy volunteers the average value of mitoPO$_2$ is 44 mmHg.

Aims: To determine the feasibility and variability of mitoPO$_2$ measurement in critically ill patients with anaemia.

Methods: We prospectively included 20 critically ill patients admitted to a mixed intensive care of Leiden University Medical Center with anaemia in whom a red cell transfusion was planned. At multiple predefined moments, before and after red cell transfusion, we assessed mitoPO$_2$ on the anterior chest wall. MitoPO$_2$ measurements were performed using a COMET monitor (Photonics Healthcare, Utrecht, Netherlands) on skin primed during 4 h with an ALA containing patch (Alacare, Photonamic, Wedel, Germany) for induction of mitochondrial PpIX. Reported values are a mean mitoPO$_2$ of 5 consecutive measures at each time point. Furthermore, hemodynamic parameters, arterial and venous blood samples were determined along with each mitoPO$_2$ measurement.

Results: A mitoPO$_2$ measurement was obtained in all but 1 participant, most likely due to excessive chlorhexidine at the measurement site. All measurements were above the signal-to-noise ratio of 25, despite the severity of critical illness assessed via APACHE IV score (range 49–171).The median mitoPO$_2$ before transfusion was 66.9 mmHg (interquartile range 61.5–77.7), while the overall median mitoPO$_2$ after transfusion was 65.8 mmHg (IQR 57.5–87.2) mmHg. The standard deviation of the mitoPO$_2$ measurements was 15.2 mmHg in the first hour after transfusion and gradually increased to 28.2 mmHg after 3 h, up to 42.5 mmHg after 24 h.

In two patients with a haemoglobin concentration below 7 g/dl, median mitoPO$_2$ increased from 71.4 (IQR 65–77.7) to 91.4 (IQR 67–97.3) mmHg after transfusion. In patients with higher haemoglobin concentrations before transfusion, median mitoPO$_2$ did not change (66.9 (IQR 61.5–69.8) vs. 63 (IQR 57–82.8) mmHg, P = 0.483).

The median heart frequency changed from 99 (IQR 83–106) before transfusion to 92 (IQR 83–106) beats per minute overall after transfusion. Likewise, the mean arterial pressure (76 (IQR 72–89) vs 79 (IQR 73–89) mmHg), central venous pressure (8 (IQR 6–9) vs 10 (IQR 7–13) mmHg), central venous oxygen saturation (64 (IQR 59–76) vs 72 (IQR 66–77) %) and pCO2 gap (0.65 (IQR 0.3–0.91) vs 0.36 (IQR 0.03–0.67) kPa) showed changes as expected.

Summary/Conclusions: It is feasible to measure mitochondrial oxygen tension in critically ill patients. The measurements seem to be most reliable in the first 3 h after patch removal. Interestingly, a higher mitoPO$_2$ in critically ill patients was seen than in healthy volunteers.

3D-S14-03

PREDICTING PERSONALIZED BENEFITS AND HARMS OF BLOOD TRANSFUSION IN CRITICALLY ILL PATIENTS

JG Van Der Bom[1,2], F Kranenburg[1,2], S le Cessie[2,3], H Putter[3], C Caram-Deelder[1] and M Arbous[2,4]

[1]Jon J van Rood Center for Clinical Transfusion Research (CCTR), Sanquin Blood Supply & Leiden University Medical Center [2]Department of Clinical Epidemiology [3]Department of Medical Statistics [4]Intensive Care, Leiden University Medical Center, Leiden, Netherlands

Background: At the intensive care unit about 30 to 40 percent of all patients receive red blood cell transfusions. Randomized trials have consistently shown that transfusion of critically ill patients with hemoglobin concentrations above 7 or 8 g/dl does not have a positive effect on the outcomes of these patients compared with postponing transfusion until the patients' hemoglobin drops below 7 g/dl. Controversy remains regarding the translation of this grade 1B evidence to the individual

critically ill patient. Guidelines advise higher hemoglobin transfusion triggers for some critically ill patients with ischemic heart disease, sepsis, or traumatic brain injury. This advice creates considerable, undesirable transfusion practice variation.

Aims: To enable the prediction of a possible effect of red cell transfusions on organ function in critically ill patients taking into account all relevant patient characteristics at all hemoglobin concentrations between 6 and 9 g/dl.

Methods: We extracted data on all hemoglobin concentrations between 6 and 9 g/dl, subsequent transfusion decisions (yes/no), sequential organ function assessment (SOFA) scores and corresponding clinical variables from electronic health records of patients admitted to the intensive care unit of the Leiden University Medical Center, The Netherlands between November 2004 and May 2016. Based on literature and clinical reasoning we selected characteristics that might modify and/or confound the association between transfusion and next-day SOFA score. These characteristics along with interaction terms for all of them with transfusion (yes/no) were entered into a linear regression model with the patients' next-day SOFA scores as dependent variable. Next we estimated the effect of a transfusion on next-day SOFA score for each decision moment by calculating the difference between the predicted SOFA with and the predicted SOFA score without transfusion.

Results: Our cohort comprised 6,024 ICU admission of 5,460 critically ill patients, 23,333 hemoglobin values between 6 and 9 g/dl, and 5,422 (23.2%) subsequent red cell transfusions. The proportion of patients receiving a transfusion decreased with increasing hemoglobin values; 67.4%, 46.5% and 10.8% for hemoglobin levels between 6 to 7 g/dl, 7 to 8 g/dl and 8 to 9 g/dl respectively. The mean difference between the next-day SOFA score with and without transfusion after adjustment for all measured confounding and effect-modification was 0.00 (95% confidence interval −0.14 to 0.13); in strata of hemoglobin values between 6 to 7 g/dl, 7 to 8 g/dl and 8 to 9 g/dl the estimated effects of transfusion on next-day SOFA scores were −0.13 (−0.54 to +0.27), +0.08 (−0.07 to +0.24), and −0.03 (−0.21 to +0.14) respectively.

Summary/Conclusions: These results show that red cell transfusion is not associated with an improved organ function score in the majority of critically patients with hemoglobin values between 6 and 9 g/dl. After external validation our model will help to decide whether or not to transfuse a critically ill patient with anemia.

3D-S14-04

HAEMATOLOGICAL FEATURES, TRANSFUSION MANAGEMENT AND OUTCOMES OF MASSIVE OBSTETRIC HAEMORRHAGE: FINDINGS FROM THE AUSTRALIAN/NEW ZEALAND MASSIVE TRANSFUSION REGISTRY

M Lasica[1,2,3], M Tacey[1], R Sparrow[1], E Wood[1,4,5] and Z McQuilten[1,4,6]

[1]Department of Epidemiology and Preventative Medicine, Monash University [2]Research and Development, Australian Red Cross Blood Service [3]Haematology, Box Hill Hospital, Melbourne [4]Haematology, Monash Health [5]Supportive Care Disease Group, Australasian Leukaemia and Lymphoma Group [6]Australia and New Zealand Intensive Care Research Centre (ANZIC-RC), Melbourne, Australia

Background: Massive obstetric haemorrhage (MOH) is defined as blood loss of ≥1000 ml during pregnancy and the puerperium with rising incidence and severity in the developed world. Dilutional coagulopathy, thrombocytopenia and hyperfibrinogenaemia can perpetuate bleeding and require prompt correction in order to reduce mortality and morbidity.

Aims: To better define current MOH transfusion management and clinical outcomes, including differences in cause of MOH.

Methods: We performed a bi-national, multi-centred, cohort study of women who received massive transfusion for MOH using the Australian and New Zealand Massive Transfusion Registry (ANZ-MTR). MOH was defined as ≥24 weeks gestation requiring ≥5 red blood cells (RBC) units within 4 h. Causes of bleeding were identified using the International Classification of Diseases (ICD-10-AM) coding system.

Results: 249 patients from 18 Australian and 5 New Zealand hospitals met the inclusion criteria. Modes of delivery were vaginal 115 (46%) or caesarean section (emergency 87 [35%]; elective 47 [19%]). Sixty-two percent occurred outside usual working hours defined as weekends as well as 6 pm–8 am on weekdays. Six patients were reported to develop an amniotic fluid embolism. Bleeding causes included obstetric trauma (n = 48, 19%), uterine atony/abnormal forces of labour (n = 56, 22%), placenta praevia (n = 51, 20%), other types of morbidly adherent placenta (n = 24, 9%) and other causes (n = 22, 8%). The majority (53%) had more than one and 48 patients had no documented cause. The median platelet count, APTT and INR were >75 × 10 × 9/L, <1.5 and <1.5× upper limit of normal, respectively at 4 and 24 h for all causes. Patients with placenta praevia and other types of morbidly adherent placenta had the highest median first fibrinogen levels (2.0 g/L [IQR 1.5–3.0] and 2.5 g/L [IQR 2.1–3.3] respectively).

Ninety-five and 87% of women with prolonged nadir APTT/INR and nadir platelet count <50 × 10^9/L, respectively, received fresh frozen plasma (FFP) and platelets, while only 74% of women with nadir fibrinogen <2 g/L received cryoprecipitate, with only 24% receiving >5 units. The median FFP: RBC ratio (IQR) at 4 h and 24 h was 0.60 (0.33–0.80) and 0.57 (0.33–0.75) respectively.

Intensive care unit (ICU) admission and/or hysterectomy occurred in 44% and 29% of cases respectively. On multi-variable analysis, emergency caesarean section (OR 4.9, 95% CI: 2.0–11.7), placenta praevia (OR 7.2, 95% CI: 2.0 – 26.4) and cases with >5 RBC units transfused before the first cryoprecipitate unit (OR 9.4, 95% CI: 3.1–28.1) were found to be independently associated with an increased risk of hysterectomy. Initial INR values of <1.5 (OR 0.44, 95% CI: 0.20–0.95, compared to INR of >1.5) were protective of ICU admission.

There were three deaths, including one due to amniotic fluid embolism. The maternal mortality ratio (MMR) was therefore 0.6 per 100,000 women.

Summary/Conclusions: This bi-national study is one of the largest cohorts of MOH described to date. Uterine atony, abnormally adherent placenta and obstetric trauma were the most common causes of MOH. FFP and platelets were more likely to be transfused than cryoprecipitate in patients with abnormal haemostasis parameters. MOH resulted in mortality and significant morbidity, including hysterectomy which was associated with emergency caesarean section, placenta praevia and later administration of cryoprecipitate.

3D-S14-05
CHANGES IN COAGULATION PARAMETERS DURING THE COURSE OF POSTPARTUM HAEMORRHAGE: A NATIONWIDE RETROSPECTIVE COHORT STUDY

A Gillissen[1,2,3], T van den Akker[3], C Caram-Deelder[1], D Henriquez[3], K Bloemenkamo[4], M de Maat[5], J Eikenboom[6] and J van der Bom[1]

[1]Center for Clinical Transfusion Research, Sanquin Research [2]Department of Clinical Epidemiology [3]Department of Obstetrics, Leiden University Medical Center, Leiden [4]Department of Obstetrics, University Medical Center Utrecht, Utrecht [5]Department of Hematology, Erasmus Medical Center, Rotterdam [6]Department of Thrombosis and Hemostasis, Leiden University Medical Center, Leiden, Netherlands

Background: Postpartum haemorrhage is a major cause of maternal morbidity, with an incidence that seems to be increasing. Data on the change in coagulation parameters during the course of postpartum haemorrhage per categorised amount of blood loss are limited. In order to determine the optimal cut-off value for initiation of treatment, it is crucial to analyse the pattern by which coagulation parameters change in relation to blood loss, and identify women diverging from this pattern who are at increased risk of severe maternal outcome.

Aims: The aim of this study was to describe changes in coagulation parameters including fibrinogen during the course of postpartum haemorrhage per categorised amount of blood loss and to compare levels of coagulation parameters during early postpartum haemorrhage between women with and without a composite severe maternal outcome.

Methods: Nationwide retrospective cohort study in 61 hospitals in the Netherlands. Women with postpartum haemorrhage (blood loss exceeding 1000 ml within the first 24 h after childbirth) who had received at least four units of red cells, or fresh frozen plasma or platelets in addition to red cells were studied. For 1039 women coagulation parameters were available. The amount of blood loss at the time of blood sampling was categorised in 7 groups: 1000–1500 ml, 1500–2000 ml, 2000–2500 ml, 2500–3000 ml, 3000–3500 ml, 3500–4000 ml and >4000 ml with 0–1000 ml as reference category. Coagulation parameters were allocated to the category representing amount of blood loss at sampling. Main outcome measures were haemoglobin, haematocrit, platelet count, fibrinogen, activated partial thromboplastin time (aPTT) and prothrombin time (PT) per categorised amount of blood loss during postpartum haemorrhage; composite endpoint of maternal morbidity (emergency peripartum hysterectomy, ligation of the uterine arteries, emergency B-Lynch suture, arterial embolization or admission into an intensive care unit) and mortality.

Results: Women in our cohort were on average 31 years of age, gave birth at a median gestational age of 39.6 weeks and 25% delivered by caesarean section. Uterine atony was the primary case of bleeding in 65% of the cases and 35% of women developed the composite endpoint of severe maternal morbidity or mortality. Haemoglobin and fibrinogen showed decreasing trends until 2.5 litres of blood loss, after which levels stabilized at 7.7 g/dL and 2.1 g/L respectively. With rising blood loss, platelet count decreased and aPTT increased, while PT remained unchanged. Low levels of fibrinogen (<2 g/L) and prolonged aPTT (39s) early in the course of bleeding (<2 L of blood loss), were associated with the composite outcome. Women

who did not develop a composite outcome of maternal morbidity and mortality only reached a fibrinogen value of <2 g/L very sporadically (blood loss above 3.5 litres).

Summary/Conclusions: Our results support the notion that fibrinogen and APTT are promising candidates to guide targeted haemostatic treatment during the early phases of severe postpartum haemorrhage.

3D-S14-06
THE CLOCK IS TICKING: USING IN SITU SIMULATION TO IMPROVE TIME TO BLOOD DELIVERY IN BLEEDING TRAUMA PATIENTS

A Gray[1], L Chartier[1], K Pavenski[2], M McGowan[3] and A Petrosoniak[1,4]

[1]University of Toronto [2]Laboratory Medicine [3]St. Michael's Hospital, Toronto, Canada [4]Emergency Medicine, St. Michael's Hospital, Toronto, Canada

Background: Massive transfusion protocols (MTP) have been widely implemented to rapidly deliver blood products to bleeding trauma patients. Every minute delay in blood product administration is associated with a 5% increase in mortality. Improving time-to-blood delivery is therefore a critical step in improving patient outcomes. We used in situ simulation (ISS) as a novel, prospective and iterative approach to identify and improve upon latent safety threats (LST) that impact time-to-blood delivery during actual trauma resuscitations.

Aims: To reduce the time to blood delivery for bleeding trauma patients using ISS.

Methods: This project consisted of twelve high-fidelity, multi-disciplinary, ISS sessions at a Level-1 trauma center in Toronto, Canada. In situ simulated MTP activations were evaluated using participant and human factor experts observations. During ISS sessions, three major LSTs were identified: 1) issues with MTP activation; 2) varied transport routes by porters between the blood bank and trauma room; and 3) inadequate prioritization of blood product administration. Process improvements for each issue were tested during subsequent ISS sessions and implemented after refinements were made. The impact of this project was measured by a retrospective chart review (January 2014 – September 2017) for all actual trauma patients requiring MTP. Cases were categorized temporally, that is, whether they occurred before, during or after the ISS QI project. Demographics, clinical, and blood bank time stamps were extracted from the medical chart and trauma and blood bank registries. Primary outcome was time-to-blood product administration from MTP activation.

Results: 185 cases were reviewed and 145 met inclusion criteria: 41 prior to, 54 during and 50 after the ISS QI project. Each group was similar in demographic data, trauma characteristics and injury severity score. Mean time-to-blood delivery from MTP activation decreased from 11.58 min before (SD 6.8), to 10.44 min during (SD 6.1) to 9.12 min after (SD 5.3). Overall, a 22% relative reduction was achieved in the time-to-blood delivery following ISS-based QI interventions (P = 0.047).

Summary/Conclusions: A comprehensive, ISS-based QI project was associated with a 22% reduction in time-to-blood delivery for trauma patients. In situ simulation represents a novel approach to the identification of LSTs and improvement related to MTP for trauma patients. This methodology should be considered as part of a QI process to test and optimize MTP and blood delivery for bleeding trauma patients.

Blood Safety – Resource Limited Countries

3D-S15-01
SITUATION ANALYSIS OF DONOR HEALTH ASSESSMENT QUESTIONNAIRE IN PAKISTAN

H Shabber[1], S Ansari[2] and S O'Brien[3]

[1]Federal Government Services Hospital and Post Graduate Medical Institute [2]Biosciences, COMSATS Institute of Information Technology, Islamabad, Pakistan [3]Epidemiology & Surveillance, Canadian Blood Services, Ottawa, Canada

Background: A Donor Health Assessment Questionnaire (DHAQ) is the key tool in blood donor selection for reducing the risk of Transfusion Transmissible Infections (TTI) and ensuring the safety of donor and recipient. Potential donors must answer this questionnaire which are accepted or deferred on the basis of their responses. A standardized, uniform, simple, unambiguous, culturally acceptable and easy to complete DHAQ ensures the collection of same information on all potential donors before each donation and should be used throughout the country. Design piloting,

validation and implementation of the DHAQ is responsibility of the national Blood Transfusion Service (BTS) of the country. A redesign of the questionnaire took place in America resulting in the development of a new Uniform Donor History Questionnaire (UDHQ) by an AABB task force in 2000, formatted to be fully self-administered. It was based on cognitive science principles to facilitate attention, comprehension and memory.

The BTS in Pakistan consisted of unorganized, isolated and poorly or completely unregulated blood establishments owned by public, private and Non-Governmental Organization (NGO) sector. Blood Centres throughout Pakistan develop their own DHAQ without following any proper standard guidelines. Some of them don't have a questionnaire or do not perform documented behavioral screening.

The Government of Pakistan initiated the process of restructuring the BTS by following WHO recommended centralized model in 2010 by establishing Safe Blood Transfusion Programme (SBTP). The first phase (2010–2015) of the project completed with the construction of 10 new Regional Blood Centres and up gradation of 60 Hospital Blood Banks. The RBCs are now in the process of operationalization. The Phase II (2016–2018) has been started which proposes expansion of the scope and coverage of the Phase I concept in the uncovered areas.

As a next step of centralization, development of a UDHQ is required. Proper and uniform donor history assessment is a vital part of transfusion safety. A national DHAQ based on cognitive science principles and tested for donor comprehension and acceptability is the need of the hour in Pakistan. It will ensure blood establishments adopt a uniform behavioral screening protocol.

Aims: To highlight the need of uniform donor history questionnaire in Pakistan.

Methodology: In order to gain an understanding of the diversity of DHAQ's and donor criteria currently in place throughout Pakistan blood transfusion centres were visited and DHAQs were collected. Questions were asked about the history taking process and observations were also recorded.

Results: A total of 15 DHAQ were collected from blood transfusion services throughout the country. 13 DHAQ were used in single-centre setting and two were used in multi-centre setting blood transfusion services. Four questionnaires were in English language and 11 were in Urdu. Lowest number of questions asked in the questionnaires was ten and highest were 36. All the DHAQ were unique in design, number and arrangement of questions.

Conclusion: The situation analysis is first step to the development of a new standardized and uniform DHAQ. This is expected to prevent TTIs and improve transfusion safety in the country.

3D-S15-02

ADDRESSING TRANSFUSION TRANSMITTED MALARIA IN KENYA

V Magutu

Human Pathology, University of Nairobi, Nairobi, Kenya

Malaria is one of the most common transmissible infections by transfusion. It poses a significant challenge to blood safety and malaria control in Sub-Saharan Africa where the disease is endemic. The majority of healthy adults living in this region have some degree of immunity to the disease and an asymptomatic low-level parasitaemia has been shown exist in a subset of the population who form the donor pool. In an area where malaria is a leading cause of death, this particular aspect of malaria control and blood safety is further complicated by inadequate blood supply. As a result many African countries, including Kenya, have yet to adopt the World Health Organization (WHO) recommendation to defer donors at risk of malaria exposure.

Another WHO recommendation that has had poor uptake in African transfusion services is the screening of donated blood for malaria. Although the infectious agent is readily identifiable and screening assays are available, they differ in their performance characteristics, resource and logistics requirements, and may themselves adversely impact on blood supply in malaria endemic areas if they were to be introduced. The routine diagnostic tests used in Kenyan clinical practice (microscopic examination of a thick blood smear, rapid malaria antigen detection kits) may not be suitable in terms of feasibility or sensitivity for the detection of low-level parasitaemia that asymptomatic donors with malaria have.

In Kenya, the National Blood Transfusion Service recommends the use of prophylactic anti-malarials with each transfusion. This approach attempts to safeguard blood supply by allowing retention of units that possibly contain the parasites, theoretically preventing transfusion transmitted malaria while circumventing the sticky issue of test selection in pre-donation screening. The documented antimalarial for use is Sulfadoxine/Pyrimethamine (SP), a drug currently reserved for prophylaxis in pregnancy and infancy due to widespread resistance. It's efficacy in the management of

TTM is therefore questionable. As an alternative, anecdotal evidence suggests that some clinicians in Kenya are now opting for 'presumptive treatment' using artemisinin combination therapy (ACT) instead of SP. The Kenyan government implemented the use of ACT as first line treatment for malaria in 2006. The national policy guiding its use is that it is reserved for laboratory confirmed cases, to curb rising antimalarial resistance and also due to the cost of artemisinin combination therapy. The use of ACT for TTM prophylaxis is therefore contrary to this policy however the lack of effective alternative prophylactic options is a significant challenge.

But is prophylaxis really necessary? A major limitation in prevention of TTM in Kenya is its actual incidence is not known. Recent prevalence studies have demonstrated a significant difference in the prevalence of malaria in Kenyan blood donors when compared with the general population. Given a documented reduction in the risk of malaria infection in Kenya, a differential evidence based policy that addresses the risk of TTM in Kenya weighed against the feasibility and sustainability of the individual control measures must be considered.

3D-S15-03

PROFICIENCY TESTING OF VIRAL MARKER SCREENING IN AFRICAN BLOOD CENTER LABORATORIES: A MULTINATIONAL STUDY

B Drammeh[1], S Laperche[2], Z Kaidarova[3], D Hindes[3], L Ozeransky[4], A De[4], M Kalou[4], B Parekh[4] and EL Murphy[5]

[1]*U.S. Centers for Disease Control, Bethesda, MD, United States* [2]*Institut National de la Transfusion Sanguine, Paris, France* [3]*Blood Systems Research Institute, San Francisco* [4]*U.S. Centers for Disease Control, Atlanta, GA* [5]*UCSF, San Francisco, United States*

Background: Previous proficiency testing studies have revealed deficiencies in viral marker screening at many African blood center laboratories. In recent years, national and international programs have made substantial investment in the formation of national blood transfusion services (NBTS) in several African countries. However it is unclear whether such investment has improved proficiency testing for viral markers.

Aims: To perform a contemporary, multinational proficiency testing of a large sample of African blood center laboratories and to compare performance according to their NBTS status, NBTS vs non-NBTS lab according to the location of the lab within or outside a hospital.

Methods: Seven African countries with varying levels of external investment in NBTS were included. All 30 NBTS centers were included and 10 non-NBTS laboratories in each country were chosen randomly after stratification for number of blood units collected per year. A blinded panel containing 25 pedigreed plasma samples including positives for anti-HIV (7), HBsAg (6) and anti-HCV (5) as well as pedigreed negatives (7) was shipped frozen to each participating laboratory. Each laboratory then performed its routine testing algorithm for screening HIV, hepatitis B and C viruses (HBV and HCV) and reported results to a coordinating center along with other data about the laboratory and its testing algorithm. Results were analyzed by each viral marker according to sensitivity, specificity and overall performance (percent correct results) and differences were tested by general estimating equations (GEE).

Results: Seven countries participated within the study's time frame. A total of 90 panels were shipped into countries and 86 (96%) laboratories confirmed receipt of a panel. Of these, 82 (95%) returned laboratory results for at least one viral marker. Of 82 labs reporting HIV, 68 (83%) had 100% sensitivity, 11 labs missed 1 positive and 3 labs missed 2 positives. Of 80 labs reporting HBV, 33 (41%) had 100% sensitivity, 9 missed 1 positive, 15 missed 2 positives and 23 missed 3 or more positives. Of 78 labs reporting HCV, 37 (47%) had 100% sensitivity, 21 labs missed 1 positive, 7 labs missed 2 positives and 12 labs missed 3 or more positives. Overall specificity was better than sensitivity for all 3 viruses. Sensitivity was significantly (P < 0.0001) higher for all three viruses at NBTS vs. non-NBTS labs. However the use of rapid tests was more common in non-NBTS labs and was also associated with poor sensitivity (P < 0.03 or lower), therefore probably accounting for much of the NBTS/non-NBTS effect. Better proficiency was also associated with a higher proportion of voluntary/non-remunerated donors but not with reported accreditation status or participation in other EQAS programs.

Summary/Conclusions: Proficiency for HIV testing has improved since previous studies but proficiency for HBV and HCV testing remains poor overall, with large variation between labs. Poor proficiency was strongly associated with non-NBTS status and the use of rapid tests. Specific remediation measures were recommended and in-country assessment will be provided to labs with poor proficiency.

3D-S15-04

HIGH RATE OF HCV AND HIV FALSE-POSITIVE RESULTS IN SEROLOGICAL SCREENING CAN IMPAIR BLOOD SUPPLY IN SUB-SAHARAN AFRICA

D Candotti[1], V Sauvage[1], P Cappy[1], M Abdallahi Boullahi[2], P Bizimana[3], G Mbensa[4], S Oumar Coulibaly[5], A Rakoto Alson[6], H Soumana[7], C Tagny-Tayou[8] and S Laperche[1]

[1]Department of Blood-borne agents, Institut National de la Transfusion Sanguine, Paris, France [2]National Blood Center, Nouakchott, Mauritania [3]National Blood Center, Bujumbura, Burundi [4]National Blood Center, Kinshasa, Democratic Republic of the Congo [5]National Blood Center, Bamako, Mali [6]National Blood Center, Antananarivo, Madagascar [7]National Blood Center, Niamey, Niger [8]Hematology, Faculty of Medicine and Biomedical Sciences of University of Yaoundé I, Yaoundé, Cameroon

Background: False-positive results in the blood screening of transfusion-transmitted viral infections remain an issue due to their impact on blood supply, especially in low-income countries where the need of blood is not always covered by blood collection.
Aims: In order to find strategies to not abusively discard non-infected donations, a study focused on HIV and HCV was conducted to estimate the frequency of false-positive reactions observed in blood screening routine in seven African countries.
Methods: A total of 16,613 blood donations tested for HCV and 16,504 for HIV collected in 2010–2012 in seven African countries were investigated: Burundi (4%), Cameroon (4%), Democratic Republic of Congo (28%), Madagascar (4.5%), Mali (11%), Mauritania (7%) and Niger (41.5%). Of the samples tested for HCV, 26.0% (0%>100% according to countries) were screened with a rapid test (RT), 71.8% (0% >100%) with a 3rd gen enzyme immunoassay (EIA), and 2.2% with a 4th gen EIA. For HIV, 52.4% were screened with a RT, 6.1% with a 3rd gen EIA and 41.5% with a 4th gen EIA. Samples reported positive for HCV (n = 456, 2.74%) and HIV (n = 249, 1.51%) were further investigated with Ag/Ab assays (Monolisa HCVAg/Ab Ultra, Genscreen HIVAg/Ab, Biorad), immunoblots (IB) (INNO-LIA HCV, Innogenetics; Geenius HIV, Biorad), and molecular investigations to confirm infection.
Results: The rate of HCV reactive samples with RTs was significantly lower than with EIAs: 0.55% (24/4,327) vs. 3.5% (432/12,286) (P < 10^{-4}). Conversely, HIV-RTs provided more reactive results than EIAs: 1.86% (161/8,648) vs 1.29% (13/1,004) with 3rd gen and 1.09% (75/6,852) with 4th gen assays (P < 10^{-4}).
Fifty-seven (16%) of 357 HCV initially reactive samples available for retesting were Monolisa reactive irrespective of the type of assay used for the screening, and 32 (56.1%) tested HCV-RNA positive.
Of the 249 HIV initially reactive samples, 40/184 (21.7%) that have been retested with Genscreen were reactive with a significant difference according to the assay used for the screening (11.4% for RT and 35% for EIA, P < 10^{-4}). Thirty eight were available for supplemental investigations: 6 were IB and RNA negative, 8 were IB indeterminate and RNA negative, and 24 IB-confirmed samples (17 HIV-RNA positive, 5 negative and 2 not tested). Overall 63% (24/38) of repeatedly positive samples were confirmed HIV positive accounting for 13% (24/184) of retested samples.
Summary/Conclusions: HCV and HIV reactivity was not confirmed by a highly sensitive EIA in 84% and 78.3% of initially reactive donations, respectively independently of the type of primary screening assay used for HCV but more frequently for HIV rapid testing. Confirmatory testing increased the rate of HIV unconfirmed reactivity to 87%. These findings underline the need of confirmatory strategies to avoid blood wastage and to reevaluate viral infection prevalences in African blood donors that may be overestimated.

New Developments in Immunohematology

3D-S16-01

ANTI-GP V AUTOANTIBODIES ARE A FREQUENT FINDING IN PATIENTS WITH IMMUNE THROMBOCYTOPENIA AND LEAD TO EFFICIENT PLATELET REMOVAL IN A MURINE MODEL

R Vollenberg[1], R Jouni[2], M Burg-Roderfeld[3], G Bein[1], T Bakchoul[2] and UJ Sachs[1]
[1]Institute for Clinical Immunology and Transfusion Medicine, Justus Liebig University, Giessen [2]Institute for Transfusion Medicine, Eberhard Karls University, Tuebingen [3]Faculty of Biology and Chemistry, Fresenius Hochschule, Idstein, Germany

Background: Immune thrombocytopenia (ITP) results from autoimmunization against platelet antigens. Resulting autoantibodies (aabs) are considered to represent a major mechanism of thrombocytopenia in ITP by inducing platelet clearance from the circulation. Several lines of evidence demonstrate that aabs against glycoproteins (GP) IIb/IIIa and Ib/IX are predominant in ITP patients, and both disease severity and treatment response rates to specific therapeutics have been associated with aabs patterns. GP V is well-characterized immune target in Varicella-associated and drug-induced thrombocytopenia, but has never been studied systematically in ITP.
Aims: To study the presence of anti-GP V antibodies in ITP and to predict their potential clinical relevance.
Methods: Patients with a suspected diagnosis of primary ITP were included once they met pre-defined clinical inclusion criteria. The presence of GP IIb/IIIa-, GP Ib/IX, and GP V-specific aabs was investigated by monoclonal antibody immobilization of platelet antigens (MAIPA) assay, both on patients' autologous platelets (direct MAIPA) and in serum (indirect MAIPA). Serum IgG fractions were tested by surface plasmon resonance (SPR) technology for the presence of anti-GP V aabs. Clearance of human platelets from the circulation in the presence of anti-GP V aabs was studied in a NOD/SCID mouse model.
Results: In 1,140 qualified patients, all three GP specificities could be tested. Platelet-bound aabs were detected in 343/1,140 patients (30.1%). Of these, 222 (64.7%) had platelet-bound anti-GP V aabs, either alone (10/222), or together with other specificities (211/222). Free anti-GP V aabs were detected in 30/222 patients by indirect MAIPA, but in 88/222 by SPR. The avidity of aabs detected by both methods (n = 29; R700/R350 = 0.73 ± 0.14) was significantly higher than the avidity for aabs detected by SPR only (n = 59; R700/R350 = 0.32 ± 0.13, P < 0.001). In the NOD/SCID mouse model, IgG prepared from both types of anti-GP V aabs eliminated human platelets with no detectable difference between the groups (mean platelet survival at t = 300 min: 40% [range 27–55] versus 35% [range, 16–46]). A comparable, dose-dependent platelet clearance was also obtained with monoclonal antibody SW16 against GP V.
Summary/Conclusions: Anti-GP V is often detected on platelets from ITP patients. Our study has important implications for both, further development of laboratory testing, and guidance for clinical decision making. Comparison between MAIPA and SPR reveals that free aabs may be more frequent than reported, since aabs appear to escape detection by standard laboratory methods because of low affinity. Anti-GP V by itself induces platelet clearance. Predicting disease severity and/or tailoring ITP therapy should not be restricted to the previously postulated difference between anti-GP IIb/IIIa and anti-GP Ib/IX, and further prospective studies are required to understand the impact of different platelet aabs on the clinical course of ITP.

3D-S16-02

ANTI-HPA-1A POTENT DONOR PLASMA FOR HYPERIMMUNE IMMUNOGLOBULIN PRODUCTION A FIGHT AGAINST FETAL AND NEONATAL ALLOIMMUNE THROMBOCYTOPENIA

M Kjær[1,2,3], K Jarås[2], C Geisen[4], C Akkøk[5], A Wikman[6], K Nielsen[7], K Walles[8], M Sonneveld[9], M Wuhrer[10], G Vidarson[9], J Kjeldsen-Kragh[2,8] and B Skogen[1,2,3]
Funded by EU's Seventh Framework Programme for Research (FP7)

[1]University Hospital North Norway [2]Prophylix Pharma AS [3]UIT-the Arctic University North Norway, Tromsø, Norway [4]German Red Cross, Frankfurt, Germany [5]Ullevål University Hospital, Oslo, Norway [6]Karolinska University Hospital, Stockholm, Sweden [7]Aalborg University Hospital, Aalborg, Denmark [8]University and Regional Laboratories, Lund, Sweden [9]Sanquin, Amsterdam [10]Leiden University Medical Center, Leiden, Netherlands

Background: The preclinical proof-of-concept study by Tiller et al. (Transfusion 2012) showed that passive administration of antibody against paternal platelet antigens induced antibody mediated immune suppression (AMIS) and prevented clinical complication of fetal and neonatal alloimmune thrombocytopenia (FNAIT) in mice.
The goal of the large European collaborate study, PROFNAIT, is to develop and monitor the efficacy as well as safety of Hyperimmune anti-HPA-1a IgG (NAITgam) manufactured from HPA-1a-immunized female donors, for the prevention of HPA-1a-immunization postpartum and FNAIT in subsequent pregnancies.
Aims: The aim of this part of the PROFNAIT project was to collect enough plasma for the manufacture of two conformance lots of Hyperimmune anti-HPA-1a IgG, and to make sure that the collected plasma had the best possible composition both with regard to safety and efficacy.
Methods: Donors included in the hyperimmune donor program were either identified by screening of existing donors, through the centers where they were diagnosed, or through the patient organization Naitbabies (naitbabies.org).
Results: In Europe, a total of 86 female potential donors were identified in Germany, Norway and Sweden. The majority of donors were FNAIT mothers (n = 69) referred to the program by their doctors, the rest were potential donors identified by screening of HPA-1a negative donors at German red cross.

From the US a total of 19,134 female plasma donors (>25 years, with a previous pregnancy) were screened for anti-HPA-1a antibodies and ten high titer donors were identified. Median antibody level in the group of high titer donors was 29 IU/ml (10–143 IU/ml). In addition, a total of 125 women (FNAIT mothers) throughout the US volunteered to donate. However, long distance to the plasma centers limited the number of donations from these volunteers. Hence, in the US, opposite Europe, the majority of plasma collections (85%) were from the screened donors. Among all the donors who were investigated, only one was identified with platelet-activating HPA-1a antibodies and anti-HNA antibodies. This donor was excluded from the program. Finally, in the pool of donors currently selected for NAITgam production (n = 27), none had anti-D antibodies, but some had anti-HLA, anti-A IgG and/or anti-B IgG. In the final pool, low level of anti-HLA (titer 1) was detected, whereas the anti-A and anti-B IgG titers were 100 and 40, respectively.

The glycosylation profiles were investigated, and there were no differences in sialylation and in fucosylation patterns between anti-HPA-1a IgG1 isolated from donors identified by screening compared to anti-HPA-1a isolated from referred donors (FNAIT mothers). However, we did find a decreased fucosylation in the total IgG from the hyperimmune anti-HPA-1a donors (81.6%) compared to the healthy population (94%). Finally, we identified decreased galactosylation in the anti-HPA-1a IgG1 isolated from the screened group compared to the referred group.

Summary/Conclusions: We have identified and qualified anti-HPA-1a positive donors who successfully have been included in the NAITgam donor program. All together, we have collected 515 L and 84 L of high titer plasma from US and EU donors, respectively.

3D-S16-03

THE NLRP3 INHIBITOR DECREASE ERYTHROPHAGOCYTOSIS BY THP-1 CELLS THROUGH OPSONIZED AND UNOPSONIZED MECHANISM

Q Li[1], F Zhao[1], J Zhang[1], G Lu[2], R Xia[3] and Z Zhu[1]
[1]Shanghai Blood Center, Shanghai, China [2]Icahn School of Medicine at Mount Sinai, New York, United States [3]Yunnan Qujing Central Blood Station, Qujing, China

Background: Phagocyte activation and accompanying erythrophagocytosis are thought to result in proinflammatory cytokines release. Two different mechanisms of senescent erythrocyte clearance have been described in the phagocytosis of aged RBCs by monocytes. These mechanisms are termed as unopsonized and opsonized phagocytoses, which are controlled by the CD47–signal regulatory protein α (SIRPα) signaling pathway and the immunoglobulin G (IgG)–Fc gamma receptors (FcγR) signaling pathway, respectively. SIRP-α, a receptor expressed on phagocytes, inhibits phagocytosis when bound to CD47 on the erythrocyte membrane. The low expression of CD47 on aged RBCs subsequently reduces the "not eat" signal, and cause such RBCs being cleared by monocytes. The aged RBCs also form Band 3 clusters and subsequently bind to antibodies and/or complements. The phagocytosis of such RBCs can be induced following the ligation of receptors, such as FcγR. The NLR family pyrin domain-containing protein 3 (NLRP3) inflammasome is the well characterized inflammasome and involved in controlling the activity of caspase-1 and the maturation and secretion of the proinflammatory cytokines, such as interleukin (IL)-1β.

Aims: The work planned to disclose whether the phagocytosis of aged RBCs would activate the NLRP3 inflammasome, and whether the suppression of NLRP3 activation by the NLRP3 inhibitor could regulate erythrophagocytosis.

Methods: THP-1 cells were cultured with or without NLRP3 inhibitor. The 42 °C-treated RBCs and an Rhmod sample were used as CD47 low expression RBCs. The anti-D treated RBCs were marked as IgG-opsonized RBCs. Erythrophagocytosis was determined by monocyte monolayer assay (MMA) and live cell imaging system. The proinflammatory cytokines expression was determined by cytometric bead array, and the activation of the NLRP3 inflammasome was tested by digital PCR and immunoblotting.

Results: The IgG-opsonized RBCs exhibited the highest clearance rate by THP-1. The CD47 expression on Rhmod RBCs was lower than that on 42 °C-treated RBCs, but the phagocytosis rate of the Rhmod RBCs was much lower than that of the 42 °C-incubated RBCs. When the NLRP3 inflammasome inhibitor existed in the culture system, the phagocytosis rates of all the tested RBCs by THP-1 were downregulated. In addition, the untreated RBCs, 42 °C-incubated RBCs, IgG-opsonized RBCs, and Rhmod RBCs all could trigger THP-1 to activate the NLRP3 inflammasome and produce proinflammatory cytokines, such as IL-1β, and tumor necrosis factor (TNF-a), which also could be decreased by NLRP3 inflammasome inhibitor.

Summary/Conclusions: The NLRP3 inflammasome of THP-1 can be activated during aged RBCs clearance both through unopsonized and opsonized pathway. The

phagocytosis rate of aged RBCs by THP-1 can be decreased by NLRP3 inflammasome inhibitor. The RBC clearance rate showed a positive correlation with the expression of proinflammatory cytokines. −1 were downregulated. In addition, the untreated RBCs, 42 °C-incubated RBCs, IgG-opsonized RBCs, and Rhmod RBCs all could trigger THP-1 to activate the NLRP3 inflammasome and produce proinflammatory cytokines, such as IL-1β, and tumor necrosis factor (TNF-a), which also could be decreased by NLRP3 inflammasome inhibitor.

3D-S16-04

ERYTHROPHAGOCYTOSIS INDUCES MHC CLASS II EXPRESSION ON NEUTROPHILS

SM Meinderts, G Baker, S van Wijk, B Beuger, J Geissler, T van den Berg and R van Bruggen
Department of Blood Cell Research, Sanquin Research and Landsteiner Laboratory, Amsterdam, Netherlands

Background: Neutrophils are innate immune cells that are the first responders in tissue injury and infection. They are particularly well known for their anti-microbial function. Nonetheless, neutrophils are versatile cells with numerous functions including innate and adaptive immune regulation. Increasing evidence indicates that neutrophils can contribute to adaptive immunity by influencing antigen specific responses. Under certain conditions neutrophils have been shown to upregulate MHC-II. Moreover, depending on the conditions, neutrophils can exhibit antigen presenting functions.

Aims: In this project we have investigated the antigen presenting capacity of neutrophils after red blood cell phagocytosis.

Methods: To measure if neutrophils produce a burst following RBC phagocytosis we used an amplex red assay, a dihydrorhodamine assay and a nitroblue tetrazolium assay. MHC-II (HLA-DR) and costimulatory molecule (CD40, CD80) expression was measured using flow cytometry, western blot and qPCR. In addition, a tetanus toxoid specific T cell proliferation assay was used to explore the capacity of neutrophils to stimulate T cell proliferation after RBC uptake.

Results: In this study we show that neutrophils express MHC-II and costimulatory molecules following RBC phagocytosis. Following RBC uptake we found that no respiratory burst could be measured and that neutrophils acquired antigen presenting cell (APC) characteristics. In a tetanus toxoid model these neutrophils were proven to illicit a T cell response.

Summary/Conclusions: RBC uptake by neutrophils induces an APC phenotype in neutrophils. These findings could suggest that neutrophils play an unexpected role in RBC alloimmunization.

3D-S16-05

NON-INVASIVE FETAL RHD SCREENING ALLOWS DISCONTINUATION OF NEWBORN RHD TESTING

M Kuosmanen, S Toivonen, K Haimila, K Sulin, A Korhonen, I Sareneva and S Sainio
Finnish Red Cross Blood Service, Helsinki, Finland

Background: Non-invasive fetal RHD test at 24–26 weeks of gestation to target routine antenatal anti-D prophylaxis (RAADP) at 28–30 weeks at women carrying an RhD-positive fetus has been offered to all RhD negative mothers in Finland since 2014. Postnatal anti-D prophylaxis has still been administered based on serological determination of newborn RhD status.

Aims: The aim of this study was to assess the accuracy of the non-invasive fetal RHD test at 24–26 weeks of gestation to evaluate whether RhD testing of newborns has been made redundant.

Methods: A prospective cohort study involving all maternity care centers and delivery hospitals in Finland between February 2014 and December 2017. Fetal RHD genotyping using cell-free fetal DNA in maternal plasma was performed with real-time polymerase chain reaction in a centralized setting. The results were systematically compared with the serological newborn RhD typing.

Results: Fetal RHD was screened from 22 667 women during 2014–2017. Three false-negative and twelve false-positive results were reported by the delivery hospitals. The false-positive results were mostly serologically negative RHD variants carried by the fetus. 1.1% of the results were reported as unclear, most due to an RHD variant carried by the mother.

Summary/Conclusions: The data of the first 4 years of fetal RHD testing in Finland indicates that 1–2 mothers in 10 000 get a false negative result. This means that if the fetal RHD test result was used to target postnatal anti-D prophylaxis, they would not be given postnatal anti-D prophylaxis, although they give birth to an RhD positive child, The rate is less than what is achieved by serological RhD determination of the newborn, which has been reported to be as high as 0.09%. An accurate fetal RHD screening test allows discontinuation of newborn testing without risking the

3D-S16-06

NON–INVASIVE PRENATAL TESTING TO ASSESS FETAL BLOOD GROUP ANTIGENS, ARISING FROM SINGLE NUCLEOTIDE VARIANTS, FOR OBSTETRIC CASES WITH ATYPICAL (NON-RHD) ALLOANTIBODIES: CAPABILITY OF DIGITAL PCR

CA Hyland[1], H O'Brien[1], E Schoemann[1], G Pahn[1,2], T Powley[2], G Millard[2], R Flower[1] and G Gardener[3]
[1]Research and Development [2]Australian Red Cross Blood Service [3]Maternal Fetal Medicine, Mater Health Service, Brisbane, Australia

Background: There is a clinical need for a non-invasive prenatal test (NIPT) that accurately assesses the fetal blood group antigen status in women who are alloimmunised against atypical (non-RhD) blood group antigens. NIPT to predict blood group antigens arising from single nucleotide variations (SNVs) is problematic because the cell-free (cf)DNA in maternal plasma is dominated by the mother's genotype. Droplet digital PCR (ddPCR) permits the detection of rare events in complex samples by partitioning the reaction into thousands of sub-reactions, minimising competition effects.

Aims: To establish proof-of-principle for the suitability of ddPCR as a platform for NIPT assessment of the fetal blood group status for antigens arising from SNVs.

Methods: Droplet digital PCR assays were developed to detect SNVs giving rise to the red cell antigens K, RhE and Rhc, and the platelet antigen HPA-1a. Probe-based assays were designed for KEL1/KEL2 and ITGB3 encoding HPA-1a/HPA-1b using AlleleID software. Published primer and probe sequences were used for RHc and RHE, and, for cffDNA control markers, SRY and hypermethylated RASSF1A. Genomic DNA and plasma cfDNA from characterised samples were used to optimise reactions for the ddPCR platform.

Alloimmunised pregnant women were enrolled with informed consent and blood samples collected into EDTA and Streck BCT tubes. Currently 43 samples from 33 subjects (GA range 10 – 28[+6] weeks) have been provided for fetal KEL1 (n = 21), RHE (n = 8), RHc (n = 3) and HPA-1a (n = 1) assessments. cfDNA was prepared from maternal plasma using a QIAGEN protocol and, for ddPCR, 10 μL added to each reaction in 7 replicates. Cord blood phenotyping or amniocyte genotyping is being used to evaluate test accuracy

Results: Optimisation demonstrated that all ddPCR assays could be performed using the same thermal cycling protocol and primer and probe concentrations (900 nM and 250 nM, respectively). To detect hypermethylated RASSF1A, the pre-PCR BstUI digest was performed directly in the ddPCR reaction for 1 h prior to amplification (contrasting with 16 h using real-time PCR).

For 21 cases tested for KEL1, six showed fetal signals predicting the K antigen. Fetal KEL1 was detected as early as 11[+6] GA for one case in which the use of Streck BCTs permitted a fetal fraction estimate of 8.36%. For RHE and RHc assays, fetal signals have been detected as early as 10 and 13 weeks gestation, respectively. Follow-up second samples have been concordant with initial findings.

The use of control markers, hypermethylated RASSF1A or SRY testing, confirmed cffDNA was present for 11 cases. Correlations with cord blood phenotype or amniocyte genotyping are currently available for 8 cases – three for KEL1, three for RHE, one for RHc, and one for HPA-1A with all matching assay predictions.

Summary/Conclusions: This study provides proof-of-principle that ddPCR reliably detects cffDNA signals, and detects signals at earlier gestation compared to real time PCR technologies. The system has the capacity to run assays using the same PCR protocol and reduced run time and sample manipulation for a universal fetal DNA control marker assay. It highlights the potential scalability, practicality and cost-effectiveness for this niche area of reference laboratory testing.

Clinical – Neonatal and Paediatric Transfusion

3D-S17-01

VOLUME EXPANSION WITH BLOOD COMPONENTS AND CRYSTALLOIDS IN NEONATES: INSIGHTS FROM A NEONATOLOGIST WORKING IN TRANSFUSION MEDICINE RESEARCH

A Keir[1,2,3]
[1]Healthy Mothers, Babies and Children Theme, South Australian Health and Medical Research Institute [2]Robinson Research Institute, University of Adelaide [3]Department of Neonatal Medicine, Women's and Children's Hospital, North Adelaide, Australia

Background: There is increasing uncertainty over the potential benefits and harms of volume expansion in paediatric and adult critical care settings. The FEAST study found increased 48-hourly mortality in critically ill children randomised to receive fluid bolus therapy. In addition, there are increasing numbers of reports of adverse effects and association with RBC transfusions in neonates, including transfusion-associated necrotising enterocolitis. Preterm infants <28 weeks' gestation in particular are considered more vulnerable to volume shifts and changes in blood pressure due to their unique physiology. The potential negative impact of volume expansion may have life-long effects and needs further careful examination.

Aims: A series of reviews and studies will be discussed with attendees.

Methods: (1) Adverse effects of red blood cell transfusions in neonates: a systematic review and meta-analysis.

(2) Are intravenous fluid boluses beneficial in neonates with suspected haemodynamic compromise? A structured literature review.

(3) An international multi-centre, observational, point-prevalence study, out to characterise current practice around the use of volume expansion in neonates (the Neo-Bolus study).

Results: (1) There is no high-quality evidence to support the use of fluid bolus therapy in late preterm or term infants with signs of haemodynamic compromise without evidence of acute haemorrhage. Fluid bolus therapy may be a marker of illness severity, has no clear clinical benefit and may be associated with adverse clinical events.

(2) No significant differences in a range of harmful outcomes between neonates exposed to restrictive and liberal RBC transfusion practice were found. However, the risks of bias identified in most of the studies and the lack of consistent reporting and definitions of events limits the conclusions of this review.

(3) 163 neonates received a bolus over 8479 eligible patient days in 41 neonatal units across Australia, Canada, Europe, New Zealand and the USA. Prevalence and types of fluid bolus therapy varied between centres; from 0% to 28.6% of admitted neonates per day, with a pooled prevalence rate of 1.5% (95% confidence interval 1.1–1.9%).

Summary/Conclusions: There is a clear need for prospective trials in neonates to evaluate the use of volume expansion, both with blood products and crystalloids. Results from PlaNeT-2/MATISSE, TOP and ETTNO are awaited and may provide additional insights. The potential benefits and harms from this commonly used therapy in neonates needs to be addressed.

3D-S17-02

COMPARISON OF HEMATOCRIT CHANGE IN PRETERM NEONATES WITH BIRTH WEIGHT BASED VERSUS FORMULA BASED PACKED RED BLOOD CELL TRANSFUSION

R Kaur[1], R Kaur[1], S Jain[2], D Chawla[2] and G Kaur[1]
[1]Department of Transfusion Medicine [2]Department of Paediatrics, Government Medical College and Hospital, Chandigarh, Chandigarh, India

Background: Conventionally the packed red blood cell (RBC) transfusion volume given to neonates is 10 ml/kg to 20 ml/kg. The weight based formulae underestimate the volume of PRBC required to achieve a target haemoglobin (Hb) or hematocrit (Hct) in preterm neonates.

Aims: The study was done to compare the rise in Hct after transfusing PRBC volume calculated either based on body weight only or using formula considering Hct of bag and Hct of preterm neonates.

Methods: This prospective study included a total of 56 preterm neonates requiring transfusion for first time having ≤ 34 weeks of gestational age. Neonates were randomized using block randomization, to receive either group 15 ml/kg of packed red blood cell transfusion (Group A) or transfusion based on formula (group B) volume

of PRBC (ml) = (Desired Hct – Initial Hct/Hct of bag) X blood volume of neonate (ml). Maximum volume of blood that was given to baby in group B was not exceeded beyond 30 ml/kg. Primary outcome of interest was rise in hematocrit 24–36 h after transfusion. Secondary Outcome was effect of transfusion on short term hemodynamics during transfusion and effect on neonatal morbidities in terms of retinopathy of prematurity, broncho-pulmonary dysplasia, intraventricular hemorrhage, periventricular leukomalacia, necrotizing enterocolitis and death.

Results: Mean Birth weight and mean gestation age was (1128.21 $\pm$ 338.88) grams and (30.20 $\pm$ 1.86) weeks. Mean APGAR score was (7.36, 8.45) at 1 and 5 min respectively. Baseline variables (birth weight, gestation age, APGAR score, maternal anemia was comparable in both groups. Two groups were similar for sickness level as mean SNAP score (Score of neonatal acute physiology) was comparable in both the groups (26.50 $\pm$ 9.74 vs 26.61 $\pm$ 10.83), P = 0.969. Sampling losses in group A and B was (6.32 $\pm$ 1.94 vs 7.18 $\pm$ 1.33), P = 0.06. Hematocrit of the bag was comparable in both the groups (66.96 $\pm$ 4.014 vs 67.46 $\pm$ 3.967), P = 0.671. Mean volume of packed RBC in group A was 18.39 $\pm$ 5.16 ml, whereas in group B it was 28.5 $\pm$ 7.1 ml, P = 0.0001. Total number of donors to which baby was exposed and day of transfusion was also comparable in two groups. Two groups were hemodynamically comparable (HR, RR, Fio2 requirement, mode of ventilation, blood pressure, hematocrit value) prior to transfusion. Post Transfusion group that received transfusion as per formula (Group B) had statistically significant change in 24 hrs post transfusion hematocrit (36.2 $\pm$ 3.98 vs 39.21 $\pm$ 4.73), P = 0.014. Need of re-transfusion was not decreased in group B. Secondary outcome (ROP, BPD, IVH, PVL, NEC, death) were also comparable in two groups. 4 babies in group A and 3 in group B died.

Summary/Conclusions: Post transfusion rise in Hct of patient in group B was significant as compared to group A but the need for re-transfusion was not decreased in group B despite transfusion of more volume of blood.

3D-S17-03

RECEIVED WITH BOTH GRATITUDE AND FEAR: LOCAL PERCEPTIONS OF BLOOD TRANSFUSION FOR CHILDHOOD SEVERE ANAEMIA IN UGANDA

A Dhabangi[1], R Idro[2], MB van Hensbroek[3], C John[4], RO Opoka[2], GE Siu[5] and WH Dzik[6]

[1]Child Health and Development Center [2]Department of Pediatrics & Child Health, Makerere University, College of Health Sciences, Kampala, Uganda [3]Department of Global Health, Emma Children's Hospital, Academic Medical Centre, University of Amsterdam, Amsterdam, Netherlands [4]Ryan White Center for Pediatric Infectious Disease and Global Health, Indiana University School of Medicine, indiana, United States [5]Child Health & Development Center, Makerere University, College of Health Sciences, Kampala, Uganda [6]Department of Pathology (Transfusion), Harvard University/Massachusetts General Hospital, Boston, MA, United States

Background: Blood transfusion is a common emergency treatment for children with severe anaemia and saves millions of children in Africa. However, the beliefs and perceptions of transfusion recipients in the region have not been well documented, yet these may influence care-seeking behaviour.

Aims: To describe local perceptions of paediatric blood transfusion in Uganda.

Methods: A qualitative study based on 16 in-depth interviews of care-givers of children transfused for severe anaemia, and six focus group discussions with community members was conducted in three regions of Buganda, Busoga and Bunyoro in Uganda between October and November 2017. Thematic analysis was supported by ATLAS.ti 7.5 software used for coding, organizing and tracking segments of data.

Results: Care-givers and community members alike held blood transfusion in high regard and valued it as life-saving. However, there were strong reservations about transfusion from widespread fear and misconceptions. Community members feared HIV transmission to their child, with some questioning the use of blood that health workers routinely drew from HIV-infected persons under treatment, and were concerned about the potential for foul play by a malicious health worker. Others were suspicious that their child may be transfused with blood from an animal, which could result in child's behaviour becoming 'wild'. Majority were aware of donor-recipient blood group incompatibilities, and perceived it to be fatal, while some believed that blood from the donor could be 'stronger' than the recipient's for reasons that the latter (child) was sick. Care-givers reported being frequently discouraged by other people who claimed that children who got transfused would always require blood transfusion each time they got sick. Challenges regarding accessing transfusion services were reported, including distant and inaccessible hospitals, scarcity of blood in hospitals especially group O blood, as well as 'under-the table' costs concerns. Besides the belief that while receiving blood a child should not be fed, peri-transfusion beliefs were minimal. However, post-transfusion care practices

including, avoiding rain, not bathing in warm water, and avoiding the heat of the sun and fire were common and were reported passionately.

Summary/Conclusions: Community members and care-givers of children with severe anaemia in Uganda regard blood transfusion highly. However, safety concerns about HIV transmission and blood incompatibility, plus knowledge gaps in the community result in suspicion. Blood scarcity coupled with poor access are major challenges to blood transfusion in Uganda, risking the lives of many children.

3D-S17-04

LATE ANEMIA IN ALLOIMMUNE HEMOLYTIC DISEASE OF THE NEWBORN: INCIDENCE AND RISK FACTORS

IM Ree[1,2], R Middelburg[2,3], A van der Bom[2,3], M de Haas[4,5,6] and E Lopriore[1]

[1]Neonatology, Leiden University Medical Center [2]Clinical transfusion research, Sanquin Research [3]Clinical Epidemiology [4]Clinical transfusion research [5]Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden [6]Immunohematology Diagnostics, Sanquin Research, Amsterdam, Netherlands

Background: Neonates with hemolytic disease of the fetus and newborn (HDFN) due to red cell alloimmunization often require red blood cell transfusions to treat late anemia during the first 3 months of life.

Aims: Our aim was to quantify the need for postnatal red cell transfusions in neonates treated with intrauterine transfusions and to design a risk model to predict late anemia.

Methods: Observational study of data collected from medical records of all 311 (near-) term neonates ($\geq$ 35 weeks of gestation) with HDFN due to maternal red cell alloimmunization admitted to the Leiden University Medical Center (LUMC) between January 2006 and December 2017. Treatment with postnatal red cell transfusions, the number of transfusions and the number of days after birth before the first transfusion was given were recorded, as well as the test results concerning potential risk factors.

Results: In neonates who had been treated with one or more intrauterine transfusion, 88% (168/191) received postnatal transfusions, compared to 61% (65/106) neonates not treated with an intrauterine transfusion (P < 0.001). The median number of postnatal transfusions per neonate was slightly higher in the group not treated with intrauterine transfusions: 2 (IQR 1–3), compared to 2 (IQR 2–3) in the intrauterine transfusion group (P = 0.036). The median time from birth to the transfusion was 16.0 days in the intrauterine transfusion group, compared to 9.0 days without intrauterine transfusion (P = 0.096). In our multivariate prediction model, treatment with intrauterine transfusion (OR 6.62, 95-CI 2.72–16.13, P < 0.001) and treatment with exchange transfusion (OR 0.12, 95-CI 0.05–0.32, P < 0.001) were the strongest predictors of postnatal transfusions.

Summary/Conclusions: Treatment with intrauterine transfusion was strongly associated with an increased risk of late anemia and postnatal transfusions in children with HDFN. Exchange transfusion was strongly associated with a lower risk of postnatal transfusion.

3D-S17-05

INCIDENCE OF ANEMIA AT DISCHARGE IN 4890 CONSECUTIVE PEDIATRIC INTENSIVE CARE SURVIVORS

C Jutras[1], M Sauthier[1], M Tucci[1], G Emeriaud[1], H Trottier[2], N Robitaille[1], J Lacroix[1], R Eltaani[2] and G Du Pont-Thibodeau[1]

[1]Department of Pediatrics, CHU Sainte-Justine [2]Research Center, CHU Sainte-Justine, Montreal, Canada

Background: Given the recent results of many randomized controlled trials advocating for a restrictive approach to transfusion therapy, transfusion practices targeting hemoglobin levels of <70 g/L are increasingly being followed in pediatric intensive care units (PICU). CHU Sainte-Justine Hospital (CHUSJ) adheres strictly to these recommendations and has one of the lowest proportions of transfused critically ill children in North America. Consequently, we hypothesize that, at CHUSJ, a large proportion of PICU survivors are anemic at PICU discharge.

Aims: To determine the incidence of anemia at PICU discharge.

Methods: This is a 5-year retrospective cohort study of all consecutive PICU survivors in a tertiary care university-affiliated pediatric hospital. Patient characteristics and the last hemoglobin level prior to PICU discharge were collected using an electronic medical record database (IntelliSpace Critical Care and Anesthesia, Philips Medical Systems, Royal Philips Electronics, Netherland). The Hb level was measured

as part of a complete blood count. Anemia was defined as per the Canadian Blood Services (CBS) diagnostic criteria.

Results: From January 7 2013 to January 7 2018, 5027 patients were admitted to CHUSJ PICU; 4890 (97.3%) survived to PICU discharge and were included in the study. 4279 (87.5%) children didn't receive red blood cell transfusion during their PICU stay. Overall, 2073 (47%) of survivors were found to be anemic prior to PICU discharge. The proportion of anemic children varied with age: 38% (n = 40) in infants <14 days of age (Hb <125 g/L), 13% (30) in infants aged 14 days to 1 month (Hb <100 g/L), 15% (46) in infants aged 1 to 2 months (Hb <90 g/L), 26% (110) in infants aged 3 to 6 months (Hb <95 g/L), 47% (421) in children aged 6 months to 2 years (Hb <105 g/L), 61% (919) in children aged 2 to 12 years (HB <115 g/L) and 57% (507) in children above 12 years old (Hb <120 g/L) (P < 0.0001). The annual overall proportion of anemic children remained stable over the 5 years (47.4 ± 1.4%).

Summary/Conclusions: A large proportion of PICU survivors are anemic at PICU discharge. This could be the result of adherence to restrictive transfusion thresholds. The long-term consequences of anemia in these children is unknown and needs to be further investigated. Specifically, it is paramount that we determine the impact of long-term anemia on the neurodevelopment of children <2 years of age.

Working Party Session on Donor and Donation

3D-S18-01
COMPLICATIONS OF BLOOD DONATION
C Napoli[1]

[1]A.O.U. (University Hospital Company), S.U.N. (II Università di Napoli, Italy), Napoli, Italy

Blood donors usually tolerate the donation well, but adverse reactions of variable severity may occur during or at the end of the blood collection. These adverse reactions can be divided into local reactions and systemic reactions. Local reactions occur are related to venous access (ie, hematomas due to extravasation from the veins). Pain, hyperemia and swelling may develop at the site of the extravasation. However, there are also trauma to the subcutaneous nerve endings. Finally, phlebitis and thrombophlebitis are rare. In contrast, the systemic reactions can be divided into mild or severe. These events are related to vasovagal reactions triggered by the pain of the venipuncture and the anxiety of undergoing the donation. The systemic reactions become clinically evident by the appearance of pallor, sweating, gastrointestinal disorders, hypotension, and bradycardia. Syncope, of variable severity, which may or may not be complicated by the onset of tonic-clonic muscle spasms can be accompanied by vomiting and loss of sphincter control. Systemic reactions can occur also during apheresis procedures requiring the use of anticoagulants such as acid-citrate-dextrose (ACD). This compound can cause hypocalcaemia, because of chelation. The lowered concentration of calcium ions leads to episodes of paraesthesia of the lips, oral cavity and limbs. These symptoms resolve after interruption of the apheresis procedure as well as the administration of calcium gluconate. Severe, but rare clinical conditions may include complex ventricular arrhythmias, convulsions and death. Thus, medical doctors involved in blood donations must be trained to prevent and treat these adverse events

3D-S18-02
NEEDLE RELATED COMPLICATIONS OF BLOOD DONATION
M Townsend

Corporate Medical Affairs, Blood Systems, Scottsdale, United States

During any routine phlebotomy, whether for whole blood or apheresis collection, a large caliber (16–18G) needle is inserted into the antecubital space. Although the targeted veins of interest are superficially located within the fossa, other deeper structures are at risk of being struck by an advancing needle, including arteries, nerves, muscles and tendons. Further, the needle need not cause direct injury of an underlying structure in order to produce pain as secondary inflammation and irritation of these structures may also induce pain. Involvement of deeper structures within the fossa may result in unusual and rare adverse events with long-lasting and sometimes devastating consequences.

Objectives of session

- Describe common adverse events secondary to needle insertion

- Describe rare adverse events, including rates and typical presentation
- Provide insight into how participation in hemovigilance programs may assist in identification of needle related adverse events

3D-S18-03
APHERESIS COMPLICATIONS
H Vrielink

See abstract 2A-01-02

The Transfusion Practitioner Role in the Stewardship of Blood

3D-S19-01
DISASTER PLANNING: THE ROLE OF THE TRANSFUSION PRACTITIONER
R Deelen[1], E Costermans[2], R Moss[3] and C Akers[4]

[1]Transfusion Practitioner, IJsselland Hospital, Capelle a/d IJssel, Netherlands [2]Nurse Practitioner Hemovigilance, UZ Leuven, Leuven, Belgium [3]Senior Transfusion Practitioner, Great Ormond Street Hospital for Children NHS Foundation trust, London, United Kingdom [4]Blood Matters Transfusion Nurse, department of Health & Human Services, Australian Red Cross Blood service, Victoria, Australia

Background: Disasters can be natural or man-made, such as industrial accidents or terrorism. Planning for them involves a coordinated, multidisciplinary approach to define and document specific tasks and responsibilities required to deal with these situations. All healthcare providers must have a plan for unexpected events that might affect their service. These plans should ensure that appropriate blood components can be located and administered in a timely and safe manner for those requiring treatment, and that if the needs are ongoing, the supply can be available.

Disaster planning for events that could influence blood supply is undertaken at the highest level of government right down to individual laboratories in small hospitals. Including the Transfusion Practitioner (TP), with their expert knowledge of the transfusion chain, can provide valuable input during planning, implementation and reviewing of disaster plans.

Aims: To describe the role a TP may undertake with the multidisciplinary/multimodal team planning for, implementing and reviewing disaster plans.

Methods: Context: TP's primary role is to promote safe and appropriate use of blood within the hospital, including extraordinary events such as internal/external disasters. The role could be localised across the whole health service, or broader, including liaison with the blood provider and government. Plans should include responses to both internal and external events, including variations in the roles and responsibilities in relation to these.

The TP would not normally be considered as part of the response team (unless working), however, have an important role ensuring that the plans are developed and understood. When planning for these events TP's can provide valuable insight and information about important and mandatory patient safety issues (guidelines/standards) required in any setting such as patient identification, logistics (movement/storage/handling), and communication channels.

Promotion and implementation of these plans is a key role of the TP. Education should include dedicated sessions or simulations about what to expect from the laboratory in a disaster and how blood would be provided. Ideally, simulation would involve all associated staff (nursing/laboratory/medical) to play out and test scenarios. The TP can assist staff to understand the outcomes of these sessions and address any issues that might arise.

While most people may think of a disaster as something occurring outside the health service, some disasters are internal such as failure of IT systems or fire in the laboratory, or being cut off from the usual blood supplier and will affect the ability of the laboratory to provide appropriate blood for patients. The TP along with the laboratory staff can advocate for these types of scenarios to be included in the disaster plan, which may include liaison with other health services or blood suppliers.

Results: –

Summary/Conclusions: Transfusion Practitioners have a role in planning for disasters. TP's have the skills to bring together knowledge and enable this knowledge to be converted into practice. They can also play a key role collecting information to evaluate disaster plans in collaboration with the broader team, to ensure safe and appropriate use of the available blood supply during these times.

3C-S19-02

THE TRANSFUSION PRACTITIONER ROLE IN MINIMISING BLOOD WASTAGE

L Bielby[1], C Denison[2] and L De Biasio[3]

[1]Blood Matters, Department of Health and Human Services, Victoria and Australian Red Cross Blood Service, Melbourne, Australia [2]Blood Stocks Management Scheme, National Health Service Blood and Transplant, London, United Kingdom [3]Ontario Regional Blood Coordinating Network, Toronto, Canada

Background: Blood and blood components can be lifesaving; however, supply is limited and relies on dedicated non-remunerated donors (in most countries). These products have a limited shelf-life and must be used appropriately, stored and handled correctly to prevent waste. Transfusion of blood is identified as one of the most over-used therapies, with much of it being inappropriate.

Transfusion practitioners (TP) include those known as transfusion nurses, transfusion safety officers, haemovigilance officers, or patient blood management (PBM) coordinators. A key aspect of the role is driving and influencing clinical blood management activities to help align practice to internationally recognised guidelines and standards, including minimising waste. Waste includes inappropriate/over use, along with component waste due to handling and storage errors or inadequate inventory management.

Aims: To describe the TP role and strategies used to minimise blood wastage.

Context: TP's play a fundamental role within the multidisciplinary team to implement, support and review practices to minimise blood waste and assist in providing safe transfusion practices. They use audit to measure and report inappropriate use, and are often the facilitator and implementer of strategies to minimise this. Strategies include; restrictive transfusion practice where appropriate to patient groups, the use of single unit transfusion in stable nonbleeding patients and promoting PBM strategies such as anaemia management to minimise transfusion. In the surgical setting encouraging practices such as group and hold rather than crossmatch to help reduce inventory stock holdings and discourage use of product, just because it is there. Educating and supporting the use of established maximum surgical blood ordering schedules.

TPs work closely with the laboratory staff and often act as the liaison between the laboratory and the clinical areas supporting practices to minimise potential waste, such as promoting the importance of cold chain management, and timely return of components if not used. Laboratory practices such as regular inventory review, use of electronic decision making ordering tools, and electronic crossmatch all minimise the potential for waste, and the TP's play a key role in helping the broader clinical community understand these processes and the importance of them. Where 'hub and spoke' principles are used for blood management and movement the TP/or equivalent work closely with the laboratory to educate and audit practice.

Results: The United Kingdom (UK) Blood Stocks Management Scheme, the Canadian 'Choosing wisely' promotions and utilisation best practice recommendations and the Australian Blood Wastage Reduction Strategy focus on optimising appropriate blood use to minimise the potential for waste. These multidisciplinary interventions have produced many tools and resources to assist laboratories and health services measure and monitor activities to minimise waste, and have reduced waste.

Laboratory staff and the TP collaboration reduced red cell waste in Victoria, Australia from 6.1% (2014) to ~2.0% (2016–17) and the UK has seen wastage rates stabilise at ~2.1%.

Summary: Minimising unnecessary blood waste is essential for a sustainable blood supply. It requires a team approach, of which the TP plays an active and crucial role to implement and support strategies across the clinical spectrum.

3C-S19-03

IS ONTRAC ON TRACK? A FIFTEEN YEAR EXPERIENCE

A Howell

ONTraC Program, St. Michael's Hospital, Toronto, Canada

The ONTraC program is a successful Patient Blood Management (PBM) network in Ontario, Canada, funded by the Ontario Ministry of Health and Long Term Care. Formed in 2002, the program has 30 PBM coordinators in 25 hospital sites across the province. These hospitals include both teaching and community hospitals and the coordinators interact with physicians, nurses, staff, and patients to promote patient blood management and alternatives to allogeneic transfusion. The targeted procedures include knee and hip surgery, cardiac surgery and gynecological procedures, but many other procedures are followed. Transfusion rates have decreased markedly since onset, for example the mean provincial transfusion rate in knee surgery was 24.5% at onset in 2002 and 1.2% in 2017. This has been accompanied by

lower lengths-of stays and infection rates. The program enhances patient safety and satisfaction whilst being at the same time cost effective and cost-efficient.

Immunobiology – The Future of Red Cell Genotyping

4C-S20-01

THE ROLE OF MOLECULAR GENOTYPING – A NEW ERA

N Gleadall

No abstract available

4C-S20-02

EXTENDED GENOTYPING OF BLOOD DONORS BY NEXT GENERATION SEQUENCING

C Weinstock[1], J Mytilineos[1], J Portegys[2], P Bugert[2], H Schrezenmeier[1] and D Fürst[1]

[1]Institute of Clinical Transfusion Medicine and Immunogenetics Ulm, German Red Cross Blood Service Baden-Württemberg – Hessen, and Institute of Transfusion Medicine, Ulm University, Ulm [2]Institute of Transfusion Medicine and Immunology, Heidelberg University, Medical Faculty Mannheim, German Red Cross Blood Service Baden-Württemberg – Hessen, Mannheim, Germany

Background: Preemptive extended phenotyping of blood donors is time consuming and expensive. Next generation sequencing (NGS) techniques enable the investigation of many genetic loci and polymorphisms of a large number of individuals in parallel. NGS is well established for human leukocyte antigen (HLA)-typing of stem cell donors, it may also be used for a cost-effective typing of blood donors.

Aims: We developed an amplicon based targeted sequencing panel for parallel typing of 768 donors on a MiSeq system (Illumina).

Methods: 33 primer pairs were designed for amplification of the genomic regions encompassing 65 polymorphic sites of the blood group systems MNS, KEL, FY, JK, LU, YT, DO, CO, DI, SC, LW, IN, JR, LAN, and VEL. In addition, two sequences within exon 1 and exon 5, respectively, of the RHCE gene were included in order to screen for RHCE variants. 5 multiplex polymerase chain reactions (PCR) were generated, each containing up to 7 primer pairs. With a second PCR, the resulting amplicons were extended for indices (donor identification) and adapters. For data analysis R/Bioconductor pipeline was used. This programme calls the blood group defining base(s) at the specified position in each target sequence and reports the genotype as well as the predicted phenotype.

Results: 768 DNA samples were typed in parallel, totalling in 25.344 PCR amplicons during the first level of the sequencing process. Finally, 80 (0.3%) of the reactions failed or resulted in a low coverage (i.e. number of final amplicons used for data analysis). For data analysis, the cut-off for the number of amplicons required for a reliable allele call was set to 15. In a typical run, however, the coverage ranged between 100 and 1300 amplicons. 570 of these samples had been typed earlier by a taqman genotyping assay. When comparing the results, 23 discrepant allele calls were found. 10 discrepant results were due to a poor amplification of the sequence of the DO gene, requiring adjustment of the primer concentrations in the primary multiplex PCR. In addition, 1 LU, 1 FY and 1 YT allele were false due to coverages near the cut-off. 8 discrepant VEL genotypes and 1 discrepant YT genotype were found to be correctly typed by the new NGS method. 1 discrepant FY genotype was shown by Sanger sequencing to be caused by a new allele, which was not recognised by NGS and was typed falsely as FY*02 by the taqman method.

Summary/Conclusions: Typing 768 blood donors parallel in one run was possible by using the Illumina technique. The newly developed test panel was found to be suitable, reliable, and cost effective. In the present setup the panel tests for frequent alleles (e.g. in the systems MNS, KEL, FY, or JK) and also screens for rare alleles or null alleles (e.g. in the systems IN, VEL, JR, LAN), but it easily can be customised by addition of new alleles or removal of unwanted alleles.

4C-S20-03

DEVELOPMENT OF A NEXT GENERATION SEQUENCING BASED ABO BLOOD GROUP ASSAY AND TYPING SOFTWARE

W Lane[1,2], H Mah[1], A Joseph[1], J Baronas[1], J Aeschlimann[3], S Vege[3], L Silberstein[1] and C Westhoff[3]

[1]Pathology, Brigham and Women's Hospital [2]Harvard Medical School, Boston [3]New York Blood Center, New York, United States

Background: ABO typing of recipients and donors is important for optimal transfusion and transplant outcomes. Although, serologic ABO typing is highly reliable, it can be limited by discordant forward and reverse typing, especially with weak antigens, ABO subtypes, and hybrid enzyme activity. In addition, living solid organ and stem cell donor evaluations often only involve a buccal swab for DNA isolation, thus preventing upfront serologic ABO typing. A combination of DNA based genotyping solutions (SSP, sequencing, etc) can be used to help resolve serologic ABO discordances as well as screen transplant donors for ABO, but these methods are time- and labor-consuming, and require interpretation by subject matter experts.

Aims: We sought to develop a targeted ABO next generation sequencing (NGS) assay, along with companion interpretive software, for automated data processing and ABO typing for known ABO alleles.

Methods: Targeted long range PCR based DNA enrichment of the ABO gene was achieved by evaluating a series of PCR primer combinations using both blood and buccal swab isolated DNA. The PCR products were run on agarose gel and Agilent bioanalyzer to determine product size and quality. Promising PCR products then underwent Illumina TruSight NGS library preparation and sequencing using an Illumina MiSeq. We previously created a curated allele database (http://bloodantigens.com) and custom bloodTyper interpretive software to determine blood groups from whole genome sequencing data. We improved on these previous efforts by further curating the ABO alleles and by adding NGS sequence read based cis/trans phasing to the bloodTyper software to determine full ABO allele haplotypes.

Results: PCR primer evaluation showed reproducible PCR products spanning ABO exons 2–7 in blood samples and 6–7 for buccal swabs, which yielded good quality NGS data. These exons encode the major ABO specificities including ABO subtypes (A_2, A_x, B_3, weak antigens (A_{weak}, A_{el}), and hybrid alleles (cisAB, B(A)). To verify the ABO NGS assay, a combination of 100 blood and buccal swab samples were tested and found to be 100% concordant with serologic ABO typing and Sanger sequencing of weak, subtype, and hybrid allele samples. We found that in most cases that targeted ABO NGS results could be fully resolved to a cis/trans phased genotyping allowing for unambiguous allele determination by the interpretative software.

Summary/Conclusions: A targeted ABO NGS based assay was developed and optimized for blood and buccal swab isolated DNA. Companion interpretive software, which automates NGS ABO analysis, was developed and correctly determined the ABO type when compared with serology and Sanger sequencing. This assay and software interpretation represents a new and improved standard for DNA based ABO testing, allowing for ABO typing when no blood sample available, and resolution of weak, subtype, and hybrid ABO alleles.

4C-S20-04

DATA VISUALIZATION OF A LARGE GENOTYPED DONOR DATABASE

W Anani[1,2] and G Denomme[1,3]

[1]Immunohematology Reference Laboratory, BloodCenter of Wisconsin [2]Department of Pathology, Medical College of Wisconsin [3]Blood Research Institute, Versiti/BloodCenter of Wisconsin, Milwaukee, United States

Background: High throughput genotyping revolutionized routine access to antigen negative donor red blood cell units. The development of large donor databases present a unique opportunity to map genetic variations of red blood cell antigens over time, locate rare pockets of antigen negative donors, and guide the locations of mobile and fixed donation sites.

Aims: Data mine a large genotyped donor database to provide analytics about common and rare donors in our region.

Methods: Donor red blood cell genotypes via molecular typing from January 2010 to December 2015 were collated with data pertaining to the donor address, age, gender, ethnicity, dates of donation, and genotyped antigens. Distance to donation sites and socioeconomic status are cited as some of the barriers to donate for minority, so we applied geolocation and data visualization of our donors to semi-quantitatively assess if these factors affect our local donors. Data were categorized by age and ethnicity and were visualized by the sum of donors in each zip code to identify any localized regions or trends of rare blood donors to include poverty index, education,

and percent of individuals living in their residence more than 1 year. Data were visualized with 3D Map (Microsoft Excel v.2016) and maps were created from Bing Maps. The donor and extracted population data were superimposed on geographic maps by zip code.

Results: Over 5 years, 54,583 donors were genotyped with 20–29 and 50–59, and 60–69 age groups being the most frequent donors. Forty-nine percent (26,943/54,583) of donors were male. The frequency of ABO groups followed the expected relative incidence: O+, A+, B+, O-, A-, AB+, B-, and AB-. Caucasians represented the largest ethnic group followed by African Americans, Hispanic, Asian, Native American, and other. Donors reported addresses were centered in Wisconsin but addresses identified donors from every US state and from most European countries. Non-Caucasian rare donors (frequency <1:1000) were younger, first-time donors clustered within specific US zip codes with high volumes of African American and Hispanic minorities, surrounded by Caucasian donors. Rare minority donors gave on average 1.2 units compared with 2.3 units for rare Caucasian donors. The median household income of rare donors and common donors were equivalent. However, education and length occupancy in homes differed. Rare donors regardless of ethnicity had an average high school education while common donors had an average college education; rare donors on average occupied their homes <1 year compared with >5 years for common donors.

Summary/Conclusions: Our large metropolitan US city tended towards ethnically segregated populations with many African American and Hispanic, young, rare, first-time donors representing the minority donors living in defined zip codes surrounded by predominately older Caucasians. Recruitment of donors to enrich the inventory with rare blood types should be tailored to particular zip codes with a focus on recruiting and retaining young donors.

4C-S20-05

SATISFYING REQUESTS FOR EXTENSIVELY TYPED RED BLOOD CELL UNITS FROM INVENTORY

J van Sambeeck[1,2,3], M Janssen[1], H Schonewille[4], N van Dijk[2,3] and CE van der Schoot[4,5]

[1]Transfusion Technology Assessment, Sanquin Research, Amsterdam [2]Center for Healthcare Operations Improvement & Research [3]Stochastic Operations Research, University of Twente, Enschede [4]Experimental Immunohematology, Sanquin Research [5]Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

Background: Red blood cell alloimmunization is one of the most important adverse events that may occur as a result of antigen incompatible blood transfusions. Alloimmunization can be reduced by matching donors and transfusion recipients for a large number of antigens. Currently, preventive matching strategies are applied to some patient groups and include only a limited number of antigens. However, the ultimate ambition might be to find extensively matched red blood cell units for all transfusion recipients.

Selecting extensively typed units from inventory, requires that the entire donor population is typed for a large number of antigens. One way to achieve this is by genotyping the entire donor population, which might become affordable in the near future.

Aims: The goal of this study was to investigate the proportion of alloimmunization that can be prevented, depending on the size of the inventory, when the donor population is comprehensively genotyped.

Methods: For multiple inventory sizes, matching strategies, and populations the likelihood that an extensively typed red blood cell unit is available from inventory was quantified. This likelihood depends on the antigen distribution in the donor and patient population, and the matching strategy applied. Moreover, based on existing literature on the immunogenicity of specific antigens in different populations, the proportion of alloimmunization events that can be prevented was computed.

Results: For inventory sizes of a small hospital (60 units), a large hospital (120 units), an academic hospital (250 units), and a distribution center (1000 units) and matching strategies up to 15 different antigens (i.e., ABO, Rh, Kell, Duffy, Kidd, Ss) results were obtained. Our mathematical model demonstrates that in a European patient population and a European donor population the proportion of alloimmunization that can be prevented was equal to 75% (stock = 60), 85% (stock = 120), 95% (stock = 250), and 100% (stock = 1000). In African patients with a European donor population these proportions were 65%, 65%, 80% and 95%, respectively. Increasing the proportion of African donors has only a limited effect on the decrease of alloimmunization events.

Summary/Conclusions: If all donors become fully genotyped, this will not only allow identification of rare donors, but it will also enable extensive preventive

matching for transfusion recipients, on a much bigger scale than currently antici-pated. This implies that alloimmunization can be reduced substantially, preventing problems during pregnancies and subsequent transfusions.

Donors and Donation – Donor Risk Assesment

4C-S21-01

BLOOD DONATION AND MSM: A POINT OF VIEW FROM THE SCREENING LABORATORY

S Sauleda

Transfusion Safety Laboratory, Banc de Sang i Teixits, Barcelona, Spain

Blood safety relies on several actions of different nature combined throughout donor selection, screening and production of blood components. The conceptual and tech-nical complexity of such actions has increased dramatically and cumulatively over the years and, once implemented, to modify or eliminate any of those measures is almost impossible. This is partially due to the strong regulations of blood donation but also to the regulators' concerns, sometimes beyond evidence, that risk to blood safety might be increased. Donor deferral for men who have sex with men (MSM) has been in place for decades in many countries and is aimed to reduce the residual risk of transfusion-transmitted infectious diseases (TTID), namely HIV-1. Permanent deferral has been replaced by temporary deferrals in some countries, the length of the deferral being variable (12 months to 5 years). Permanent or temporary, MSM deferral policies are a controversial debate. Spain is one of the few countries that apply a gender neutral deferral, based on sexual risk practices (4 to 12 months). Spain is also one of the Western European countries with highest HIV-1 prevalence (10 cases per 100,000 inhabitants annually), which is reflected in high HIV-1 preva-lence and incidence in blood donors. Mandatory screening markers are, among others, anti-HCV, HBsAg, anti-HIV-1/2 and HCV RNA, the latter implemented in 1999. HIV RNA and HBV DNA are not mandatory by law, but recommended by the Transfusion Safety Scientific Committee of the Spanish Ministry of Health and all blood donations are presently HCV/HIV/HBV NAT screened in routine either in indi-vidual NAT (ID-NAT) or in minipools of 6 donations (MP-6). From 2005 to 2016, the Spanish surveillance NAT group has reported 52 HIV-1 positive donors in window phase, which equals to 1 out of 400,000 donations screened. Regional data from Cat-alonia show 1 HIV-1 window phase out of 300,000 donations and several anti-HIV-1 positive donors are intercepted annually (7.7 per 100,000 donations), most of them being male regular donors with MSM practices. The fact that most of the HIV-1 pos-itive donors donate in a hospital-based blood center, rather than in a mobile unit, and the short time elapsed since the previous eligible donation suggest that the cur-rent selection criteria have limited effectiveness, and that safety regarding HIV infec-tion relies mainly on NAT and serological screening. Indeed, this is demonstrated by the Spanish Hemovigilance System as the last HIV-1 post-transfusion transmission is documented back in 2005. Two recipients were infected from an HIV window phase donation missed by a first generation MP-44 NAT. Improvements in the sensi-tivity and design of the NAT systems minimize the risk of false negative results due to low viral load or mutated sequences and have correctly addressed HIV residual risk in Spain. However other TTDI might still pose a threat to blood safety, such as the recent outbreaks of hepatitis A virus in Europe, linked to MSM practices. The controversial debate is therefore still open.

4C-S21-02

INFECTION PRESSURE IN MEN WHO HAVE SEX WITH MEN AND THEIR SUITABILITY TO DONATE BLOOD

TJ van de Laar[1], W van Bilsen[2], A Matser[2], K van den Hurk[3], E Slot[1], M Schim van der Loeff[2], H Zaaijer[1,4] and M Prins[2,4]

[1]Department of Blood-borne Infections, Sanquin [2]Department of Infectious Diseases and Research, Public Health Service of Amsterdam [3]Department of Donor Studies, Sanquin [4]Amsterdam Infection and Immunity Institute, Academic Medical Centre, Amsterdam, Netherlands

Background: Deferral of men who have sex with men (MSM) from blood donation is highly debated.

Aims: To assist in defining MSM donor deferral policies, we investigated the suit-ability of MSM to donate blood. We hypothesized that MSM with self-reported low-risk behavior pose a low threat to blood safety if their infection pressure is compara-ble to that of male donors.
Methods: We compared the antibody prevalence of 10 sexually and transfusion trans-missible infections (TTI) among 583 MSM from the Amsterdam Cohort Studies and 583 age-matched repeat male blood donors. The MSM were classified as low-risk (lr) or medium-to-high-risk (hr) based on self-reported sexual behavior and as eligible or non-eligible using Dutch donor deferral criteria for permanent exclusion. Infection pressure was defined as the number of antibody-reactive infections, giving class A infections (HIV-1/2, HBV, HCV, HTLV-1/2, syphilis) double weight, while class B infec-tions (CMV, HSV-1/2, HHV-8, HEV, Parvovirus B19) were given single weight.
Results: Repeat donors had a lower median infection pressure than eligible lr-MSM and eligible hr-MSM (2[IQR-1-2]) versus 3[IQR 2-4), P < 0.001). Low infection pres-sure (infection pressure <3) was found in 76% of donors, 39% of eligible lr-MSM, and 27% of eligible hr-MSM. The prevalence of class A infections did not differ between donors and eligible-lr MSM but was significantly higher in eligible hr-MSM and non-eligible MSM. Recently acquired class A infections were detected in hr-MSM only. Compared to blood donors, CMV, HSV-1/2, and HHV-8 were more prevalent in all MSM groups (P < 0.001), and prevalence increased with higher levels of risk behavior.
Summary/Conclusions: Infection pressure correlates with self-reported sexual risk behavior in MSM. Although lr-MSM might form a low threat for blood safety with regards to class A infections, the high seroprevalence of human herpes viruses in lr-MSM may represent sexual risk-taking that might compromise blood safety, and warrants further investigation.

4C-S21-03

THE USE OF THE ABO RISK–BASED DECISION MAKING FRAMEWORK IN SUPPORTING DONOR SELECTION DECISIONS

G Mallinson[1], S Brailsford[2], K Davison[3] and C Newstead[4]

[1]Joint UK Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC), Sheffield [2]NHSBT/PHE Epidemiology Unit, NHS Blood and Transplant [3]NHSBT/PHE Epidemiology Unit, Public Health England, London [4]Department of Nephrology and Transplantation, Leeds Teaching Hospitals National Health Service Trust, Leeds, United Kingdom

Background: During 2016/2017 the UK Department of Health asked the advisory committee tasked with ensuring the safety of blood, tissues and organs in the UK (SaBTO) to review the donor selection guidelines for men who have sex with men, commercial sex workers, other higher risk sexual partners, skin piercing, injecting drug use and endoscopy for blood, tissue and stem cell donors. These exposures and behaviours have been associated with a potential increased risk of acquiring blood borne infections, for example, hepatitis B virus (HBV). SaBTO set up a donor selec-tion working group to review these criteria and report back with recommendations as to whether they were still appropriate and proportionate.
Aims: The review used an evidence based approach to make recommendations for donor selection based solely on the risk of transmission of a blood borne infection from the donation rather than the previous risk behaviour of the donor. The SaBTO donor selection working group used the Alliance of Blood Operators Risk Decision Making Framework (ABO RBDMF) to guide the review process.
Methods: The working group considered the available data on infection risk, rates of infection in donors, current tests and window periods and information on compli-ance with current criteria. A tolerable risk of transmission was defined as being no greater than predicted by current modelled predictions for undetected infections in the blood supply for HBV, HCV, HIV and syphilis. This was modelled for a range of selection criteria and the framework used to assign where this was tolerable.
The working group included SaBTO members, expert scientists and clinicians and key stakeholder groups representing both patients and groups disproportionately affected by the criteria. The review process started with an open meeting to describe the planned process and allow feedback from interested parties to be included.
Results: A range of recommendations were made by SaBTO to the UK Departments of Health. All the recommendations relating to sexual partners were accepted but it was not possible to reduce the deferrals currently in place for piercing, injecting drug use or endoscopy because of the legal requirements in the blood safety regula-tions. Taking into account the risk assessments, ethical and societal considerations SaBTO recommended reducing the selection criteria for MSM, commercial sex work-ers and higher risk sexual partners to 3 months since last sex. A communications strategy was put in place to ensure that interested parties were aware of the announcement.

Summary/Conclusions: The ABO RDMF was used to support the recent donor selection criteria review and proved useful in ensuring the assessment was carried out in a logical manner with essential areas such as stakeholder participation, communication, ethics and societal considerations being considered. The framework was also useful in assessing tolerable risk.

The new donor selection criteria were implemented in November 2018 across England, Scotland and Wales.

4C-S21-04

HIV RESIDUAL RISK IN THE UK: MODELLING THE IMPACT OF A THREE MONTH DEFERRAL OF DONORS WITH HIGHER RISK SEXUAL BEHAVIOURS

K Davison[1], M Katz[2], C Reynolds[3] and S Brailsford[3]

[1]NHSBT/PHE Epidemiology Unit, Public Health England [2]Global and Public Health Analytical Branch, Department of Health and Social Care [3]NHSBT/PHE Epidemiology Unit, NHS Blood and Transplant, London, United Kingdom

Background: During 2017, the UK Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) reported on their review of donor selection guidelines. They recommended that selection criteria for donors with high risk sexual behaviours (HRSB) should be reduced from 12 to 3-months. The risk of not detecting an HIV window period (WP) infection on donation testing, HIV residual risk, with a 3-month deferral was modelled for the review; any additional risk was considered to be due to donors who did not adhere to the guidelines, i.e. non-compliant. The methodology was similar to that used for the 2011 assessment of risk for changing deferral of men who have sex with men (MSM) from lifetime to 12-months.

Aims: During 2017, the UK Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) reported on their review of donor selection guidelines. They recommended that selection criteria for donors with high risk sexual behaviours (HRSB) should be reduced from 12 to 3-months. The risk of not detecting an HIV window period (WP) infection on donation testing, HIV residual risk, with a 3-month deferral was modelled for the review; any additional risk was considered to be due to donors who did not adhere to the guidelines, i.e. non-compliant. The methodology was similar to that used for the 2011 assessment of risk for changing deferral of men who have sex with men (MSM) from lifetime to 12-months.

Methods: The number of donations from compliant and non-compliant HRSB donors under the current 12-month deferral was estimated by applying the weighted responses to the UK blood donor survey to the number of donations tested in the UK 2012–2015. HIV risk was calculated as observed incidence/100,000 person years multiplied by window period (9 days). For a 3-month deferral, general population sexual behaviour data was used to determine the number of donations from HRSB 4–12 m and HRSB <3 m donors i.e. the additional number of compliant, and remaining number of non-compliant. For the worst-case, the remaining number non-compliant donors (HRSB <3 m) was increased in proportion to the increase in compliant. The observed HIV incidence from avidity testing was used to calculate HIV risk among non-compliant HRSB donors; for the worst-case, the upper bound of the 95% confidence interval of incidence was used to estimate risk. For each group of non-compliant HRSB donors, the difference in HIV risk between the best- and worst-case was added to the current value across all donations to give overall risk for reasonable worst-case under a 3-month deferral.

Results: The increase in non-compliant HRSB donors expected following implementation of 3-month deferral ranged from zero (best-case), to 5% for partner-HEC, - CSW or -FPM and 54% for MSM (worst case). No change was detected for partner-BBV due to low numbers.

HIV risk was estimated as 0.18 per million donations tested under a 12 month deferral of HRSB donors; for a 3-month deferral under the best-case scenario this would remain unchanged but increase almost 4-fold to 0.67 per million donations tested as worst-case, mostly due to non-compliant MSM.

Summary/Conclusions: Implementing a 3-month deferral of donors with HRSB could have no impact on HIV risk in the UK. Even as a worst case, risk was <1 per million donations; this was considered tolerable from the standpoint agreed by SaBTO donor selection working group and the change was made in November 2017.

4C-S21-05

IMPLEMENTATION OF A SCRIPT FOR PRE-DONATION INTERVIEWS: IMPACT ON BLOOD SAFETY

JO Mitchel[1], B Custer[2], Z Kaidarova[2] and K van den Berg[3]

[1]Donor Services, South African National Blood Service, Mpumalanga Zone, South Africa [2]Epidemiology and Health Policy Research, Blood Systems Research Institute, San Francisco, United States [3]Specialised Therapeutic and Transfusion, South African National Blood Service, Eastern Cape, South Africa

Background: Donor selection plays a crucial role in ensuring blood safety. Since the emergence of the HIV epidemic, selection strategies are focussed on preventing window period infections by deferring donors who engaged in recent high risk behaviour. Strategies used include donor education, direct and indirect questioning of the donor regarding risk behaviour. Use of these approaches is widely accepted, often as precautionary measures, but evidence of the efficacy of these practices is limited.

Aims: This study evaluated the impact on blood safety of using a scripted interview to conduct one-on-one donor eligibility assessments in South Africa.

Methods: We conducted a pre-post implementation cross-sectional evaluation study to determine the impact of using a scripted interview on pre-donation high risk deferral (HRD) and recently acquired HIV (RAH) infections among accepted blood donors. We compared two 18-month periods before (unscripted period, November 2013 to April 2015) and after the implementation of the interview script (scripted period, June 2015 to November 2016). Chi-square tests were used for statistical significance assessment, and multivariable models were developed to determine odds ratios separately for each outcome (HRD and RAH) while adjusting for covariates, including sex, age, race, collection zone, and donation history.

Results: There were 3,172,286 donor presentations during the two 18-month periods, of which 52.2% (1,657,024) were made during the scripted period. The odds of HRD were 1.07 times greater during the scripted period (OR: 1.07; 95% CI: 1.05 – 1.08). Female donors (OR: 0.56; 95% CI: 0.55–0.56) had a 44% lower odds of HRD than male donors. All zones had lower odds of HRDs when compared to Egoli zone, with the lowest odds in Kwazulu-Natal (OR: 0.58; 95% CI: 0.57–0.60). A separate model evaluated the odds of RAH infection, which showed an odds of RAH of 0.88 times lower (OR: 0.88; 95% CI: 0.79 – 0.97) during the scripted period. The odds of RAH were higher among females (OR: 2.06; 95% CI: 1.85–2.29) compared to males and among Black (OR: 26.91; 95% CI: 21.35–33.93) and Coloured (OR: 7.33 95% CI: 5.23–10.26) donors compared to White donors. Significant differences by collection zone were evident.

Summary/Conclusions: The use of a script resulted in increased odds of HRD with a concomitant reduction in RAH infection. The lower odds of HRD, yet almost double odds of RAH among females might be indicative of differing societal standards regarding not only sexual behaviour but also willingness to declare such behaviour to others during one-on-one interviews. In addition, sexual disparity in South Africa (SA) contributes to a lack of knowledge among females of potential high risk behaviour of their sexual partners. The significant greater odds of RAH among Black and Coloured donors parallel the HIV infection trends among the general population in SA. Geographically certain areas (predominantly those with a greater rural population) demonstrated lower odds of HRD, but greater odds of RAH infection. The reasons for these differences is likely multi-factorial, including socio-economic differences, but also potentially different operational considerations. While other potential unmeasured confounding factors cannot be excluded, this study found improvement in blood safety with the implementation of a scripted donor interview.

Management and Organisation – Blood and Product Supply

4C-S22-01

TOWARDS A SAFE AND SUFFICIENT BLOOD SUPPLY IN AFRICA

D Kyeyune[1] and H Hume[2]

[1]NAKASERO Blood Bank, Uganda Blood Transfusion Service, Kampala, Uganda
[2]University of Montreal, Montreal, Canada

Achieving universal health coverage, including essential service coverage, is target 3.8 of the United Nations Sustainable Development Goal 3; an index of essential health service coverage indicators includes the proportion of facilities with access to

essential medicines, including blood and blood components. The World Health Organization (WHO) estimates that at least 10 donations per 1000 population are required to adequately fulfill a country's blood transfusion requirements. According to the 2016 Global Status Report for Blood Safety and Availability (GDBS 2016), the median whole blood (WB) donation rate in high income countries (HIC) in 2013 was 32.1 donations/1000 population while in low-middle and low income countries (LMIC/LIC) it was 7.8 and 4.6, respectively. In order to achieve WHO donation goals and provide safe blood, WHO encourages (among other things) the coordination of blood collection and processing systems under the ministry of health, collection of all blood from voluntary non-remunerated donors (VNRD) and testing of all blood donations for HIV and hepatitis B and C viruses (HBV, HCV) in a quality-controlled manner. According to GDBS 2016, 127 (71%) of responding countries indicated that there is a unit with their country's ministry of health for blood services but 63 countries (38 in Africa) received funding from external sources to support these services. The GDBS 2016 also reports that 71 countries, 22 in Africa, still collected<50% of their blood supplies from VNRD and depended on family/replacement donors (FRD) for the majority of their blood supply. With respect to testing for HIV, HBV and HCV, the GDBS 2016 reports that 174 to 176 countries had a policy of screening all donations for HIV, HBV and HCV. In spite of these policies 13 countries reported not being able to test 100% of units collected, only 66% of LIC reported that the testing was performed in a quality assured manner; several LIC perform this testing using rapid diagnostic tests some of which have low sensitivities. Pathogen reduction (PR) of plasma and platelets are now in clinical use in some HIC but not in LIC or LMIC. PR of WB has been shown, in Ghana, to reduce the risk of transfusion-transmitted malaria, an infectious agent common in LIC for which no testing is currently performed. With respect to component production, GDBS 2016 reports that 97% of WB donations collected in HIC versus 50% in LIC is separated into components. In spite of the WHO recommendation, it can be argued that complete conversion of an LIC's blood supply from WB to components is not always the best option. The Uganda Blood Transfusion Service (UBTS) – in spite of being in a LIC – has achieved some of the WHO goals, albeit with the aid of the President's Emergency Plan for Aids Relief (PEPFAR). UBTS is a semi-autonomous organization of the Ugandan Ministry of Health whose mandate is to provide blood free of charge to all Ugandan hospitals and patients. UBTS collects blood exclusively from VNRD with >50% of donations being from repeat donors; all donations are tested serologically for HIV, HBV and HCV. Total blood donations in 2016–217 were 239,040, approximately 5.8 per 1000 Ugandans. In this talk the steps taken by UBTS to achieve its successes will be discussed along with the challenges it and other LIC/LMIC face in striving to continually improve blood safety and sufficiency, including a discussion of VNRD versus FRD, the potential role of PR technologies and the optimal mix of WB versus components.

4C-S22-02

'BIG DATA' APPROACH FOR THE COLLECTION OF COMPARATIVE DATA ON BLOOD UTILISATION FROM THREE UK NHS TRUSTS WITH THE AIM OF IDENTIFYING TARGETS FOR QUALITY IMPROVEMENTS IN TRANSFUSION PRACTICE

AS Dhesi[1], R D'Souza[2], M Kaur[3], N Watkins[2], R Royston[4], K Pendry[4,5], Y Scott[6], A Charlton[3,6], S Staples[7] and M Murphy[7,8]

[1]NHS Blood and Transplant, London [2]NHS Blood and Transplant, Cambridge [3]NHS Blood and Transplant, Newcastle [4]Manchester University NHS Foundation Trust [5]NHS Blood and Transplant, Manchester [6]The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle [7]Oxford University Hospitals NHS Foundation Trust [8]NHS Blood and Transplant, Oxford, United Kingdom

Background: The traditional approach to the collection of comparative data on blood utilisation to support clinical benchmarking is laborious because it involves obtaining information from multiple electronic systems and/or manually from clinical records. 'Big data' refers to the collection of extremely large data sets that are too difficult to process using traditional database and software techniques. Electronic health records and developments in pathology informatics support the collection of such large data sets which can be linked and analysed to support quality improvement initiatives in transfusion medicine.

Aims: The aim of this feasibility study was to determine if large amounts of data from three NHS Trusts could be collected and merged to allow transfusion practice to be benchmarked.

Methods: Clinical, laboratory and transfusion data from patients discharged from three NHS Trusts (Manchester, Oxford and Newcastle), in the financial year 2016/17, were gathered from Patient Administration Systems, Laboratory Information Management Systems and Haemonetics Blood Track (available in two Trusts). Data were

uploaded, along with various reference data tables, into a data warehouse. Using analytical business intelligence software and structured query language, data links were made to generate outputs relevant to transfusion practice.

Results: There were 748,982 patient spells in the dataset with 91,410 components transfused across the three Trusts. Benchmarked results included the number of blood components transfused per 1,000 bed days. This parameter can be used as an enhanced comparator of blood usage between hospitals rather than the number of components issued to hospitals by the blood service or the number of components transfused in a given time. Red cell utilisation was 42.4, 40.4 and 49.5 units/1,000 bed days in the 3 Trusts, and platelet utilisation was 11.69, 7.76 and 11.66 units/ 1,000 bed days.

Information on blood component use showed overall 60.4% O D-negative RBC units were transfused to recipients that were not group O D-negative. Excluding patients with an unknown (blank) ABO/D group this rate drops to 33.6%. Data from one Trust shows for emergency transfusions, 88.3% O D-negative RBC are transfused to recipients with unknown ABO/D group.

Further detailed information about where blood was used was analysed according to diagnostic (ICD-10), procedure (OPCS4) and healthcare resource group (HRG) codes. This provided information about where to focus patient blood management efforts. For example, one Trust found their cardiac platelet usage (7.26% of total platelet use) was higher than the other two Trusts (2.82% and 2.37%).

Some challenges with data management remained, including variances in data format in hospital information systems. However, compared to traditional approaches to collect blood utilisation information there are incremental benefits with time, effort and staff resource.

Summary/Conclusions: Comprehensive comparative data on blood usage, including standardisation of denominator data such as hospital bed days, allows direct comparison of transfusion practice between hospitals and individual clinical services. This allows the identification of targets for quality improvement initiatives.

Additional insights into how blood is used might also support demand planning by blood services allowing more accurate prediction of blood use and adjustment of blood collection activities.

The use of big data is the first step to developing machine learning to further improve transfusion practice.

4C-S22-03

A PROSPECTIVE STUDY OF BLOOD UTILIZATION IN ELECTIVE SURGERIES FOR FORMULATION OF MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE (MSBOS) AT A TERTIARY CARE TEACHING HOSPITAL IN CHANDIGARH, INDIA

M Devnani[1], S Bawa[2], A Gupta[1], A Jain[3], V Suri[4] and S Aggarwal[5]

[1]Hospital Administration, Post Graduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh [2]Health and Family Welfare, Government of Himachal Pradesh, Nahan [3]Transfusion Medicine [4]Obstetrics and Gynecology [5]Orthopedics, Post Graduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh, India

Background: Arbitrary and excessive requisition of blood for elective surgeries is a common practice leading to wastage of blood. To be on the safe side, surgeons request more packed red blood cells (PRBCs) than required for elective surgeries. Maximum Surgical Blood Ordering Schedule (MSBOS) is an evidence based method allowing efficient use of blood stocks, optimal utilization of blood bank resources and reducing blood wastage. This study was undertaken at a tertiary care teaching hospital in India to determine MSBOS for certain elective surgeries. Around 45,000 surgeries are performed in the institute annually.

Aims: To study blood requisition and utilization pattern of nine elective surgical procedures in three surgical departments (Surgery, Orthopedics, and Gynecology) and determine MSBOS.

Methods: All patients undergoing nine elective surgeries -Abdominal Hysterectomy (AH), Vaginal Hysterectomy (VH), Exploratory Laparotomy-Gynecological (ELG), Exploratory Laparotomy-Surgical (ELS), Whipple's procedure (WP), Frey's Procedure (FP), Splenectomy, Total Hip Replacement (THR), and Total Knee Replacement (TKR) – from 1st June 2015 to 31st August 2015 were included in this prospective study. Data of blood requisition, issuance, transfusion, and return within 24 h for each patient was collected prospectively from patient record, operating room and blood bank. Descriptive analysis was performed to determine CT Ratio, Transfusion Probability, Transfusion Index (Ti) and MSBOS for each surgical procedure and altogether. The study was approved by institute review committee.

Results: A total of 536 patients underwent these surgeries during the study period, out of which 67.9% were females. Mean age of patients was 48.6 years (SD 14.8).

Total 1380 PRBC units were requested but only 813 (58.9%) were issued by blood bank. Mean PRBC units requested per surgery was 2.57 (max 3.33 for Splenectomy and min 2.06 for VH). Out of 813 units issued, 244 (30%) were transfused to 207 (38.6%) patients. Maximum 51.47% TKR patients received transfusion whereas only 22.2% Splenectomy patients were transfused. Out of 569 units not-transfused, only 297 (52.2%) were returned to blood bank within 24 h. There was no statistically significant difference (P = 0.3) in pre-transfusion hemoglobin of patients transfused (6.9 g/dl) and not-transfused (7.1 g/dl). Total 824 cross-match were performed. CT ratio for all surgeries was 4.18 (max 7.4 for Splenectomy, min 2.53 for AH). Overall Transfusion Probability was 35.17% (max 51.47% for TKR, min 22.2% for Splenectomy), and Ti was 0.41 (max 0.62 for TKR, min 0.28 for Splenectomy). The MSBOS for elective surgeries was as follows: AH 0.74, VH 0.45, ELG 0.57, ELS 0.58, WP 0.49, FP 0.42, Splenectomy 0.41, THR 0.96, TKR 0.94.

Summary/Conclusions: The study shows that MSBOS for all nine elective surgeries is less than one which is much lower than the actual PRBC requisitions being sent for these elective surgeries. Keeping in view the large volume of surgeries in the institute, implementation of MSBOS would have huge benefits in terms of efficient use of blood and blood bank resources. This study provides evidence for formulation of MSBOS based blood utilization policy at institute level.

4C-S22-04
A PROVINCIAL IMMUNE GLOBULIN SCREENING PILOT FOR NEUROLOGY

D Evanovitch[1], L Young[2], W Owens[3] and L Shepherd[4]

[1]Regional Manager [2]Project Coordinator [3]Program Manager, Ontario Regional Blood Coordinating Network-ORBCoN, Hamilton [4]Laboratory, Kingston General Hospital, Kingston, Canada

Background: In 2015, the Ontario Ministry of Health and Long-Term Care (MOHLTC) and Immune Globulin Advisory Panel (IGAP) examined different screening methodologies for IG for several reasons:

1. IG utilization and costs continue to grow
2. Concerns about the sustainability of this growth.
3. A 2015 compliance audit demonstrated a need for improvement in appropriate IG utilization
4. The need for patient reassessment for those on long-term therapy to determine if the treatment and dosage continue to achieve the expected clinical response
5. The expertise to screen requests across all specialties is not available at every hospital
6. An IG audit conducted in 2012 indicated that 11.6% of Ontario's IVIG use was for unapproved conditions

The IGAP preferred the Exceptional Access Program (EAP) model currently in use for drugs due to its availability at all IG hospitals that issue IG and its familiarity to most physicians. Neurology was selected for the Immune Globulin Screening Pilot (IGSP) because provincial champions were identified and were willing to support it.

Aims: The objectives of the IGSP were to reduce inappropriate use and wastage of IG, ensure the minimum effective dose was administered, improve patient outcomes by ensuring that treatment is effective, gain an understanding of the increased utilization of IG, raise awareness of IG use and costs, ensure dose correction for obese patients and develop a screening model that may expand to other specialties.

Methods: The EAP electronic request technology was not available to this pilot, so a paper-based, faxing system was developed to fill this gap. The pilot ran from May 30 2016 to January 31 2017.

All IG neurology requests were initially screened by an IGSP assessor (pharmacist). The order was approved within 24 h if the guidelines were met. All other requests were forwarded to an anonymous neurologist reviewer for approval or rejection. An urgent process was developed for critical patients and an appeal process was available.

All renewals also required that an Outcome Questionnaire be completed and submitted with the new request to ensure that the treatment continued to be effective and that a minimally effective dose had been applied.

Results: Ninety-two hospitals submitted 1,478 requests which represented 1,167 patients. Eleven requests were rejected, 1,187 requests were approved and 187 requests had dose adjustments. The pilot potentially conserved 72,848 g of IG at a cost saving of $4.5M (CAN). A compliance assessment determined that only 51% of the IGSP approved dose was the actual dose administered by the hospitals. The final cost saving was $2.2M (CAN) when this compliance rate was applied along with EAP costs.

Summary/Conclusions: The pilot was a partial success. It provided uniform, expert screening, inappropriate requests were denied or adjusted, awareness of IG treatment and its cost increased, patient outcomes were monitored and cost savings were

realized. The manual process was tedious and unsustainable. An IG screening model can have a positive effect on patient outcomes and utilization, but the requisite technology must be available to support it.

4C-S22-05
THE USE OF SMART APPLICATIONS TO IMPROVE BLOOD DONORS RECRUITMENT AND RETENTION

MY Raouf and R Sharma

Blood bank, Dubai Health Authority, Dubai, United Arab Emirates

Background: Increasing blood donor recruitment and retention is of key importance to transfusion services to cope with the increasing demand for blood and components in presence of stringent donor eligibility criteria and quality requirement in the blood collection. Building National sustainable voluntary non remunerated blood donation program in among Dubai's National Agenda.

Aims: To improve blood donors recruitment and retention Dubai Blood Donation center has conducted customers satisfaction surveys to evaluate its existing services and has developed an initiative based on voice of the customers and their needs and exceptions which were integrated into planning and implementation of the initiative .

Methods: Dubai blood donation center has introduced a smart mobile applications "DAMMI" on September 2017 that is available on Apple & Android systems. This application allows intended donors to read about blood donation process and journey; educational material, benefits of blood donation and eligibility criteria. Online donors history questionnaire is available in Arabic & English languages. Where the donor can answer the questionnaire and submit it to the blood center by a generated barcode. Donors can also register their details in case they are willing to donate during emergencies and can get notifications from Dubai Blood Bank through such application. To evaluate this initiative we have selected few key performance indicators to evaluate the effectiveness, efficiency and quality of this service.

Results: 8430 donor have used the smart applications inside our center and 3570 donors has down loaded DAMMI application on their smart phones to fill up the donors history questionnaire. Registration service delivery time has been reduced from 4.8 min to 1 min. Waiting time for educational material and fill up questionnaire has been reduced from 23 min to 6 min. Incidents reported due to documentation errors during registration procedure has been reduced from 19% to 0%. Blood donor notifications for infectious diseases according to FDA guidance has been improved from 40% compliance to 100%. Customers happiness survey has shown that customers satisfaction for: speed of service has improved from 79% to 97%., for professionalism of staff has been improved from 78% to 99%, for service information has improved from 83% to 91% and for accessibility to information from 82% to 98.5% .

Summary/Conclusions: The smart mobile application has improved customers satisfaction in our services by making educational material available on mobile phones where they can read it carefully and giving the opportunity to blood donors to fill up donors questionnaire online while they are at home or at their offices with confidentiality. This process can shortened the service time to make blood donation procedure shorter and more convenient to blood donors to encourage their retention. The smart application allows public to register their information to donate in cases of emergencies and disasters. This allows the blood bank to have a wide data base of people who are willing to donate with their locations and blood group. Dubai Blood Bank will proceed to phase two of this application with more features to improve its services.

Blood Products – Frozen Platelets

4C-S23-01
FROZEN PLATELETS: CURRENT PRACTICE, EVIDENCE, EVIDENCE GAPS AND CLINICAL RESEARCH PROGRAMS UNDERWAY

MC Reade[1,2]

[1]Faculty of Medicine, University of Queensland, Brisbane [2]Joint Health Command, Australian Defence Force, Canberra, Australia

Platelets are essential for haemostasis. Liquid-stored platelets have a shorter shelf life (5 days) than other blood components (42 days for red cells and 12 months for fresh

frozen plasma), so outer metropolitan hospitals, rural hospitals and deployed military hospitals usually cannot justify maintaining platelet units on-site, as this would inevitably waste a resource in high demand elsewhere. In response, the Netherlands Military Blood Bank built on earlier US Navy research to refine a process to freeze (using dimethylsulfoxide as a cryopreservative), store (for up to 2 years) and reconstitute (in plasma) platelets for use in military operations. Experience with 1,143 cryopreserved platelet units transfused into 349 patients in Afghanistan suggests they were both safe and effective in treating active bleeding (Noorman et al., 2016), although no comparisons with liquid-stored platelets or whole blood were made. There are also several instances in civilian practice in which the ability to transfuse platelets has been judged to outweigh any unquantified risk associated with the cryopreserved product, including in Poland, the Czech Republic, France and the United States. However, while extensive preclinical assessments and one phase I human study of cryopreserved platelets have been performed, to date there has only been one clinical trial involving bleeding patients published. This US Navy-sponsored study (Khuri et al., 1999) randomised 73 patients to cryopreserved or liquid-stored platelets for treatment of bleeding after cardiac surgery. No adverse effects were observed in the 24 patients who received cryopreserved platelets. Blood loss with cryopreserved platelets was significantly less, despite lower post-transfusion platelet increments and a tendency towards decreased platelet survival. While uniformly encouraging, this evidence base is insufficient to justify regulatory approval. Several international trial groups are seeking to address this deficiency, including the Czech military and the US Department of Defense/Dartmouth University. In 2015 the Australian Red Cross Blood Service and the Australian Defence Force commenced a clinical trial program, the Cryopreserved vs. Liquid Platelet trial (CLIP), designed to evaluate the effectiveness, safety and cost-effectiveness of cryopreserved platelets in comparison to liquid-stored platelets. The Australian pilot trial ceased enrolment in December 2017, with a New Zealand variant of the protocol due to run through 2018. In the Australian pilot, 121 high-risk cardiac surgical patients were randomised, of whom 42 were transfused platelets. Study groups were well-balanced at baseline. There were no adverse events attributed to platelet transfusion. Medical complications that might have been related to cryopreserved platelet transfusion, but which are also common after high-risk cardiac surgery, such as fever, infection, acute respiratory distress syndrome, and deep venous thrombosis, were present in similar proportions in the two trial groups. There were non-statistically significant trends to superiority in several bleeding-related outcomes, including blood loss, requirement for red cell transfusion, and need to return to the operating theatre for bleeding. The results justify progression to a definitive phase III trial, CLIP-II.

4C-S23-02

INVESTIGATION OF DIFFERENT RESUSPENSION SOLUTIONS FOR THAWED CRYOPRESERVED PLATELETS: AN INTERNATIONAL STUDY

L Johnson[1], L Dumont[2,3], J Petrik[4], D Crimmins[5], F Noorman[6], T Shereen[1], M Barber[2], D Dumont[2,3], R Geisler[2], K Grindle[2], A Morrison[7], L McMillan[7], C Casey[8], R Evans[8], P Flanagan[5], D Marks[1] and On behalf of the BEST Collaborative[9]

[1]Research and Development, Australian Red Cross Blood Service, Alexandria, Australia [2]Geisel School of Medicine at Dartmouth, Lebanon [3]Blood Systems Research Institute, Denver, United States [4]Research Development & Innovation, Scottish National Blood Transfusion Service, Edinburgh, United Kingdom [5]Clinical Components Development, New Zealand Blood Service, Auckland, New Zealand [6]Military Blood Bank, Leiden, Netherlands [7]National Science Laboratory, Research Development & Innovation [8]Processing and Testing, Scottish National Blood Transfusion Service, Edinburgh, United Kingdom [9]Biomedical Excellence for Safer Transfusion (BEST) Collaborative, Lebanon, United States

Background: Cryopreserved platelets are now manufactured in many blood centres globally, in an effort to improve storage logistics and/or support military deployments. However, post-thaw processing methods, particularly the volume and type of solution used for resuspending the thawed platelets vary among countries. While plasma, saline and various platelet additive solutions (PAS) have been shown to support post-thaw platelet recovery in separate studies, the most appropriate resuspension solution remains to be defined. Plasma provides the advantage of coagulation factors and fibrinogen to additionally support coagulation in bleeding patients. The use of a non-plasma based solution provides the advantage of improved safety and a more standardised composition. Further, it was hypothesised the inclusion of glucose would support extended storage following thawing. As such, an international multi-centre study with participants from Australia (AUS), New Zealand (NZL), Scotland (SCT) and the United States of America (USA) was performed to compare the quality of platelets resuspended in different solutions.

Aims: To determine the suitability of three different solutions for the resuspension of cryopreserved platelets in an international context.

Methods: A three-arm pool and split design was used to cryopreserve (5–6% DMSO at 80°C) and resuspend thawed apheresis platelets in site-specific solutions (saline for USA; plasma for AUS, NZL and SCT), Intersol or Intersol + 18 mM glucose (n = 6 in each arm, per site). In vitro quality and function were tested at each site using the same protocols, prior to freezing, immediately after thawing and at 24 h post-thaw (stored at 22°C). Collated data were analysed using a two-way ANOVA to assess the combined effects of resuspension solution and country.

Results: The post-thaw platelet content varied among countries (AUS: 260 ± 8 x 10^9/unit; NZL: 217 ± 8 x 10^9/unit; SCT: 226 ± 3 x 10^9/unit; USA: 287 ± 5 x 10^9/unit), but this was due to the pre-freeze platelet content, rather than the resuspension solution. As a result, the mean platelet recovery immediately after thawing was similar among sites (site-specific: $84 \pm 7\%$; Intersol: $86 \pm 6\%$; Intersol+ glucose: $84 \pm 7\%$), although use of PAS reduced platelet loss during 24 h of post-thaw storage when compared to plasma. The resuspension solution did not lead to differences in platelet activation markers, including P-selectin (CD62P) and phosphatidylserine (annexin-V/lactadherin). Thromboelastography (TEG) parameters, including R-time and maximum amplitude, were similar among the three resuspension solutions. Minor differences in quality parameters were detected among the production sites, which may be due to variations in donors, production techniques and/or in vitro measurements.

Summary/Conclusions: Although internationally manufactured cryopreserved platelets differ in composition, these differences are slight and may not be of consequence. Interestingly, the resuspension solution did not substantially influence platelet recovery, activation or function even after 24 h of post-thaw storage. This study demonstrates that all fluids tested are suitable for the resuspension of cryopreserved platelets, and that glucose does not improve storage. This allows thawed platelets to be flexibly adjusted in volume and/or composition to support different patient or logistic requirements.

4C-S23-03

RELEASE OF BIOLOGIC RESPONSE MODIFIERS FOLLOWING CRYOPRESERVATION OF PATHOGEN REDUCED AND NON-PATHOGEN REDUCED PLATELET CONCENTRATES

N Tynngård[1] and P Sandgren[2]

[1]Research and Development Unit in Region Östergötland, Linköping [2]Department of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden

Background: Due to the risk of replication of contaminating pathogens, platelets are stored for a maximum of 5 days. It can be prolonged to 7 days using pathogen inactivation (PI) technologies such as the INTERCEPT Blood System but even with the use of pathogen reduction technologies, 7 days is still a short storage time, and can cause logistic and supply problems. Cryopreserved platelets (CPPs) could be an alternative to meet such demands as well as function as backup stock in crisis situations. However, activation or lysis of platelets results in secretion of biologic response modifiers (BRMs). Consisting of both cytokines and other biomolecules, these BRMs are thought to activate autocrine and paracrine pathways to influence key cellular functions of both donor and recipient cells.

Aims: The aim of this study was to investigate the impact of cryopreservation on BRM release and how cryopreservation affected platelets treated with the INTERCEPT Blood System in this regard. In addition, the correlation between BRM release and the platelet surface markers was also investigated.

Methods: Platelet concentrates with 35% plasma and 65% platelet additive solution (SPSS+) were prepared by buffy coat technology. Twelve units were treated with the INTERCEPT Blood System and 12 units used as non PI-treated controls. The units were cryopreserved and BRM concentrations analysed before- and after cryopreservation. White blood cell (WBC)-associated BRMs INF-gamma, IL-12 (p40), IL-12 (p70) and TNF-alpha as well as platelet-associated BRMs IL-1beta, IL-7, TGF-alpha, RANTES, VEGF and sCD40L were investigated. Correlation analysis were also made between the BRMs and the platelet surface markers assessed by flow cytometry (P-selectin and the active conformation of GPIIb/IIIa measured by PAC-1 binding as well as the platelet mitochondria transmembrane potential measured by JC-1 binding).

Results: The concentration of all BRMs increased significantly (P < 0.05) after cryopreservation with exception of TGF-alpha and IL-12 (p40). PI-treated CPPs had significantly lower increase in RANTES (increased from 97978 ± 49115 pg/ml before cryopreservation to 226524 ± 43628 pg/ml after cryopreservation) than control CPPs (increased from 87590 ± 57088 pg/ml before cryopreservation to

282187 ± 44825 pg/ml after cryopreservation). No or only weak correlations (r < 0.6) were found between the platelet surface markers and IL-12 (p40), IL-12 (p70) and TGF-alpha. Strong correlations (r > 0.6) were found for the other BRMs and P-selectin (P < 0.05) as well as for JC-1 binding except sCD40L. No or only weak correlations (r < 0.6) were found between spontaneous PAC-1 binding and the BRMs whereas there were also strong correlations between ADP-induced PAC-1 binding and several of the BRMs.

Summary/Conclusions: Cryopreservation resulted in increased accumulation of BRMs and generally to a similar degree in control and PI-treated CPPs. BRM accumulation correlated to changes in platelet surface markers. INTERCEPT-treated CPPs may reduce the patients safety risks upon transfusion. However, the clinical relevance of these findings needs to be further evaluated.

4C-S23-04

CRYOPRESERVED DOXORUBICIN–LOADED PLATELETS (PLT–DOX) AS TARGETED CELL–BASED DELIVERY SYSTEM FOR CANCER THERAPY: A TROJAN HORSE TRANSLATIONAL APPROACH

Y Wu[1], C Huang[1], C Changou[2], L Lu[3], H Goubran[4] and T Burnouf[1]

[1]Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering [2]Graduate Institute of Translational Medicine, Taipei Medical University [3]Department of Radiation Oncology & Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering, Taipei Medical University Hospital & Taipei Medical University, Taipei, Taiwan, Republic of China [4]Division of Oncology, College of Medicine, University of Saskatchewan, Saskatchewan, Canada

Background: It is increasingly evident that platelet (PLTs), which are abundant anucleated cells circulating in blood, play a detrimental role in cancer progression. Membrane glycoproteins present on PLTs can target and interact with coagulation factors in the tumor micro-environment and cancer cell surface markers, leading to a detrimental PLT-cancer cell activation loop, culminating in "tumor cell-induced platelet aggregation", platelet degranulation and release of their content. This supports the scientific rationale of a "Trojan Horse" anti-cancer strategy using drug-loaded platelets as a novel physiologically based and immuno-transparent smart targeted drug delivery system (TDDS). To achieve this goal it is required to develop clinically-compliant loading and PLT storage procedures ensuring (a) meaningful drug loading capacity, (b) maintenance of platelet function, (c) long-term storage, and (d) suitable drug release kinetics in the tumor micro-environment.

Aims: To develop a procedure for manufacturing clinical-grade frozen DOX-loaded PLT for targeted drug delivery treatment of cancer.

Methods: Therapeutic-grade platelet concentrates (PCs) were obtained from volunteer donors (Taipei Blood Center, Guandu, Taiwan). PCs were centrifuged to pelletize the PLTs. The pellet was resuspended with 100 μM DOX in platelet additive solution (PAS) and the mixture incubated at 37°+/- 0.5°C for 1 h to encapsulate DOX (PD). PD pellet was suspended in 6% dimethyl sulfoxide (DMSO) and frozen at −80°C (FPD) until use. FPD was thawed at 37°C +/- 0.5°C for 1 min and resuspended with PAS followed by centrifugation to remove excess DMSO. The entrapment of DOX in PD and FPD was observed by deconvolution microscopy. The presence of PLTs surface markers was determined by Western blot. Functionality was assessed by thromboelastography (TEG). DOX entrapment efficiency (% EE) and in vitro release of DOX from PD and FPD in PAS (pH 7.4; control group), PBS (pH 7.4, 6.5, 5.5) and breast cancer cell cultured conditioned medium was examined by HPLC with fluorescence detection (470/585 nm). Human breast (MDA-MB-231), lung (A549) and colon (HCT-116) cancer cells were treated with various concentrations of PD, FPD, free DOX, PLT, or frozen PLT (controls) for 48 h and then analyzed by CCK-8 assay to determine viability.

Results: Deconvolution microscopy showed similar DOX entrapment in PD before and after freezing. DOX encapsulation efficiency was approximately 50 ± 2.2% and 40 ± 3.2% in PD and FPD, respectively. Western blots showed that CD41, CD61 and PAR-1 markers were expressed by both PD and FPD. In the TEG assay, maximum amplitude (MA) on FPD was similar to that of PLT and PD. DOX was released more efficiently at an acidic pH 5.5 mimicking that of the tumor micro-environment and in the cancer cell conditioned medium containing tissue factor microvesicles. MDA-MB-231, A549 and HCT-116 cells viability was affected by PD and FPD as efficiently as by free DOX and significantly more than by liposomal DOX.

Summary/Conclusions: These data support the rationale and feasibility to use cryopreserved platelets as a targeted delivering platform of anti-cancer agents for translational applications.

4C-S23-05

PLATELET ADHESION AND AGGREGATION RECEPTORS ARE ALTERED BY THE COMBINED IMPACT OF UVC PATHOGEN INACTIVATION AND CRYOPRESERVATION

L Waters[1,2], M Padula[2], D Marks[1,3] and L Johnson[1]

[1]Research and Development, Australian Red Cross Blood Service [2]Proteomics Core Facility, University of Technology Sydney [3]Sydney Medical School, The University of Sydney, Sydney, Australia

Background: Conventional storage of platelets at room-temperature (20–24°C) limits their shelf-life to 5 days. Modifications to storage, including cryopreservation (−80°C) and pathogen inactivation (PI), may facilitate extension of shelf-life and improve product safety. Cryopreservation and PI have been shown individually, although differentially, to alter the abundance, conformation and glycosylation profile of the platelet adhesion and aggregation receptors, GPIbα and GPIIb/IIIa. Given the pivotal roles of these glycoproteins in mediating platelet function, it was important to establish the combined effect of these storage modalities.

Aims: The aim of the study was to determine the effect of PI-treatment of platelets prior to cryopreservation, focussing on the impact of combined treatment on platelet glycoproteins.

Methods: Two buffy-coat derived platelet units were pooled and split to form matched pairs (n = 8). One unit remained untreated and the other was UVC pathogen inactivated with the THERAFLEX UV-Platelets system according to manufacturer's instructions (MacoPharma). Both were cryopreserved at −80°C using 5–6% dimethylsulfoxide and resuspended in a unit of plasma after being thawed at 37°C. Platelets were sampled for testing immediately following thawing (post-thaw) and after 24 h of storage at room-temperature (post-storage). The abundance and conformation of GPIbα (anti-CD42b-HIP1 and anti-CD42b-AN51, respectively), GPIIb/IIIa (anti-CD41a and PAC-1, respectively), and the amount of surface bound fibrinogen under resting conditions (anti-fibrinogen) were measured by flow cytometry. Exposure of specific glycan residues were measured using the following lectins: Sambucus nigra (SNA) for sialic acid, Ricinus communis agglutinin (RCA) for galactose and succinylated wheat germ agglutinin (sWGA) for N-acetyl-D-glucosamine (βGlcNAc). Statistical comparisons were performed using paired two-sided t-tests.

Results: The post-thaw recovery of PI-treated platelets (62.6 ± 1.9%) was significantly lower than untreated platelets (71.3 ± 2.5%; P < 0.0001), which declined further during storage. Post-thaw abundance of GPIbα (HIP1) and GPIIb/IIIa on PI-treated platelets was similar to untreated platelets (P = 0.1368 and P = 0.7651, respectively). However, reduced AN51 binding indicated a change in the conformation of GPIbα on PI-treated platelets immediately following thawing (P = 0.0202). GPIbα (HIP-1 and AN51) was re-expressed on the membrane during 24 h of storage, although recovery was lower in PI-treated platelets (P = 0.0231 and P = 0.0075, respectively). PAC-1 binding to PI-treated platelets was higher than untreated platelets post-thaw (P = 0.0017), and increased 3-fold during subsequent storage (P < 0.0001), indicating greater platelet activation. PAC-1 binding correlated with an increase in fibrinogen binding post-thaw and post-storage (r = 0.7326; P < 0.0001). Further, PI-treated platelets bound the most fibrinogen following post-thaw storage (P = 0.0309). Lectin binding, including binding of SNA to sialic acid residues, was reduced on the PI-treated platelets compared to untreated platelets immediately after thawing (P < 0.05 for all lectins). However, this recovered during storage, such that both groups were similar after 24 h.

Summary/Conclusions: PI-treatment prior to cryopreservation alters the post-thaw platelet phenotype. The increased abundance of activated GPIIb/IIIa and fibrinogen binding may enhance aggregation of PI-treated cryopreserved platelets. However, the loss of GPIbα and desialylation of platelet proteins could lead to more rapid clearance of PI-treated cryopreserved platelets.

Blood Safety – Haemovigilance

4C-S24-01

INDIAN EXPERIENCE OF INTRODUCING A HAEMOVIGILANCE SCHEME

A Bisht

Haemovigilance Programme of India, National Institute of Biological Ministry of Health & Family Welfare, NOIDA, India

Background and Objective: Haemovigilance Programme of India (HvPI) at the national level was launched on 10th December 2012 by National Institute of

Biologicals (NIB), Ministry of Health & Family Welfare, Government of India as the National Coordinating Centre - HvPI .The key objectives outlined in the HvPI are i) Monitor Transfusion Reactions ii) Create awareness amongst health care professionals iii) Generate evidence based recommendations iv) Advise Central Drugs Standard Control Organization (CDSCO) for safety related regulatory decisions v) Communicate findings to all key stakeholders and vi) Create National & International Linkages.

Implementing Haemovigilance Programme of India The main characteristics of this programme are in accordance with WHO guidelines for adverse event reporting and learning systems. It is non-punitive, confidentiality of the reporter is maintained, it is independent of punishing authority, data is reviewed by experts and the intent is to improve processes and systems and to make the participants responsive to recommendations. Since this national programme was first of its type in India, one of the challenges was to disseminate awareness about the programme which was achieved through CMEs, workshops and newsletters. The next major challenge was to have a software to facilitate collection and collation of data in TRRF from various enrolled centres and to transmit this data to HvPI. This challenge was overcome by development of an indigenous Haemo-vigil Software which facilitated online reporting by centres. Initially, a simplified one page Transfusion Reaction Reporting Form (TRRF) was introduced to encourage reporting. A well structured committees with defined role and responsibilities provides oversight to this programme. NCC-HvPI has come out with its first report on,"Analysis of Transfusion Reactions Reported from January 2013 to April 2016 and key recommendations for blood safety" .During the analysis of Transfusion Reactions reported, it was found that review process was restrained due to inadequate information & to improve the quality of data, a more detailed TRRF was introduced. Online Reporting in this new format was initiated from 1st May 2016. Looking to the success of recipient Haemovigilance Programme, National Blood Donor Vigilance Programme was launched & reporting of reactions via Donor-Vigil software was initiated in June 2016. The most significant outcome of the programme has been the steady increase in the number of centres reporting to the HvPI since the launch of the programme. This reflects the increasing confidence in the programme on reporting of sensitive data and its outreach to the transfusion medicine community and clinicians. One of the objectives of the programme is to Create International Linkages. In this direction NIB has taken a leap by collaborating with Royal Government of Bhutan. NIB officials had undertaken visit to Bhutan from 07th to 11th November, 2016 with regard to INDO-BHUTAN CME on Haemovigilance for Establishment of Haemovigilance System in Bhutan. IT Cell of HvPI had developed a dedicated Haemo-Vigil Software for Bhutan which was officially handed over to them on the last day of the CME. Bhutan has initiated the Haemovigilance Program in their country with the 1st pilot phase w.e.f July-December 2017 in 4 identified centres. Further, India is a member of International Haemovigilance Network (IHN).

Conclusion: Haemovigilance Programme of India envisage to protect and promote public health by ensuring safe blood transfusion practices in the country.

4C-S24-02

PUTATIVE ALLERGIES WITH METHYLENE BLUE TREATED PLASMA IN HAEMOVIGILANCE DATA: A REAPPRAISAL

P Renaudier[1], A Schumacher[2], N Malvaux[3], A Heinricy[4], M Van der Zwalmen[4], L Scheer[4], F Merny[4], J Leveque[5], P Courrier[1] and J Faber[1]

[1]Direction [2]Laboratory [3]Plood Production [4]Blood Collection [5]IT, Blood Transfusion Center - Luxembourg Red Cross, LUXEMBOURG, Luxembourg

Background: Methylene Blue (MB) is one of the widely used methods of plasma inactivation and considered as safe and effective. However, observations from the French haemovigilance data have raised the question of an increased rate of allergic reactions in plasma recipients a decade ago. We aim at retrospectively reviewing these reactions in addition with the data from the last 10 years.

Aims: We aim at retrospectively reviewing these reactions in addition with the data from the last 10 years.

Methods: Haemovigilance reports of the AFSSAPS and later the ANSM are considered along with those of the EFS. Rates of adverse reactions along with their 95% confidence intervals and their time trends are computed.

Results: *Period of 2008–2011:* rate of allergies to MB plasma was higher (8.9/100,000 units) compared to other types of plasma (5.6/100.000 units). The rate of allergic reactions of grade 3–4 and high imputability was decreasing over the time for MB plasma (3.9/100,000 units in 2009) while maintained for other types of plasma (5.1/100,000 units), achieving the same level during 2010–2011 (32.9/100,000 units; 34.7/100,000 units, respectively), for allergic reactions of all grades and imputability 2–3. In addition, the 95% confidence intervals for these reactions

to all types of plasma overlap during the entire observed period (no statistical difference).

Period of 2012–2016: number of allergic reactions to all types of plasma, all grades and imputability 2–3, has significantly increased compared to the previous years (48.5/100,000 units; 36.3/100,000 units; 34.0/100,000 units; 58.0/100,000 units and 67.6/100,000 units; respectively).

Summary/Conclusions: 1) a reporting bias could have taken place as a result of a strengthened biological exploration of allergic reactions to MB plasma only; this bias, if it is the case, would invalidate the comparability of the MB and non-MB groups. (2) Until 2008, MB plasma was exclusively produced by apheresis in France, which results in more allergies than whole blood plasma (Saadah N. et al. Br J Haematol 2018). Update of the French data does not confirm the previous conclusions, which were not identified in the ISTARE database either. In conclusion, there is no longer evidence point in considering that the MB plasma is responsible for a greater number of allergies.

4C-S24-03

CLASSIFICATION OF TRANSFUSION REACTIONS USING DEFINITIONS FROM ISBT WP ON HAEMOVIGILANCE

O Flesland, C Steinsvåg and A Espinosa

Reporting and Learning Systems Unit, Norwegian Directorate of Health, Oslo, Norway

Background: The Norwegian Haemovigilance system uses the ISBT-WP on Haemovigilance definitions of transfusion reactions from 2011, incorporating corrections to TRALI definitions as adopted June 2013. Transfusion reactions are reported from the clinicians to the blood banks. The blood banks do the necessary laboratory analyses and forward the reports to the haemovigilance system using an internet based form, where the reporter can select from a list of symptoms and a list of transfusion reactions. The ISBT definitions are shown in the form as a help to the reporter. There are two options if no other definitions are suitable, Unclassifiable complication of Transfusion (UCT) and our local "Can't conclude". In the Haemovigilance system each report is validated by at least one medical specialist in transfusion medicine, including a check of the classification against the definitions.

Aims: The aim of this study is to see to what extent reported transfusion reactions in 2016 and 2017 can be classified using the currently used definitions, compared to the 10 year period 2004 – 2013, and to characterize the transfusion reactions reported that do not fit the definitions.

Methods: All transfusion reaction reports from 2016 and 2017 to the Norwegian haemovigilance system were analysed. Data were compared with already published data from 2004 to 2013. https://helsedirektoratet.no/publikasjoner/overvaking-av-blod-i-norge.

Results: From 2004 to 2013 117 reports were classified as UCT and 344 as "Can't conclude". That means that 461 (15.7%) of the total 2937 reports did not fit a definition.

In 2016 to 2017 we had 18 reports classified as UTC and six "Can't conclude". That means that 24 (9.2%) of the total of 262 reports did not fit a definition. Patients with transfusion reactions classified as UTC/can't conclude had the same age distribution as the others, but more were female (63 vs 52%).

There were relatively more life-threatening reactions, but no deaths, in the unclassified group. Otherwise severity was the same. Of the 24 patients with unclassified transfusion reactions 21 recovered completely and outcome for the last three was unknown at time of reporting.

Imputability was weaker in the unclassified group. None of the 24 had imputability Definite, and only two had imputability Probable.

The 24 patients with UTC/can't conclude had recorded a total of 56 symptoms (average 2,3).

The symptoms were nausea/vomiting (11), tachycardia (9) chills or rigors (8), respiratory distress (6), increase in blood pressure (4), chest pain (4), dizziness (3), and headache (2). In addition there were nine other symptoms, each experienced only by one patient.

The other 238 patients had 676 symptoms (average 2.8).

Summary/Conclusions: After evaluation of the reports by a transfusion medicine specialist in the haemovigilance system, only 9% of transfusion reactions are classified as UTC/can't conclude when we use the ISBT-WP definitions. The unclassifiable reactions are mostly mild reactions where the patient recovers completely and imputability is low. In our opinion the current ISBT-WP definitions of transfusion reactions work well.

4C-S24-04

KOREAN HAEMOVIGILANCE SYSTEM – TEN YEARS OF OPERATION RESULTS

J Hyun[1], S Choi[2], J Kim[2], Y Hong[3], H Kim[3], T Kim[3], J Park[3], K Park[3] and K Han[3]

[1]Department of Laboratory Medicine, Hallym University College of Medicine, Hwaseong-si [2]Division of Human Blood Safety Surveillance, Korea Centers for Disease Control and Prevention, Cheongwon-Gun [3]Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

Background: We have set up and operated a national haemovigilance system supported by the Korean Ministry of Health and Welfare (MOHW) but independently operated by the Korean Society of Blood Transfusion (KSBT) since 2007.

Aims: We intended to report the 10 years of operation results of the Korean haemovigilance system.

Methods: In 2007, we started to develop the Korean haemovigilance system as a research fund for the Korean Centers for Disease Control and Prevention. We defined the scope of the reporting events and developed the reporting forms. During the next 2 years (2008–2010) of pilot study, we made a homepage of Korean haemovigilance system and 46 institutions participated and reported voluntarily. We developed the on-line reporting system and the data has been collected on the website since 2011. In 2014, we included the participation of haemovigilance system into the checklist of blood management fee which was newly created. We revised the categories of transfusion reaction and updated the reporting forms in 2017. We hold an explanatory meeting for participating organizations every year.

Results: A national haemovigilance system formally launched in 2010. It is supported by the Korean MOHW but, is independently operated by the KSBT. Although the Korean haemovigilance system is a voluntary reporting system, the participation is included in the accreditation checklist by the Korea Institute for Healthcare Accreditation and Assessment for Certification in Laboratory Excellence by the Korean Laboratory Medicine Foundation. Participation is also required for the institutions to receive the blood management fee. These requirements have dramatically increased the number of participating institutions.

All adverse events including transfusion reactions, near-misses and incidents are reported to the haemovigilance system. After 10 year of operation (including 2 years' pilot study), a total of 14,625 adverse events have been reported. Overall 13,754 transfusion reactions were reported. Febrile non-hemolytic transfusion reaction (8,125, 59.1%) and allergic reaction (3,752, 27.3%) were the most frequently reported adverse reactions and 50 cases (0.4%) of transfusion-related acute lung injury, 31 cases (0.2%) of acute hemolytic transfusion reaction, 20 cases (0.1%) of delayed hemolytic transfusion reaction, 17 cases (0.1%) of delayed serologic transfusion reaction were reported. Transfusion-associated circulatory overload, transfusion-associated dyspnea and hypotensive reaction were newly categorized in 2017 and 2, 92, and 26 cases were reported respectively. There were 882 reports of incidents: near miss 754 (85.5%), incidents without adverse reactions 105 (11.9%), and incidents leading to adverse reaction 23 (2.6%). About the half of incidents (54.2%) occurred in related to blood sampling, 21.7% occurred during transfusion in the ward, and 9.6% occurred during performing pre-transfusion tests in blood bank.

Summary/Conclusions: We have set up and successfully operated the national haemovigilance system for 10 years including 2-year pilot study. Participating institutions increased considerably and accounted for about 80% of transfusion in Korea in 2017. We expect that the data from the haemovigilance support the development of blood safety strategies in Korea.

4C-S24-05

THE FREQUENCY OF PATIENT REGISTRATION ERRORS AND THEIR IMPACT ON TRANSFUSION SAFETY

S Ning[1], M Yan[2] and J Callum[3]

[1]Department of Medicine, McMaster University, Hamilton [2]Department of Laboratory Medicine and Pathobiology, University of Toronto [3]Sunnybrook Health Sciences Centre, Toronto, Canada

Background: Errors remain a major cause of adverse transfusion events world-wide. Data from the 2016 Serious Hazards of Transfusion reported that errors accounted for 87% (2688/3091) of all reports. While errors can occur at various points along the transfusion chain, accurate patient registration is a key first step. However, data pertaining to registration errors is limited. The frequency, patterns, and impact of patient registration errors remain unclear and require further study.

Aims: To provide a descriptive overview of patient registration errors affecting the Transfusion Medicine service of an academic hospital in Ontario, Canada; To highlight the clinical impact of patient registration errors with an illustrative case.

Methods: Patient registration errors impacting the Transfusion Medicine service of an academic hospital (Sunnybrook Health Sciences) in Toronto, Ontario, Canada were reviewed from 2008 to 2017. An illustrative case was investigated and summarized.

Results: Over a 9 year period, there were a total of 146 patient registration errors which impacted the blood bank, of which 111 (75%), 20 (13.6%), 4 (2.7%), 3 (2.0%), and 8 (5.4%) were detected by blood bank technologists, nurses, patients, physicians, and others, respectively. The majority of registration error discoveries occurred at the time of sample receipt or unit request (n = 108, 74.0%), while 15 (10.3%) of the errors were detected at the time of the bedside check. Most common errors were duplicate patient records (35/146), wrong name spelling or name order (35/146), and registration under the wrong hospital identifier (27/147). A total of six errors reached the patient. In one case, a patient with historical anti-Jka antibody was not matched for Jka. In two cases, error led to delay of surgery.

Case: A 23-year-old male with sickle cell disease was admitted to an Ontario hospital for acute pain crisis. His red blood cell (RBC) phenotype (C-c+E-e+, Kell-, Fya-, Fyb-, Jka+, Jkb+, S-, s+) was known and he was registered with the National Sickle Cell Registry. His history of allo-anti-E mandated extended matched (Rh, Duffy, Kidd, S) RBCs for all transfusions as per local policy. On admission, he was erroneously registered with his first and last name in reverse order and assigned a new medical record number; this error led to a lack of patient history at both the hospital and the national registry level. Anti-E was not detected on his screen, and he received two RBC units matched only for Rh antigens (2 units S+, 1 unit Fya+). The registration error was serendipitously identified by a clinical staff prior to further transfusions required for acute chest syndrome, leading to significant delays in procuring appropriately matched products. He was discharged from hospital three days later without detectable new alloantibody formation.

Summary/Conclusions: Patient registration errors are common, detected by both laboratory and clinical staff, and can pose serious harm to patients. Accurate patient registration is a key component of safe transfusion practice.

TP Survey and Abstracts

4C-S25-01

SURVEY OF ISBT MEMBER COUNTRIES TO ASSESS THE ADOPTION OF THE TRANSFUSION PRACTITIONER ROLE

AS Dhesi[1], R Deelen[2], L Bielby[3], R Moss[4] and C OReilly[5]

[1]NHS Blood and Transplant, London, United Kingdom [2]IJsselland Hospital, Capelle a/d Ijssel, Netherlands [3]Victoria and Australian Red Cross Blood Service, Melbourne, Australia [4]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom [5]BC Children's and Women's Hospitals, Vancouver, Canada

Background/Aims: Transfusion Practitioner (TP) is a term that describes healthcare professionals (HCP) whose key role is driving and influencing clinical blood management and safety activities. This includes patient blood management (PBM) initiatives, with the common aim of supporting safe and appropriate care for patients. The ISBT Clinical Working Party (CWP) established the TP Forum (TPF) in 2015 to support the role development across member countries. Over this time, it has become clear that there is significant variation in staff groups filling the role. To understand these variations a survey was undertaken in 2017.

The aims of the survey were to gain an understanding of: which countries have TP roles (or equivalent); the differences in the TP role across ISBT member countries, where these roles are in place; the challenges/barriers for adoption/development of the TP role and the resources the ISBT TP Forum Steering Committee (TPFSC) could develop to support the role.

Methods: A survey was developed by the TPFSC with input from CWP Chairs and members. Two cycles of review were undertaken to agree questions and check functionality and format using SurveyMonkey®. The survey was distributed by ISBT office to all ISBT members, and promoted via newsletters and social media. Respondents were asked to cascade the survey.

Results/Discussion: Five hundred and eighty-two responses received from 84 different countries. The TP role exists in 67 countries, 41 countries do not have the TP role, and eight indicated they did not know. Of note, there were conflicting responses received from within countries, perhaps highlighting differences in role, or understanding of the role.

The TP role has many different titles; the most commonly reported title was TP, followed by Haemovigilance Officer then Transfusion Safety Nurse. Overall, 108 different job titles were indicated. Of the 436 respondents with a TP, 178 indicated the TP spent more than 50% of their time in another role.

The main reported activity of the TP role was policy and procedure development, followed by education, Hospital Transfusion Committees involvement and then audit activity. Fewer TPs are involved in blood manufacturing development and work associated with websites and research.

Eighty-eight respondents (41 countries) indicated they did not have a TP role, with the main barrier being financial, followed by lack of support for the role. Eight respondents indicated they previously had a TP and this role was no longer in place, due to a variety of reasons such as lack of support for role, national/organisational cutbacks and other priorities within transfusion medicine.

Fifty-four percent of the respondents were aware of the TPF prior to the survey, and support the development of tools to support education, audit and specific training for TPs. Regional/national campaigns and programmes to support safe and appropriate blood use were reported by 85% of respondents, with 90% reporting they have national guidelines for transfusion.

Summary/Conclusion: This survey provides insights to where and how the TP functions and provides the TPFSC with valuable information to develop tools to support further development of the role.

4C-S25-02

THIS BLOOD THAT IS NOT MINE: MEANING AND PARADOXES OF BLOOD TRANSFUSION. AN ANTHROPOLOGICAL CLINICAL STUDY OF RECIPIENTS' FAMILY

L Gomez Cardona[1], S Fortin[1], M Tucci[2] and J Lacroix[2]
[1]Université de Montréal [2]CHU Sainte-Justine, Montréal, Canada

Background: The administration of blood products is a therapy frequently used within a number of clinical contexts and it has significant impact on the healthcare system. Transfusion affects not only people's health status, but also self-identity as well as social relations within medical settings. In addition, blood products also raise ethical and legal issues (Kleinman 1994, Starr 1998). Few researchers have focused on the perspectives of the patients receiving blood transfusions and their families.

Aims: In an explorative study, Fortin (Transfusion 2016;56:130-8) documented non-clinical factors (symbolism associated with blood, relations between patients and their professionals and amongst health professionals themselves) that seemed to influence the decision to administer a transfusion and the experience of receiving a blood transfusion. We aimed to enhance this study through precise observation of the role of sociocultural and biomedical environments in which the decision-making process and experience of blood transfusion procedures occur. Our purpose was to characterize the representations that patients and their families attribute to blood transfusions as well as their perspectives regarding blood transfusion procedures.

Methods: We undertook a qualitative trial based upon ethnographic fieldwork consisting of 63 semi-structured interviews (18 children and 45 adults) and a case-study approach of 5 families. The population includes 42 patients followed medically and who require the administration of blood products and their families, and 15 healthcare providers. Attention was paid to acquire a cohort representative of the sociocultural diversity in Montreal. The blood transfusion receivers were divided into two categories requiring medical care. In the first group, we enrolled patients who received multiple blood transfusions as a result of a chronic condition over a long-term basis (example: sickle cell disease). Patients in the second group received blood transfusion over a shorter term, such as in the context of an intensive care unit admission. The data collected underwent a thematic analysis on three levels (individual, horizontal and transverse).

Results: We found a variety of ideas and ambiguity surrounding blood and its transfer (meanings, values). Some respondents believe that the blood of donor carries or contains his individual characteristics. The context surrounding blood transfusion and the therapeutic course also affect transfused patients and their families. Most respondents disagree with the current anonymity of the blood donation system and some would prefer to donate their own blood for their children. Several doctors stated that they do not take into account the symbolic aspects of blood for parents and patients when they prescribe a transfusion.

Summary/Conclusions: A better knowledge of the sociocultural and relational aspects of blood transfusion in a plural clinical context might provide precious information to physicians and nurses. Ethnography should help to better understand the impact that medical procedures like transfusion have on different populations and on the daily lives of people. We see the need to sensitize caregivers about the realities of parents and the ideation they have pertaining to blood transfusion.

4C-S25-03

RURAL AND REGIONAL BLOOD MANAGEMENT IN QUEENSLAND, AUSTRALIA: THE ROLE OF A TRANSFUSION NURSE

S Kay
Clinical Governance, Darling Downs Hospital and Health Service, Toowoomba, Australia

Background: Darling Downs Hospital and Health Service (DDHHS) is the major referral centre for central and western Queensland. It covers over 90,000 square kilometres with 26 facilities that service over 300,000 people. Seven sites provide birthing services, four host Queensland Pathology laboratories, and five sites hold emergency O negative red cells. In late 2014, a Transfusion Nurse (TN) was employed to cover the DDHHS. At this time there was no standardisation, nor central coordination of activities/resources related to blood management.

Aims: To implement rural and regional blood management practices by:
- Measuring and understanding current practices and issues related to blood management
- Increasing awareness of safe and appropriate blood management
- Increasing staff confidence and compliance with procedures/practices across DDHHS.

Methods: In 2014, the TN visited all sites to gather information about current practices and the challenges faced by staff around blood management; including suggestions for improvement.

Policies and procedures were reviewed and updated to align with National standards/guidelines. Audits were undertaken at four key sites to measure practice compliance with policy.

Results: Some challenges expressed related to access to information, blood/blood products, support (medical, specialist transfusion medicine/haematologist), and education programs. Another challenge was lack of familiarity (experience) where infrequent transfusions were administered.

Some strategies used to address these challenges include:
- Developing a 'One Stop Blood Shop' intranet page providing links to blood management resources.
- Commencing education through targeted in-services and workshops. Initially, two workshops were planned, however due to demand, 12 were given in 1 year across all DDHHS sites. Further workshop requests continue within and outside the DDHHS, as staff become more aware of the TN role and the value of the education.
- Establishing close working relationships with/between all laboratories and sites, and connections with pharmacists, General Practitioner Networks, and consumer groups, proving to be a key component to promote blood management.
- Linking with other TNs through state and national networks for support and information sharing.
- Commencing an obstetric patient blood management clinical practice improvement project in partnership with the Australian Red Cross Blood Service to address iron deficiency anaemia.

As a consequence of these strategies, participants express increased knowledge, feeling confident about blood management, and knowing where to access resources. One key site has reduced red cell use significantly from 10/100 separations in 2014 to 4/100 separations in 2017. The use of single unit transfusion has increased from 27% of transfusion in 2014–15 to 38% in 2016/17 and the incidence of giving more than two unit transfusions reduced from 25% to 19% in the same timeframe.

Summary/Conclusions: The TN position covers a large number of sites and distance. Establishing this dedicated position has enabled DDHHS to provide staff with increased knowledge to increase patient safety by reducing blood use and increasing compliance to policy because of staff knowledge, confidence, and competence about blood management and blood safety. Ongoing work and engagement is necessary not only to maintain practice but also to continue to make improvements into the future.

4C-S25-04

PROVIDING A NEW TREATMENT OPTION FOR PATIENTS WHO NEED IMMUNOGLOBULIN THERAPY IN VICTORIA, AUSTRALIA

K Bastin[1], L Bielby[1], C Akers[1], B Glazebrook[1], J van Diemen[1] and J Daly[2]
[1]Blood Matters, Australian Red Cross Blood Service, Melbourne [2]Clinical Services and Research, Australian Red Cross Blood Service, Brisbane, Australia

Background: Subcutaneous immunoglobulin (SCIg) is a well-established form of treatment for patients with primary immunodeficiency (PID) allowing for

self-administration outside the hospital setting. There is significant evidence demonstrating its effectiveness in improving trough levels of immunoglobulin and subsequent increase in health related quality of life. Patients report increased compliance with treatment and reduction in overall cost of care.

SCIg was approved for use in Australia for the treatment of patients with PID and secondary immunodeficiency in 2013. Health services must apply to be an approved treatment site; however, uptake has been slow in most states of Australia. To increase uptake, the Victorian government offered seed-funding in 2017 to 12 health services to start-up SCIg programs, which was accepted by 11. Blood Matters employed a Project Nurse in November 2017 to support and assist with the development of these programs.

Aims: To assist and support health services to implement SCIg programs across Victoria.

Methods: The Project Nurse role includes:
- identifying sites with eligible patients
- promoting the benefits of SCIg at those sites, to clinicians and patients
- identifying and reducing barriers to program development
- providing education on SCIg and assist with a train the trainer education model
- providing tools and resources that are easily accessible through a central repository

Results: To date, 13 health services are approved to administer SCIg, six sites have an established program, and seven are developing programs. It is estimated at seed-funded sites, over 1500 patients are potentially eligible to receive SCIg; however, individual assessment is required at a health service level to determine the patient's interest and capability to undertake this self-therapy. In quarter one 2016/17, 1517 patients were eligible by diagnosis for SCIg, with 51 recorded as receiving SCIg, this has now increased to more than 80 in February 2018.

Important links have been established with AusPIPS (Victorian PID advocacy and support group) and these interactions will be strengthened throughout the project.

Health services have reported positive feedback from patients receiving SCIg, particularly related to choice of therapy, where they can tailor treatment around their life, rather than their life around their treatments.

Financial barriers have been identified for health services without seed-funding; costs associated with set-up and development of a program, equipment, consumables and the reduced funding currently received from intravenous immunoglobulin treatment admissions.

A comprehensive work plan has been developed, outlining site visits to support and promote SCIg uptake, development of tools, and key performance indicators. Initial information and resources have been made available on the Blood Matters website https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/speciality-diagnostics-therapeutics/blood-matters/scgi-implementation-program

Summary/Conclusions: Given the infancy of the project there is still considerable work to be done to embed SCIg programs across Victoria. Initial feedback from patients receiving SCIg is positive and more formal evaluation of the response to treatment will be incorporated in the project. It is anticipated that as patients become more aware of this treatment option, they may help drive uptake. Strategies will need to be developed to assist sites where there are perceived/real financial barriers to uptake.

4C‐S25‐05

INCLUSION OF FERRITIN LEVELS IN A DECISION SUPPORT FOR RED BLOOD CELL TRANSFUSION

C Sanadi[1], A Damani[2], S Solomon[2], L Bortignon[2] and N Shehata[3]

[1]Mount Sinai Hospital, Toronto, Canada [2]Transfusion Medicine Services, MLT [3]MD, MSc, Mount Sinai Hospital, Toronto, Canada

Background: Red blood cell (RBC) transfusion may be requested for patients with iron deficiency anemia if the hemoglobin concentration is perceived to be low. The inclusion of ferritin levels in a RBC transfusion decision support may prompt clinicians to request iron supplements when the ferritin concentration is low instead of RBC transfusion and help to identify clinical services that are requesting RBC transfusion for iron deficiency to direct educational initiatives.

Aims: The aim of this study is to determine the frequency of measurement of ferritin levels prior to transfusion and the frequency of RBC transfusion for iron deficiency following the implementation of computerized decision support. We excluded patients who required a massive transfusion protocol and RBC exchange transfusion.

Methods: This was a retrospective study at a tertiary care -university affiliated center. Data for RBC units transfused and serum ferritin levels were extracted from August 1, 2015 to July 31, 2016 after a decision support for RBC transfusion was implemented. We included patients who had ferritin levels available within 48 h of RBC transfusion and who had ferritin values below 30 µg/L as this level was considered to be diagnostic for iron deficiency.

Results: During this interval 4174 RBC units were transfused to 3979 patient. A ferritin level was available in 5.5% of patients. 57 units were transfused to 46 patients with ferritin levels below 30 µg/L. Of these, 64% of the RBC units were requested for patients in the Emergency room, 16% in General Medicine, 9% by the preoperative unit, 4% in the outpatient department, 3% by ICU and 2% each by the pregnancy and oncology services. The hemoglobin (Hgb) ranges prior to RBC transfusion were as follows: 5 patients had Hgbs ≤50 g/L, 12 patients had Hgbs 51–60 g/L, 23 patients had Hgbs 61–70 g/L, and 6 patients had Hgbs 71–80 g/L. The main indication cited for the majority of these 57 transfusions were low Hgbs and bleeding.

Summary/Conclusions: Investigating for iron deficiency does not occur frequently when RBC transfusion is requested. Several services transfused RBCs instead of iron for iron deficiency. Future modifications to the decision support include prompts for checking iron indices prior to RBC transfusion. Education regarding patient blood management is warranted based on our findings.

Blood Supply Management

4C‐S26‐01

EFFECTIVE COLD CHAIN MANAGEMENT

R Tocchetti

Transfusion Medicine, SA Pathology, Adelaide, Australia

Blood supply chain includes the storage and transport of blood and blood products at and between donor collection/processing centres, transfusion service laboratories and hospitals where the transfusion event occurs.

This blood supply chain requires a strict maintenance of the correct temperature. Maintenance of the correct temperature of blood and blood products during this blood supply chain is referred to as blood cold chain. This chain is a vitally important factor in the maintenance of blood cell viability, preservation of cell function and prevention of bacterial contamination, as such, compliance ensures availability of safe and effective blood and blood products. Non-compliance leads to unsafe blood and blood products and wastage of a precious resource.

Correct temperature is achieved using a combination of dedicated and validated blood refrigeration equipment and transport containers. Blood refrigerators and freezers are specialized equipment and ideally treated as critical medical devices that have been correctly specified, validated, qualified and maintained for the specific use of blood storage. Importantly, blood refrigeration equipment must have continuously temperature recording devices and alarm systems. Blood transport boxes are similarly specialized and must also be specified, validated and qualified for blood transport in all the common and also possible temperature environments and transport periods required.

Most importantly, to facilitate the correct use of blood refrigeration equipment and transport boxes, trained staff and maintained processes and quality systems must exist throughout every link of the blood cold chain between the donor and the patient. Training must be at all levels and links of the blood cold chain and quality systems must include regular auditing and system testing.

With the advent of more centralized donor collection/processing centres and decentralization of sites where transfusion is being performed, the blood supply cold chain is ever so important. Effective blood cold chain is an important part of the strategy to promote universal access to safe blood and blood product transfusion no matter where the recipient is.

A cost-effective blood cold chain can only be achieved if technologically appropriate storage and transport equipment is affordable and accessible at all levels of the health care system and blood supply chain.

Blood cold chain appears to be simple and uncomplicated but it is not, it is a complex process that involves many important steps and many people. Like any process, the chain is only as strong as its weakest link, and a failure of any link will result in the collapse of the chain. Of critical importance is the establishment of a culture with all people involved in the blood supply chain - a culture, the centre of which is 'why?' – 'to have safe and effective blood and blood products available to patients'.

4C-S26-02
OUTCOME OF SURVEY ON BLOOD PRODUCT WASTAGE IN DEVELOPING COUNTRIES

M Yazer

No abstract available

4C-S26-03
CHALLENGES TO EMERGENCY TRANSFUSION IN DEVELOPING/RESOURCE CONSTRAINED COUNTRIES

D Kyeyune[1] and H Hume[2]

[1]Nakasero Blood Bank, Uganda Blood Transfusion Service, Kampala, Uganda
[2]University of Montreal, Montreal, Canada

Blood transfusion is a critical component of any health care system. In high income countries (HIC) the majority of red blood cell (RBC) (or rarely whole blood, WB) transfusions are prescribed for patients with complex surgical procedures, trauma or cancer while in low income countries (LIC), more than 50% of RBC or WB transfusions are given to patients (usually children <5 years old) with malaria or women with obstetrical haemorrhage or for trauma.

One could argue that every RBC or WB transfusion, in any setting, should be an "emergency" transfusion i.e. that not administering the transfusion would result, within a short time period, in a significant adverse effect on the patient's clinical course. The need for transfusion in the majority of settings in HIC can be predicted and blood shortages are rare; true "emergency" transfusions are less common in HIC than in LIC and when they occur the blood necessary to respond to the emergency is available. In contrast, the majority of requests for RBC or WB transfusions in LIC are true emergencies and blood supplies are mostly at levels that would be considered a state of severe shortage in HIC.

In order to manage this double impact of very limited blood supplies with frequent emergency needs, RBC/WB transfusions are often given with much stricter indications in LIC/LMIC than in HIC (e.g. WHO recommendations for RBC/WB transfusions for children in LIC with acute anemia indicate that transfusions should only be given to children with hemoglobin (Hb) levels of 40–60 g/L if they are symptomatic and usually not at all if the Hb level is >60 g/L). In spite of these restrictions, children in LIC die from lack of blood: 2 recent studies have shown that acutely ill children with severe anemia who are not transfused have a significantly increased risk of dying (BMC (2015) 13:21, 52% versus 4% if transfused and BMC Hematology (2017)17:19, 29% versus 10%). Likewise it has been estimated that in sub-Saharan Africa (SSA) approximately 26% of women with post-partum haemorrhage die due to lack of blood (BJOG 2008; 115:1331-9).Alternately, other studies from LIC have shown that RBC/WB transfusions have been given without appropriate indications; this issue deserves further scientific evaluation.

Other issues that deserve further study include inventory management and blood wastage at both the blood supplier and hospital levels. Examples at the blood supplier level include improved blood donor selection procedures, decreasing underweight collections and ensuring a supply of safe small volume units for neonatal and paediatric patients. At the hospital level, examples include coordination of inventories and blood use among different sectors within a given institution and decreasing wastage of blood sent to wards or theatre but not transfused. Other approaches to ensuring the best use of the very limited blood supplies in LIC include better communication and collaboration between blood suppliers and users, effective national and hospital-level blood transfusion committees and the implementation of patient blood management strategies (e.g. late cord blood clamping, correction of iron deficiency during pregnancy and prior to elective surgery) and massive transfusion protocols (including the early use of tranexaminic acid for traumatic and obstetrical haemorrhage). This presentation will focus on these and other strategies to respond to emergency requirements for RBC/WB transfusions in the presence of limited blood availability, particularly in SSA.

Clinical – Hemoglobinopathies

4D-S27-01
PREVENTION AND MANAGEMENT OF RED BLOOD CELL ALLOIMMUNIZATION IN THALASSEMIA

AA Pourfathollah

Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine,, Iranian Blood Transfusion Organization, Tehran, Iran, Islamic Republic of Iran

Since Iran is located on the "thalassemia belt", the prevention and treatment of thalassemia major is one of the priorities of national health governance in the country. Currently there are more than 18000 patients of thalassemia major in Iran.
- Provides constant compatible, safe and adequate blood and blood products for thalassemia patients.
- Prevention and treatment of thalassemia major is one of the priorities of national health governance in the country
The national thalassemia prevention plan was started in 1997. Considering the few number of new patients, it has been proved as one of the successful plans in developing countries. The prevalence of alloimmunization among Iranian thalassemia patients has not been decreased from 1994 to 2013 in Iran. However, the rate is considerably low comparing to other countries. Although there are some strategies to reduce the risk of RBC alloimmunization, finding compatible RBC units for patients with thalassemia has remained a big challenge. IBTO provides constant compatible, safe and adequate blood and blood products for thalassemia patients. Also, pre-storage leukoreduction is applied to all thalassemia patients. There is reference and subsidiary clinical centers throughout the country which provide health services to the patients according to the protocols set by the Iranian Ministry of Health.

As a part of mitigation strategy to manage the alloimmunization, IBTO is recommended to perform matching protocol for K antigen of Kell system for the most prevalent of Rh alloantibody in patients with thalassemia like D, C and E of Rh system. Secondly, personalized medicine and giving the most appropriate transfusion before the formation of alloantibody prevents the severe complications to find the compatible RBC units. Lastly, performing the screening programme to find the donors with the same phenotype of RBC-specific antigens may be helpful to make a pool of donors with the same expression of the most immunogenic RBC antigens such as Kell and Rh other than D antigen.

4D-S27-02
THE TRUE COST OF TRANSFUSION IN THALASSAEMIA STUDY (TRUSTT)

N Waters[1], K Burns[1], H Haysom[1], A Higgins[1], R Tahiri[1], K Rushford[2], T Dunstan[2], K Saxby[3], Z Kaplan[2], S Chunilal[2], Z McQuilten[1] and E Wood[1]

[1]Department of Epidemiology and Preventive Medicine, Monash University [2]Monash Medical Centre, Monash Health [3]Centre for Health Economics, Monash University, Melbourne, Australia

Background: Beta thalassaemia major is an inherited disorder of haemoglobin requiring life-long red blood cell (RBC) transfusion therapy. Information is required to understand the true costs of this support as part of overall management, and the cost-effectiveness of new treatments being developed for this condition. However, no current Australian or international data are available. Determining the true cost of transfusion requires a comprehensive investigation of the complex range of activities required in providing RBC support to a specific transfusion-dependent patient cohort, as various factors influence the cost (e.g. inpatient/outpatient setting), including laboratory, clinical and governance activities, and inputs required to deliver the service.
Aims: To accurately determine the total cost of RBC transfusion support for adult transfusion-dependent thalassaemia patients at Monash Medical Centre (MMC), a thalassaemia treatment centre in Melbourne, Australia.
Methods: A time-driven activity-based costing (TD ABC) study of clinical, laboratory and administrative processes for RBC transfusions for transfusion-dependent adult thalassaemia patients at MMC was performed. Detailed process maps were developed for every procedure undertaken over 1 month (March 2017). Direct and indirect costs (personnel, consumables, equipment, clinical and testing procedures) were calculated, including costs of governance, managing long-term consequences of transfusion, and other complications.

Detailed process maps and corresponding flowcharts were developed to provide a step-by-step description of the entire transfusion pathway including pre-transfusion phlebotomy, laboratory procedures, patient day admission for RBC administration, and treatments and processes directly related to the transfusion. Direct observations to verify process maps and timing of the processes were conducted. Expert opinion was obtained where processes were unable to be timed. All activities, resources, staff, equipment, consumables and overheads were included and a cost and sensitivity analysis was performed.

Results: Thirty-one complete processes were mapped including prescription, sample collection, laboratory activities including inventory management, administration and follow-up of RBC transfusion. For iron chelation, 79% patients received deferasirox, 18% desferrioxamine, 3% received both. All process steps, staff and consumables required to provide 478 RBC transfusions to 117 adult patients (average 2.8 RBCs per admission) with thalassaemia major over 1 month, including frequencies, and direct and indirect overhead costs, contributed to the per-RBC unit cost of AUD $1,004 (95% CI 1003, 1006).

Summary/Conclusions: The TD ABC method provides an accurate measurement of the cost of transfusing a unit of RBC to patients with transfusion-dependent beta thalassaemia major. Considering staff time, equipment, consumables and other resources, the cost of transfusing a unit of RBCs in this setting is more than double the published manufacturing cost of the RBC unit. This study also provides detailed process maps and a costing method which will be adaptable for costing studies of other blood components, in other hospital settings and in other patient groups, including other chronically transfused patient populations such as myelodysplasia. Detailed cost data determined as part of this study will be valuable for clinicians, hospital management, governments, blood services, patients and the broader community.

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4D-S27-03
RED CELL ALLOIMMUNIZATION IN EPISODIC AND CHRONICALLY TRANSFUSED THALASSEMIA INTERMEDIA

M Yan[1], H Merkeley[2] and C Cserti-Gazdewich[1,3]

[1]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto [2]University of British Columbia, Vancouver [3]Laboratory Medicine Program, University Health Network, Toronto, Canada

Background: Red blood cell (RBC) alloimmunization occurs more often in patients with hemoglobinopathies. The propensity in sickle cell disease (SCD) is especially pronounced owing to the inflammatory milieu when RBC transfusion is indicated, and the differences in the donor base versus host antigen profile (if not addressed with prophylactic matching). Episodic transfusions in SCD associate with a higher rate of alloimmunization and hemolysis (per RBC unit) compared to patients in a chronic transfusion regimen. Whether patients with thalassemia intermedia (TI) share similar alloimmunization risks with episodic RBC transfusions is unknown. TI includes β-TI (a clinical severity between β-thalassemia trait and β-thalassemia major), and Hemoglobin H Disease (HHD, in which 3 of 4 α-chains are affected). Patients with TI do not require transfusions from birth but may require them episodically during illness, or on a chronic basis later in life to treat complications.

Aims: The primary objective of the study is to evaluate the frequency of RBC alloimmunization in patients with β-TI or HHD receiving episodic RBC transfusions.

Methods: A retrospective review of all TI patients followed at the Red Blood Cell Disorders Clinic between January 1999 to September 2017 was conducted at an academic institution in Toronto, Canada. Patients with β and/or δ mutations resulting in a TI phenotype, or α mutations resulting in HHD, were included in the review. Non-transfused patients were excluded from the study. Information regarding transfusion history and frequency, antibody investigation results, and age at first transfusion was collected. Chronic transfusion was defined as receiving more than one unit of RBCs per month for at least 3 months. Transfusions at our institution for thalassemia were Kell-negative and matched for RhD.

Results: Seventy-four patients with TI (59 β-TI (80%) and 15 HHD (20%)) were reviewed for the study. Forty-four patients (59%) were female. In addition to transfusions administered at our institution, 62 patients (84%) also received transfusions at other institutions. Forty patients (54%) had only received episodic transfusions with a median of 0 (interquartile range (IQR), 0–1) RBC units, and a mean of 2.0 (±4.7) units transfused at our institution. Thirty-four patients (46%) had received chronic transfusions with a median of 89 (IQR 7–209) units and a mean of 131 (±162) units transfused at our institution. The mean age of chronic transfusion initiation was 30 (±18) years old. RBC antibodies were detected in 17 patients (23%)

with 12 of these patients (71%) having multiple antibodies. The frequency of RBC alloimmunization in patients receiving episodic transfusions was 18% (n = 7) compared to 29% (n = 10) in chronic transfusions (P = 0.27). Forty-six antibodies were detected, of which 18 (39%) had specificities targeted against RHCE antigens.

Summary/Conclusions: Despite a limited exposure to RBC units, patients with TI receiving episodic RBC transfusions have an increased risk of alloimmunization, specifically against Rh antigens. Provision of Rh- and Kell-matched units to these patients may mitigate the risk.

4D-S27-04
IDENTIFICATION OF GENETIC BIOMARKERS FOR ALLOIMMUNIZATION IN SICKLE CELL DISEASE USING NEXT GENERATION SEQUENCING

SM Meinderts[1], J Sins[2,3], J Gerritsma[2], M de Boer[1], K van Leeuwen[1], M Tanck[4], B Biemond[3], A Rijneveld[5], J Kerkhoffs[6], S Pakdaman[7], A Habibi[8], R van Bruggen[1], T Kuijpers[1,2], E van der Schoot[9], K Fijnvandraat[2,10], F Pirenne[7] and T van den Berg[1]

[1]Department of Blood Cell Research, Sanquin Research and Landsteiner Laboratory [2]Department of Pediatric Hematology, Immunology and Infectious Diseases, Emma Children's Hospital, Academic Medical Center, University of Amsterdam [3]Department of Hematology [4]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam [5]Department of Hematology, Erasmus MC, University Medical Center, Rotterdam [6]Department of Hematology, Haga Hospital, The Hague, Netherlands [7]Etablissement Français Du Sang Ile de France, INSERM U955, University of Paris Est-Créteil, Hôpital Henri Mondor [8]Reference Center for Sickle Cell Disease, Hôpital Henri Mondor, Créteil, France [9]Department of Experimental Immunohematology [10]Department of Plasma Proteins, Sanquin Research and Landsteiner Laboratory, Amsterdam, Netherlands

Background: Virtually all sickle cell disease (SCD) patients rely on blood transfusion as main treatment strategy. However, frequent blood transfusion poses to the risk of alloimmunization; a severe complication that can lead to blood transfusion reactions and potentially lethal delayed hemolytic transfusion reactions (DHTR). Not all patients develop alloantibodies after repeated transfusion. It appears that alloimmunized patients (responders) represent a genetically distinct group that is more prone to RBC sensitization. On average 30% of patients will alloimmunize while other patients remain tolerant despite high transfusion exposure (non-responders). A promising strategy to reduce alloimmunization in SCD is prophylactic matching. In order to reduce costs and make this logistically feasible the strategy should be reserved for SCD patients most at risk of developing alloantibodies. To predict which patients will turn out to be responders identification of genetic biomarkers for alloimmunization is necessary.

Aims: The aim of this study was to evaluate whether SNPs in genes previously associated with alloimmunization, antibody-mediated graft rejection or antibody-mediated autoimmune diseases are associated with RBC alloimmunization in a cohort of SCD patients.

Methods: In this case-control study, DNA samples from 2 cohorts of transfused SCD patients were combined (France and the Netherlands). Cases had a positive history of alloimmunization, having received ≥1 RBC unit. Controls had a negative history of alloimmunization, having received ≥20 RBC units. Single nucleotide polymorphisms (SNPs) and copy number variation of the FCGR2/3 gene cluster were studied in a FCGR-specific multiplex ligation-dependent probe amplification assay. In addition we have genotyped 784 SNPs in 119 genes using next generation sequencing (NGS). Frequencies were compared using logistic regression. 285 patients were included (141 controls, 144 cases).

Results: The non-classical open reading frame in the FCGR2C gene (FCGR2C.nc-ORF) was strongly associated with a decreased allo-immunization risk (OR 0.26, 95% CI 0.11–0.64). This association persisted when only including controls with exposure to ≥100 units (OR 0.30, CI 0.11–0.85), and appeared even stronger when excluding cases with Rh or K antibodies only (OR 0.19, CI 0.06–0.59). During the genotype analysis of the 784 selected SNPs using NGS 2979 additional SNPs were picked up. Statistical analysis is currently being performed on these 3763 genotyped SNPs.

Summary/Conclusions: In conclusion, SCD patients with the FCGR2C.nc-ORF polymorphism have over a threefold lower risk for RBC allo-immunization compared to patients without this mutation. This protective effect was strongest for exposure to antigens other than the immunogenic Rh or K antigens. In the next coming weeks we expect to find more polymorphisms associated to alloimmunization in SCD.

4D-S27-05

USE OF A CLOUD–BASED SEARCH ENGINE OF A CENTRALIZED DATABASE TO IDENTIFY HISTORICAL ANTIGEN–NEGATIVE UNITS IN HOSPITAL INVENTORIES

G Denomme[1,2], S Reinders[3], A Treml[4,5], J Gottschall[1,2,4,5] and W Anani[2,4]

[1]Immunohematology Reference Laboratory [2]Blood Research Institute [3]Information Services, Versiti/BloodCenter of Wisconsin [4]Department of Pathology, Medical College of Wisconsin [5]Froedtert Hospital, Milwaukee, United States

Background: Minor blood group antigen information on red cells units provides valuable information to hospitals for alloimmunized patients and antigen-matched transfusions. Regulatory labeling can be exorbitantly expensive to meet the demand. Access to unlicensed historical phenotype and mass-scale red cell genotype results provides an option for the end-user to confirm the antigen-negative status on specific units. However, historical antigen information provided on packing slips is cumbersome: units from each shipment need to be set aside and the documentation transferred for reference. We created an electronic access program that queries the blood center centralized database of historical phenotype and mass-scale red cell genotype screen results to find antigen-negative units in local inventories.

Aims: To provide hospitals with a cloud-based end-user search engine that queries a blood center centralized database of red cell phenotypes and genotypes to identify historical antigen-negative units in their local inventories.

Methods: The cloud-based electronic query was developed to mimic the process used to phenotype units. A hospital operator scans the ISBT unit number barcode on a set of group-compatible blood units from the local inventory into designated fields, and selects the desired antigen-negative criteria from a list along with number of units required. The query is electronically sent to the blood center and reports back in real-time those unit IDs that match the search criteria. If the search criteria are not met, the query can be performed with additional units, the antigen-negative criteria can be relaxed, or the order can be electronically 'pushed' to the blood center. Using the ISBT unit number, the blood establishment computer system identifies any red cell phenotype or genotype information linked to the donor. Pattern matching is used to determine if the genotype information satisfies the full request. Once the argument is completed for all units in the query, the search then lists the oldest units first until the number of units required is satisfied. Matched units are displaying to the operator.

Results: The facilities were located 4 to 210 miles away from the blood center. Hospital beds ranged from 25 to 585 with blood bank inventories holding at least 25 units or more. Search criteria ranged from 1 to 6 antigen-negative types among the common RH, MNS, Kell, Duffy, and Kidd antigens. Approximately 40% of blood donor units leaving the blood center have phenotypes or red cell genotypes that include the Rh, MNS, Kell, Duffy, and Kidd common antigens. For the 4 years ending 2017, 938 of 5,070 searches found 3,297 antigen-negative units among 28,939 units scanned. Successful searches correlated with the antigen-negative frequencies. Percent success/partial success rates by single antigen ranged from 76% to 31% (E>K>C>Jk[b]>Fy[a]>Jk[a]>S>N>M>Fy[b]). The success/partial success rates for R1 or R0 with up to 3 additional antigen-negative attributes was 31% and 42%, respectively.

Summary/Conclusions: Cloud-based access to an historical phenotype and red cell genotype information at the blood center provides valuable information that significantly reduces end-user confirmatory phenotyping. The process provides real-time data on units in hospital inventories while limiting shipping delays of blood from the blood provider.

Donor Safety

4D-S28-01

DONOR HEALTH: IMPROVING THE SAFETY AND EFFICIENCY OF BLOOD DONATION

E Di Angelantonio

Public Health and Primary Care, University of Cambridge, Cambridge, United Kingdom

Every year in Europe there are approximately 12 million blood donors donating about 20 million units of blood, and this product is transfused in more than 10% of all hospital stays that include a procedure. Over the past 20 years, efforts in blood transfusion have mainly focused on improving viral safety and on establishing a better use of blood products for patient benefits. Although these efforts must be maintained, there is also a need to develop plans to ensure that the blood supply is adequate and to maintain donor health and well-being.

Using randomised trials and other robust methodology, we have assessed 2 key questions: (1) How can the time interval between blood donations be more personalised? (2) Can the risk of anaemia and iron deficiency be reduced by optimizing approaches to haemoglobin testing to allow donation?

To address the first question, I will describe results from the ~50,000-donor INTERVAL trial, an open randomised pragmatic trial to determine whether blood can be safely and acceptably collected from donors more frequently than present practice in England and at similar intervals to current custom in some other countries. Donors aged >17 years with internet access, including equal numbers of men and women were recruited at routine donor sessions in the 25 static donation centres between June 2012 and June 2014. Men have been randomly assigned to standard 12-wk vs 10-wk vs 8-wk inter-donation intervals and women have been assigned to standard 16-wk vs 14-wk vs 12-wk inter-donation intervals. The primary endpoint is the number of blood donations made. A key secondary endpoint is donor quality of life (assessed by the Short Form-36).

To address the second question, I will describe results from the ~30,000-donor COMPARE study, a within-person comparison of 5 different approaches to measure haemoglobin levels in blood donors. Haemoglobin levels were measured using a gravimetric finger-prick copper sulphate test, a post-donation strategy whereby haemoglobin levels at the previous donation are used to predict likely haemoglobin levels at the current donation, a HemoCue® test of capillary blood, two non-invasive spectrometry strategies, as well as a venous sample analysed by a "gold standard" automated cell counter. The primary outcome is a combination of sensitivity and specificity of each testing strategy in detecting haemoglobin levels beneath the minimum thresholds.

Findings from these studies will provide evidence to develop a more personalised approach to blood donation to improve donor safety and minimising the risk of iron deficiency.

4D-S28-02

GENERALIZED ALLERGIC REACTIONS IN BLOOD DONORS

M Townsend, H Kamel and M Bravo

Corporate Medical Affairs, Blood Systems, Scottsdale, United States

Background: Allergic reactions in donors are well recognized and described in hemovigilance systems. Local allergic reactions include rash and itching at the site of skin disinfection or application of adhesive bandage. Generalized allergic reactions (GARs) may be expressed as more widespread rash, hives and itching, swelling of the face, neck or throat, wheezing or in extreme cases anaphylaxis. Severe allergic reactions have been associated with ethylene oxide sterilization of apheresis kits and hydroxyethyl starch use in granulocyte collections. Because of the rarity of such reactions, few rates have been published. Daurat reported a rate of 2.3 GARs per 100,000 systemic allergic events among apheresis platelet collections and none in WB collections (Transfusion 2016).

Aims: To determine the rates of GARs in our system.

Methods: We analyzed allogeneic apheresis and WB needle-in collections between 1/1/2015 to 12/31/2017. GARs were identified based on signs and symptoms of having "generalized rash/hives/ itching" reported by staff and/or Medical Director classification of "allergic, systemic" consistent with AABB/IHN/ISBT definitions. Record review was performed on each case to assess appropriateness of classification based on recorded observations, signs and management by staff, outside medical care or donor deferral due to the adverse event. Other donation information including type of apheresis collection and device used were reported. Rates of GARs were calculated per 100,000 needle-in WB and apheresis collections (AC) overall and stratified based on procedure type (2RBC vs. non-2RBC collections (including Plasma, Platelet and other multi-component procedures).

Results: Twelve GARs among 673,988 needle-in AC for a rate of 1.8 per 100,000 and none among 1,747,269 WB collections were identified during the 36-month analysis period. Seven of the events were associated with 2RBC collections (n = 339,303) for a rate of 2.1 per 100,000. Five of 268,639 (1.9 per 100,000) were associated with platelet or platelet combination apheresis collections. There were no systemic events associated with plasma or plasma combination apheresis collections (n = 66,046) or with WB collections (n = 1,747,269). Of the 12 events, 6 donors were deferred from further AC. Two events required outside medical care with 1 case reporting use of epi-pen, 5 required anti-histamines and 6 cases resolved spontaneously. Severity of symptoms ranged from hives over body and extremities (8), swollen lip (2), throat tightness (1), and trouble swallowing/throat tightness/chest tightness (1).

Summary/Conclusions: While GARs are rare, concerns for safety may dictate that donors suffering such reactions may need to be deferred from future automated donations. Rates for systemic allergic reactions in our system were not significantly

different for separator manufacturer or for type of collection (2RBC vs. platelet combinations). Rates in our system are comparable to those reported by Daurat, however, those data included only apheresis platelet collections and did not include apheresis 2RBC collections. Rates of rare reactions are subject to limitations from small numbers of events.

4D-S28-03

PREDICTIVE VALUE OF FERRITIN AND ZINC PROTOPORPHYRIN FOR SUBSEQUENT LOW–HAEMOGLOBIN DEFERRAL

S Zalpuri[1], T Timmer[1], W de Kort[1], M Heymans[2] and K van den Hurk[1]

[1]Donor Studies, Sanquin [2]Epidemiology, VUMC, Amsterdam, Netherlands

Background: Whole blood donation involves the risk of body iron store depletion through the loss of haemoglobin (Hb). Hb levels though, do not accurately reflect a donor's true iron status. Alternative markers for body iron stores, like zinc protoporphyrin (ZPP) and Ferritin present as opportunities to supplement or replace Hb as a measure for loss of iron with every donation. The World Health Organisation (WHO) has already advised monitoring ferritin levels in donors. A combination of Hb, ZPP and/or Ferritin as predictive markers for potential donor deferral could be advantageous in terms of donor health and efficient in terms of blood banking practices.

Aims: We aimed to estimate and compare the predictive value of ferritin, ZPP and Hb individually, and in combination with each other for low-Hb deferral at the subsequent donation.

Methods: The study population consisted of repeat donors from Donor InSight-III (DIS-III). DIS-III is an observational cohort study among repeat donors, aimed at gaining insight into genetic determinants of Hb level and donation-related iron deficiency. We selected a subset of donors who had made at least one follow up donation attempt after participation in the study, were whole blood donors and were below the age of 70. We constructed logistic regression prediction models using the predictors Hb, ZZP and Ferritin as primary predictors of interest; and deferral at previous donation, age, BMI, donation history prior to the study period and the season of donation as additional predictors of interest. Low-Hb deferral at the next donation was used as the outcome. All analyses were stratified for sex. Wald statistic, Nagelkerke R^2 and Area under the curve (AUC) were presented for the prediction models. The prediction models were internally validated.

Results: A total of 608 male and 605 female donors were included from the DIS-III study population. Mean ferritin levels were 51.2 µg/L and 37.8 µg/L; mean ZPP levels were 61.3 µmol/mol and 67.9 µmol/mol in males and females respectively. An odds ratio (OR) of 1.02 (95% confidence interval (CI) 1.01–1.03) for ZPP was observed for both men and women. An OR of 0.95 (95% CI 0.93–0.97) and 0.97 (95% CI 0.94–0.99) for ferritin was observed for men and women respectively. The internally validated area under the curve, AUC for ZPP (men-0.61, women-0.66), ferritin (men-0.70, women-0.73) and Hb (men-0.76, women-0.79) were estimated. Next, with a backward selection procedure, ZPP was deemed as not a significant predictor and a final model was built with significant secondary predictors previous donation history and age. The AUC of this final model (Hb, Ferritin, previous donation history and age) improved to 0.80 for men and 0.81 for women.

Summary/Conclusions: Hb and ferritin demonstrated a higher predictive value for a subsequent low Hb deferral than ZPP, and adding previous donation history and age as predictors improved the predictive value of the model. Additional outcomes like subsequent Hb levels should also be considered to evaluate the value of ferritin and ZPP as potentially practical predictors in daily blood bank setting.

4D-S28-04

PROMOTING DONOR HEALTH AND STABLE COLLECTIONS: A PILOT FERRITIN TESTING PROGRAM IN MALE PLATELETPHERESIS DONORS

BR Spencer[1], J Haynes[1], E Notari[1], G Foster[1], G Holley[2], B Deisting[2], C Winton[2], D Krysztof[2], W Steele[1] and S Stramer[2]

[1]Scientific Affairs, American Red Cross, Rockville [2]Scientific Affairs, American Red Cross, Gaithersburg, United States

Background: Most single donor platelet (SDP) donors transition to plateletpheresis donation after a history of whole blood (WB) or double red cell apheresis donations (DRC). Recruitment often follows identification of a high platelet count, a marker associated with iron depletion (ID). With an allowable donation frequency of 24 per

year and estimated red cell loss up to 54 ml per donation, SDP donors may be at risk for ID. Unrecognized ID could adversely impact donor well-being. If uncorrected, ID could lead to donor loss through increased deferrals following a higher minimum hemoglobin for male donors required by the US FDA (Final Rule) and ultimately impact the SDP supply.

Aims: To evaluate impact on donations and return behavior under a pilot ferritin testing program providing donors low ferritin test results.

Methods: Test and Control subjects were male SDP donors between May 2015-May 2017, with no WB or DRC donations, and considered at risk for ID based on finger-stick hemoglobin <13.5 g/dL. Starting March 2016, Test subjects were mailed a letter reporting low ferritin results (≤26 ng/ml) and recommending iron supplementation ("LF letter"). Annualized rates of donation and low hemoglobin deferral were summarized before and after receipt of the LF letter in Test subjects. Comparable "pre-"and "post-" intervention estimates were developed for Control SDP donors before and after Final Rule implementation (May 2016). Differences in means between Test and Control groups were tested using Analysis of Variance (ANOVA). Approximately 2/3 of LF letters to Test subjects were sent after Final Rule implementation. Eligibility for both groups required 2 SDP procedures minimum during their respective pre-intervention period. An electronic survey to the Test donors inquired about iron supplementation practices.

Results: Test (N = 1272) and Control (N = 878) donors had SDP donation rates prior to the evaluated intervention of 13.9 vs 12.3 annually, respectively [F (1,2148) = 44.75, P < 0.0001]. After receipt of the LF letter, annualized donation rates in Test donors declined by 19.3%. The decline in donation rates was much sharper in Controls, falling by 48.6%. Failure to return was 8.9% for Test subjects after receiving the LF letter and 23.4% for Controls following Final Rule implementation (chi-square = 86.2, 1df, P < 0.0001). The proportion of visits resulting in low hemoglobin deferral increased from 2.0 to 3.2% in Test donors and from 3.7 to 5.6% in Control donors. Only 20% of Test donors reported taking supplemental iron when they received the LF letter; 65% of those not taking iron reported initiation of iron supplementation following the letter.

Summary/Conclusions: These data suggest that many donors were responsive to notification of low ferritin and attendant messaging on iron supplementation. Test subjects, who also were subject to the Final Rule's higher hemoglobin requirements, experienced a decline in donation rates less than half as large as Control donors. Failure to return was more than twice as high in Controls. Ferritin testing potentially benefits donor health and a stable blood supply. Further analyses are needed to assess the impacts to donor behavior after implementing a ferritin testing program.

4D-S28-05

PLASMA SUPPLY MANAGEMENT: SAFE AND SUSTAINABLE PLASMAPHERESIS

R Norda[1], J Castren[2], G Follea[3], G Marano[4], G Rautmann[5], J Epstein[6] and J Pink[7]

[1]Clinical Immunology and Transfusion Medicine, Uppsala University Hospital, Uppsala, Sweden [2]Finnish Red Cross Blood Services, Helsinki, Finland [3]French Blood Transfusion Society, Paris, France [4]Italian National Blood Centre, Rome, Italy [5]European Directorate for the Quality of Medicines &Health Care, Strasbourg, France [6]Food and Drug Administration, Silver Spring, MD, United States [7]Australian Red Cross Blood Services, Kelvin Grove QLD, Australia

Background: The European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS) of the Council of Europe (CoE) appointed a working group (WG) to address plasma supply management (PSM). The WG PSM was tasked to gather data to support a revision of the "Guide to the preparation, use and quality assurance of blood components" (the CoE "Guide," currently in its 19th ed https://register.edqm.eu/freepub). Previous surveys and literature reviews indicated wide practice variations and a paucity of supportive evidence.

Aims: To define the range of current practices and obtain operational and donor safety data, the WG PSM conducted a survey of blood establishments (BEs) performing plasmapheresis to collect plasma for fractionation (PfF).

Methods: The survey covered eligibility criteria and medical assessment of donors, collection volume and frequency, blood tests, management of red cell loss, donor panel demographics, capture and recording of adverse events, equipment used, staff qualification and supervision, site requirements, productivity measures, and key performance indicators used. After a limited pilot to field-test utility of the questionnaire, the survey took place from September to December 2017. The survey was submitted to BEs via representatives of the Member States (MS) and observers to the CD-P-TS, and by relevant professional networks.

Results: A preliminary analysis of the survey data focused on comparison of plasmapheresis practices with the recommendations in the CoE Guide. There were 36

responses from 25 countries including 24 responders from 16 countries who reported collection of PfF by plasmapheresis (17 responses from 9 CoE MS, and 7 responses from 7 countries outside CoE). 21 respondents reported a total of 2,869,419, plasmapheresis collections during the last fiscal year. The Guide allows 25L annual collection volume excluding anticoagulants: 10 reporters are more stringent, 7 allow larger volumes and 7 are aligned. The Guide allows 33 plasmapheresis procedures per year: 14 reporters are more stringent, 7 allow a larger number and 2 are aligned. The mean number of annual donations per donor was <5 in 7/11 respondents with more stringent number of procedures. Among the 7 respondents that allow more than 33 procedures per year, all had a mean number per donor >5 and 3 had a number more than 10. The Guide allows maximum collection of 750 ml excluding anticoagulant: 7 reporters are more stringent, 9 allow a larger volume depending on donor size and 7 are aligned. Overall adverse event rates per 10,000 collections reported by 14 respondents ranged widely with 7 reporting less than and 7 >100/10,000.

Summary/Conclusions: Collection of PfF by plasmapheresis is common among MS of the CoE, contributing to the supply of PfF, but practices vary widely and are not always aligned with recommendations in the Guide. Further analysis of the survey data should yield correlation between collection practices and outcomes relevant both to donor safety and plasma availability. Incorporation of evidence-based recommendations for plasmapheresis in the Guide is anticipated to advance progress toward a more robust supply of PfF while safeguarding donor health.

Accreditation, Standards and Good Practice – Improving Transfusion Services

4D-S29-01

THE CHALLENGES OF IMPLEMENTING THE EUROPEAN GOOD PRACTICE GUIDELINES FOR BLOOD COMPONENTS IN THE BLOOD ESTABLISHMENTS OF SLOVENIA

P Mali

Blood Transfusion Centre of Slovenia

4D-S29-02

THE AFRICA SOCIETY FOR BLOOD TRANSFUSION STEP-WISE ACCREDITATION PROGRAMME: ORGANIZATION, ACHIEVEMENTS AND CHALLENGES

C Tayou[1], M Farouk[2], L Bust[3] and D Mvere[4]

[1]Africa Society for Blood Transfusion, Yaoundé, Cameroon [2]Africa Society for Blood Transfusion, Cairo, Egypt [3]Africa Society for Blood Transfusion, Cap town, South Africa [4]Africa Society for Blood Transfusion, Hararé, Zimbabwe

Background: Despite improvement of blood safety indicators in the 54 African countries, the latest WHO survey reports that the cumulative transfusion transmitted infection median seroprevalence is 7.3% and reaches up to 37.3% in some areas. Transfusion adverse events are found in up to 21% of patients. Most of African blood services are still running their daily activities without any quality management systems in place (WHO, 2017). Africa Society for Blood Transfusion (AfSBT) is a professional body created in 1997 with a mission advocating for the highest ethical and professional standards and skills in blood transfusion across the African continent, enabling safe, universally accessible and sustainable national blood programmes in participating countries. Its strategic objectives include developing and supporting the implementation of the AfSBT Step-wise Accreditation Programme that endorses operating standards of the highest quality for the practice of blood transfusion and takes cognizance of the disparate states of development of blood services in Africa.

The AfSBT Step-Wise Accreditation Programme: the programme was established in 2009 to provide blood services at virtually any stage of blood safety development with a step by step accreditation/certification mechanism that is different to the common "all or none" approach. Step 1 Certification is provided to a facility that meets minimum (basic) quality and operational requirements; Step 2 Certification is a recognition for meeting intermediate quality and operational requirements and Step 3 corresponds to full accreditation when quality and operational requirements at international

standard are met. The programme is based on locally relevant Standards prepared and reviewed biannually by a sub-group of experts in the field established by the Africa Society for Blood Transfusion (AfSBT) in collaboration with AABB.

Outcome: Since 2014, a total of 23 blood services in 20 countries were enrolled in the process of certification and accreditation among which 8 were from French-speaking and 12 from English-speaking countries. AfSBT assessors conducted 26 assessments among which 19 baseline (initial), 3 progress and 4 formal assessments led by AABB assessors. Two countries have been accredited (Step 3) and 3 facilities got certified at Step 2.

Challenges: Despite a rising interest in the AfSBT Step-wise accreditation program, AfSBT is facing limited funding to run the program as external funding and support is running out. Quality culture, quality systems and staff capacity building of are still to be reinforced in African blood services prior to formal assessments. Continuous improvements in blood transfusion field, dictate regular revision of the Standards so that they match new technology, international regulations, and emerging blood transfusion associated risks.

Adverse Reactions – Immunological Crosstalk

4D-S30-01

ITP, FROM PATHOPHYSIOLOGY TO TREATMENT

M Michel

No abstract available

4D-S30-02

A POTENTIAL ROLE IN PLATELET DESTRUCTION IN AUTOIMMUNE THROMBOCYTOPENIA: ANTIBODY MEDIATED GLYCAN MODIFICATION ON PLATELETS AND MEGAKARYOCYTES

T Bakchoul[1], I Marini[2], R Jouni[3], F Rigoni[3], K Sevke-Masour[3] and U Sachs[4]

[1]Center for Clinical Transfusion Medicine [2]University of Tübingen [3]Otfried-Müller Straße 4/1, Center for Clinical Transfusion Medicine, Tübingen [4]University of Giessen, Giessen, Germany

Background: Immune thrombocytopenia (ITP) is a bleeding disease caused by autoantibodies (AAbs) directed against platelet (PLT) glycoproteins. Recently, an Fc-independent platelet clearance via Ashwell-Morell receptors, which recognize glycan changes on platelet surface, has been proposed as a new mechanism of ITP in mice.

Aims: In this study, we investigated the impact of AAbs from ITP patients on glycan pattern of megakaryocytes (MKs) and platelet and analyzed the subsequent effect on their survival in vivo.

Methods: MKs were differentiated from hematopoietic stem cells after cultivation with thrombopoietin. MKs and PLTs were incubated with ITP-sera and the modification in glycan pattern was assessed by flow cytometry using two lectins: Ricinus communis agglutinin (RCA) and Erythrina cristagalli lectin (ECL). The impact of glycan pattern modification on survival of human platelets was analyzed using a NOD/SCID mouse model.

Results: After incubation with ITP-sera a different patterns of glycan modification were observed on platelet surface: 9/37 sera induced high ECL binding, while 8/37 sera showed decrease in RCA binding. Interestingly, a subgroup of ITP-sera was able to change glycan pattern on MKs surface (3 fold increase in RCA-binding compared to control). The injection of AAbs accelerated clearance of human PLTs from the circulation in vivo. The destruction of human PLTs by ITP-AAbs was largely reduced by a neuraminidase inhibitor that prevents glycan changes on PLT surface (PLT survival after 5 h: 60% vs 40%).

Summary / Conclusions: Our results indicate that AAbs from ITP patients are able to induce changes in glycan patterns on both MKs and PLTs surfaces. The mechanism of antibody-mediated modification of glycan patterns seems to contribute to platelets destruction as well as to interfere with PLTs production from MKs.

4D-S30-03

HOW DO ANTI-ERYTHROCYTE ANTIBODIES AMELIORATE IMMUNE THROMBOCYTOPENIA – EXAMINATION OF ANEMIA, PHAGOCYTOSIS AND INFLAMMATORY ACTIVITY IN A MURINE MODEL

R Khan[1,2] and A Lazarus[1,2,3,4]

[1]Laboratory Medicine and Pathobiology, University of Toronto [2]Laboratory Medicine, St. Michael's Hospital [3]Medicine, Division of Hematology, University of Toronto [4]Canadian Blood Services, Toronto, Canada

Background: Immune thrombocytopenia (ITP) is an autoimmune disorder that causes thrombocytopenia (decreased platelet levels) primarily due to the presence of antiplatelet antibodies. Anti-D therapy (treatment with an antibody against Rhesus-D factor on RBCs) has been proven to ameliorate ITP but it comes with limitations - as a human-derived product, it is limited in quantity and will always carry a theoretical risk of transferring emerging pathogens. These limitations can be essentially eliminated if anti-D was to be replaced by a recombinant antibody but in order to achieve that, it is important to first elucidate the mechanism of action through which anti-D ameliorates ITP. TER119, an antibody against glycophorin A associated protein (present on RBCs), is used widely to model the anti-D effect in mice. Past work with TER119 has shown that it is able to ameliorate ITP successfully in vivo and inhibit platelet phagocytosis in vitro; however it is also associated with anemia and we have observed that it can also decrease body temperature in some mice, an indication of undesirable inflammatory activity.

Aims: To determine whether these effects are required for the amelioration of ITP and to potentially help determine the characteristics of therapeutic RBC antibodies, another anti-RBC antibody was tested.

Methods: M1/69 (anti-murine CD24) was tested for therapeutic efficacy and potential side effects in a murine model of ITP as well as tested for its ability to induce in vitro phagocytosis.

Results: We demonstrate here that M1/69 increases platelet counts in passive ITP consistently across various mouse strains but does not always induce anemia or lead to a decrease in the body temperature. Similar to TER-119 and other therapeutic RBC antibodies in a murine model of ITP, M1/69 induced phagocytosis of RBCs and when bound to RBCS, inhibited opsonized-platelet phagocytosis by RAW264.7 macrophages.

Summary / Conclusions: It may be possible to use the inhibition of platelet phagocytosis in vitro as a predictor to determine the ability of an anti-RBC antibody to ameliorate ITP in vivo, and that anemia and inflammatory activity may not be required for ITP amelioration by anti-RBC antibodies. Further characterization of RBC antibodies is required to solidify the current conclusion as well as elucidate their mechanism of action in ITP.

4D-S30-04

CANDIDA ALBICANS DECREASES AUTOPHAGY OF HUMAN PLATELETS

Q Chen[1], Z Duan[2] and M Li[2]

[1]Transfusion Research Department, Jiangsu Province Blood Center [2]Department of Medical Mycology, Institute of Dermatology, Chinese Academy of Medical Science & Peking Union Medical College, Nanjing, China

Background: It is becoming increasingly clear that platelets play roles in initiating and modulating inflammatory and immune responses against infection. Autophagy is not only a process that maintains cellular homeostasis and metabolism, but also a key regulator of immunity. It has been demonstrated that canonical autophagy could constitutively present in resting platelets and be induced upon platelet activation.

Aims: To clarify whether *Candida albicans* could influence autophagy in human platelets and to determine the underlying mechanisms.

Methods: Human platelets were challenged with heat-killed *C. albicans* in the presence or absence of chloroquine (CQ) in vitro for 8 h. Western blotting was used to analyze LC3-II accumulation and p62 protein level. β-Actin served as the loading control. Calcofluor white (CFW) is a useful tool for analyzing the localization of *C. albicans*. So CFW was used to stain *C. albicans* and to make it exhibited fluoresce when exposed to ultraviolet light. Antibody against p62 was used to detect the expression and distribution of p62. Images were collected with an OLYMPUSFV1000 laser scanning confocal microscope.

Results: We found that the level of LC3-II accumulation was increased in platelets after treatment with lysosomal inhibitors CQ for 8 h, indicating the basal autophagy level. The LC3-II accumulation was decreased in platelets challenged with heat-killed *C. albicans* in the presence of CQ for 8 h compared to cells incubated with CQ alone.

p62 is a receptor for cargo destined to be degraded by autophagy. The p62 is able to bind ubiquitin and LC3, and is used to target autophagosomes and clear ubiquitinated proteins. We found that the level of p62 was significantly increased after the treatment with *C. albicans* in the presence or absence of CQ. The immunofluorescence assay also proved these findings, with the fluorescence of p62 was enhanced and wrapped around *C. albicans*.

Summary / Conclusions: Our data suggest that *C. albicans* may inhibit autophagy flux in platelets. The underlying mechanisms of *C. albicans* influence autophagy in platelets and the role of ubiquitin-binding autophagic adaptor p62 in protects against *C. albicans* infection needs to be further studied.

4D-S30-05

ERYTHROCYTE ANTIGEN LOSS DEFINES ANTIBODY-MEDIATED IMMUNE SUPPRESSION: STUDIES WITH WILD-TYPE AND IGG FC REGION DEGLYCOSYLATED ANTIBODIES IN MICE

Y Cruz-Leal[1,2], D Marjoram[2] and A Lazarus[1,2,3]

[1]Canadian Blood Services, Ottawa [2]St Michael's Hospital [3]University of Toronto, Toronto, Canada

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, epitope masking and immunological deviation. Recently, antigen (Ag) loss (also known as Ag modulation) has been proposed as a potential mechanism of AMIS in a KEL immunoprophylaxis model; where Fcγ receptors and/or complement were required. On the other hand, we recently demonstrated in a model system that immunoglobulin G Fc glycans are not essential for AMIS and the presence of Fc glycans is considered important in Fcγ receptor and complement function. However, the relevance of Ag-loss as a predictor of AMIS effect and the impact of antibody glycosylation in this process have not been assessed.

Aims: The aims of the present work is to study the ability of wild type and deglycosylated antibodies specific to different portions of an experimental Ag to induce i) AMIS activity, ii) RBC clearance and iii) Ag modulation and to determine if a relation exists between AMIS activity and one of these mechanisms.

Methods: Transgenic HOD mice possess erythrocytes 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 24 h selected HEL-, OVA- or Duffy-specific antibodies were administered. Mice were bled at 2, 24, and 48 h and the percentage of HOD-RBC in circulation and HOD-Ag levels on the surviving RBC assessed by flow cytometry. HEL-specific IgM and IgG antibody responses were measured by ELISA after HOD-RBC transfusion.

Results: Antibodies specific for different portions of the HOD-Ag induced AMIS independent of their ability to clear RBC. Strikingly however, all HOD-specific antibodies able to fully inhibit the HEL-specific IgM response induced a significant early Ag-loss. A deglycosylated variant of the Duffy-specific monoclonal antibody (CBC-512) was able to induce AMIS and loss of the Ag, even though was unable to promote RBC clearance. Comparing HEL-specific antibody responses with RBC clearance and Ag-loss demonstrated that AMIS induced by HOD-specific antibodies correlated with their ability to cause Ag-loss but do not with erythrocyte clearance.

Summary / Conclusions: Ag loss was highly related to AMIS induction while RBC clearance was a dispensable requirement for AMIS. These findings demonstrate that Ag-loss is a good predictor of AMIS activity in the HOD model.

Working Party Session on Rare Donors/Terminology/Immunohaematology

4D-S31-02

NAME THAT SPECIFICITY: INVESTIGATING AND IDENTIFYING COMPLEX AND EXOTIC RH VARIANTS

T Peyrard[1,2,3]

[1]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine [2]UMR_S1134 Inserm Université Paris Diderot [3]Laboratoire d'Excellence GR-Ex, Paris, France

Rh is a blood group system of high clinical relevance as most alloantibodies are known to be involved in hemolytic transfusion reactions and HDFN. Rh is one of two most complex systems with MNS. The first reason for this complexity lies in the fact that Rh is encoded by two genes, RHD and RHCE. The second reason is an atypical tail-to-tail orientation of those genes, which facilitates material exchange during meiosis. The major molecular background at the origin of the Rh complexity is the gene conversion mechanism. However, many other molecular events, such as deletions, insertions, splice variants or point mutations were also reported to give rise to a large number of RHD and RHCE variants. All of those gene alterations may result in the loss or weak expression of one or several existing epitopes and/or the production of new epitopes. Of note, some rare Rh variants may originate from the alteration of another gene, RHAG, such as Rh_{null} of the regulator type and Rh_{mod}.

The two paralogous RHD and RHCE genes (10 exons) encode RhD and RhCE proteins, respectively. Rh currently comprises 55 antigens, with 14 high- and 27 low-prevalence antigens. Among those 55 antigens, 41 (75%) are encoded by RHCE, 6 (11%) by RHD and 8 (14%) by both genes (e.g. the G antigen).

The complexity of the D antigen lies in the great number of phenotypic variants (weak D and partial D phenotypes) and an even greater number of allelic variants. As of today, 149 weak D (DEL excluded) and 126 partial D phenotypes are reported. D-negative blood is required in partial D, which is usually not a problem, but it can be a challenge if the patient is c- and/or e-.

The complexity of the RhCE protein is much more challenging in transfusion medicine, because many variants correspond to rare blood types. As of today, 155 RHCE alleles have been reported. The most clinically significant RHCE alleles are mainly encountered in people of African descent: RHCE*ceAR, RHCE*ceEK, RHCE*ceBI and RHCE*ceSM that code for the rare Hr^S- type (RH:-18); RHCE*ce^S (also called RHCE*-ce48C,733G, 1006T) that codes for the rare Hr^B- type (RH:-34); RHCE*Ce-D(4)-Ce, included in the R^N haplotype, encoding the rare Sec– type (RH:-46); RHCE*ceJAL encoding the rare RH:-57 type; RHCE*ceCF encoding the rare RH:-58 type; RHCE*-ceAG encoding the rare RH:-59 type; RHCE*ceMO encoding the rare RH:-61 type, and RHCE*ceTI encoding partial c and partial e (with no reported lacking high-frequency antigen as of today).

Another degree of complexity is due to the fact that all of those previous rare RHCE variants code for partial e (and most, if not all, for partial c) but the alloanti-e (and alloanti-c) potentially developed are usually not mutually compatible. The anti-e made by RHCE*ceAR, RHCE*ceEK, RHCE*ceBI or RHCE*ceSM is called anti-hr^S (anti-RH19) and anti-e made by RHCE*ce^S is called anti-hr^B (anti-RH31). Unfortunately, all alloanti-e for the other RHCE variants have no specific names and are called "anti-e-like", which is confusing. In addition, all anti-Hr^S are not mutually compatible depending on the encoding allele (as is also the case for anti-hr^S), which makes things even more complex.

Another complexity in the Rh system resides in pseudo-reactivity. Indeed, some RHCE variants may express D epitopes (e.g. RHCE*ceCF, RHCE*ceHAR) and conversely (e.g. expression of C in DIVa and by the RHD*DIIIa-CE(4-7)-D hybrid allele). As a result, each time an unexplained Rh reactivity occurs with no molecular alteration observed when sequencing the corresponding gene, the second gene of the haplotype needs to be investigated.

4D-S31-03

MAKING IT ALL HAPPEN FOR PATIENTS WITH RARE BLOOD

V Yahalom[1,2]

[1]Transfusion & Apheresis, Rabin Medical Center, Petah Tikva [2]National Blood Group Reference Laboratory, Magen David Adom - National Blood Services, Ramat Gan, Israel

Red Blood Cell (RBC) transfusion is one of the most common medical procedures performed amongst hospitalized patients in developed countries. A rare blood type is defined by the ISBT working party (WP) as the absence of a high frequency (HF) antigen or multiple common blood group antigens found in less than 1:1000 individuals. Nevertheless, certain blood types are extremely rare around the globe (Rh Null, D–, Ko, K:-22, U negative), while others differ in their prevalence amongst diverse populations [pp, Jr(a-),Vel negative, Yt(a+)]. Rare blood types are usually discovered when serum reacting with all screen and panel reagent cells in the presence of a negative auto control is encountered. Patients with rare blood types and an antibody to a HF antigen or a rare combination of multiple common antibodies who require blood for elective procedures and especially for emergency situations, pose a significant challenge to all those involved in their care and in the identification and provision of rare blood units. A rare blood type, especially in the presence of an antibody should be confirmed by reference laboratories which have experienced technologists, unique resources (rare RBC's, anti- sera and fluids) and technologies (enzyme treated cells, inhibition tests, molecular testing and others) and knowledge of the rare blood types and their clinical significance amongst local ethnic groups. Following, identification of a HF antibody or a rare combination of common antibodies, communication with the clinical team is essential to verify the necessity of transfusion and the time in which RBC's provision is required. Rare RBC's units can be provided by supplying liquid RBC units which may be available in the Blood Center, thawing units from a local/national frozen inventory, calling known rare blood donors to donate, screening the index case family or another targeted population. If rare blood is unavailable locally or nationally, a clinical decision should be made as to the best available therapeutic option until compatible blood can be attained nationally or internationally through contact with the International Rare Donor Panel – IRDP (ibgrl.blood.co.uk/services/international-rare-donor-panel) and/or by direct contact with members of the ISBT working party for rare blood (www.isbtweb.org/working-parties/rare-donors). Despite different donor criteria, testing requirements, language barriers, working hours and holidays, the mutual goal of supplying rare blood to patients in need results in a coordinated chain of efforts and communication locally and/or internationally which enable timely provision of rare RBC's around the globe.

4D-S31-04

CATALOGING BLOOD GROUP VARIATION WITH THE HELP OF NEW TOOLS

ML Olsson

No abstract available

Working Party Session on Cellular Therapies

4D-S32-01

THE CURRENT STATUS OF HUMAN PLATELET LYSATES: PRODUCTION AND MANUFACTURE

T Burnouf

Taipei Medical University, Taipei City, Taiwan, Republic of China

Scientific evidence demonstrates that human platelet lysate (HPL) can substitute for fetal bovine serum (FBS) in the cell therapy field as a valuable, clinically compliant, supplement of growth media for the in vitro propagation of human cells, such as mesenchymal stromal cells (MSCs). HPL contains a plethora of growth factors released by platelets, as well as additional nutrients and cell-growth promoting agents originating from both plasma and platelets. The clinical advantages of HPL in this application encompass the avoidance of the risks of xeno-immunization and zoonotic infections associated with materials from animal origin such as FBS. In addition, scientific studies have identified that ex vivo expansion of MSCs from different tissue sources may actually be more

efficient in a medium supplemented with 5–15% (v/v) HPL than with 10–20% FBS: the cell proliferation is stronger, the cell population doubling time is shorter, and the CFU-F size increased. In addition, the use of HPL maintains the clonogenicity, the immunophenotype, the in vitro trilineage differentiation capacity, and the in vitro T cell immunosuppressive properties of expanded MSCs. Thus, an increasing number of protocols for clinical-grade expansion of human cells is likely to rely on the use of HPL supplementation, especially as regulations recommend avoiding FBS. This implies a continuous, if not increasing need to define and implement production and manufacturing methods to ensure HPL quality, safety and consistency. Most HPL preparations are manufactured, by blood establishments or commercial suppliers, using "expired" platelet concentrates originally collected for transfusion purposes. When reaching the expiry date, the platelet concentrates devoted to HPL production are frozen and stored. The platelet concentrates are then subjected to several freeze and thaw cycles (e.g. 3 cycles at −80/+37°C) to induce platelet lysis and are pooled. The pool can be either directly clarified by centrifugation/filtration, or may undergo a serum-conversion treatment to clot and remove fibrinogen, prior to sterile filtration, dispensing, freezing, and storage. Main variables in HPL manufacturing methods include the collection procedure of the platelet concentrates (from whole blood or apheresis), the use of a platelet additive solutions (which implies a dilution in the plasma nutrients), the pool size (currently up to 16, or up to 40 to 50 donations may be pooled to improve standardization, depending upon jurisdictions), the implementation of a pathogen inactivation treatment (as performed by some blood establishments to enhance the safety platelet concentrates for transfusion), and the removal of fibrinogen (to avoid gelation of the growth medium during cell culture). The impact that process alternatives may have on cell propagation needs further understanding. Regardless of these variations, the manufacturing process should be done under conditions complying with GMP when/if the HPL is used for clinical-grade cell expansion for subsequent transplant to patients. Further developments in HPL manufacturing technologies are expected, aiming at improving product standardization and virus safety. In addition, international consensus and regulations on quality control and safety criteria of HPL preparations will be increasingly needed as their use in cell therapy, tissue engineering, and regenerative medicine is expanding.

4D-S32-02

CLINICAL INDICATIONS, EFFICACY, AND QUALITY CONTROL OF AUTOLOGOUS PLATELET RICH PLASMA (PRP)

CS Cohn[1] and M Koh[2]

[1]Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, United States
[2]ST George's University Hospitals NHS Foundation Trust, London, United Kingdom

Background: Autologous Platelet-rich plasma (aPRP) is a poorly regulated blood component often produced at the patient's bedside and used for indications such as chronic and acute orthopedic injuries, wound and incision-healing and rheumatologic diseases. Platelets contain growth factor and cytokines, which are thought to play a role in reducing inflammation and aid the healing process. Most aPRP is made using small bench-top centrifuges with cartridges that deliver uneven platelet enrichment. Thus, the consistency and quality of aPRP is questionable and lower yielding PRP may have decreased efficacy. Blood components are held to stringent standards regarding their safety, efficacy and content. Since PRP is an autologous product, no similar standards apply. The lack of standards, and highly heterogeneous nature of PRP make it difficult to develop evidence for its use, and guidelines for its isolation. Quality control (QC) measures imposed during processing could help clinicians to develop a consistent and efficacious approach.
Aims: To our knowledge, there are no published reports of QC protocols for PRP. We developed a survey to better understand PRP usage, and the QC measures taken by hospitals using PRP.
Methods: A survey was designed to assess aPRP manufacture, usage and quality control (QC) measures taken prior to its use. A survey was developed with input from content experts. The survey was sent to members of BEST and ISBT. Survey respondents were encouraged to forward the survey to colleagues, thus a true denominator is unknown. A total of 62 completed and partially completed surveys were received.
Results: Responses came from 13 countries, but most came from the United States. Of the respondents, 35% reported aPRP use in their hospital. aPRP was used predominantly for outpatients, though >40% of hospitals also used aPRP in the in-patient setting. In most hospitals, aPRP was used by 1–5 MDs; however, 3 hospitals had >10 MDs using aPRP. The aPRP was used for orthopedics, wound/incision repair, rheumatology and other indications. In the US the aPRP was manufactured outside of the blood bank, while outside the US aPRP was isolated by blood bank personnel. Nearly all the aPRP manufacturing was done with no quality control (QC) measures (97%); however, 3 respondents assessed the final product prior to release. These QC measures included a platelet count to measure the enrichment of the platelet fraction, culturing the product and infectious serology testing. In some cases, if the

aPRP failed QC it could still be used, pending an MD's approval. In the 3 hospitals conducting QC on the final aPRP, the testing was done by the blood bank.
Summary / Conclusions: PRP is used in hospitals throughout the world for a wide variety of indications. The blood bank is involved in its manufacture in some countries, but in the US aPRP is made outside of the blood bank. Quality control of aPRP production and the final product is not done in most hospitals. To improve the consistency and efficacy of PRP, more stringent QC measures need to be in place.

4D-S32-03

NOVEL NEW PLATELET DERIVED PRODUCTS: SCIENCE, REGULATION AND THE EVOLVING ROLE OF BLOOD BANKS

MB Koh

Cell Therapy Facility, Blood Services Group, Health Sciences Authority, Singapore, Singapore

The central role orchestrated by platelets in inflammation as well as the understanding that platelets are rich in growth factors and other cytokines have resulted in the manufacture of novel platelet derived products for eventual clinical therapeutics. These platelet derived products include human platelet lysates (HPL), most extensively used as ancillary materials for supporting mesenchymal stromal cell growth/proliferation in cell therapy and platelet rich plasma (PRP) widely used in orthopaedics, often via direct injection into joints. These products are currently often manufactured in blood banks evolving into new roles beyond the traditional production of standard blood components and increasingly adopting a more active role in supporting cellular therapy. The demand for these platelet based products has also resulted in large scale commercial manufacture by various companies as potential xeno-free alternatives to foetal bovine serum in cell culture. On the other hand, point of care devices have been developed to transform the field of PRP for clinical use from central production into ones made within individual clinics and centres with the inevitable issues of variability and consistency. The science of platelet physiology is now well understood but less so are the specific mechanisms of action when injected clinically, partly as there has been an initial lack of rigour in running robust clinical trials. In addition the significant variations in individualised production including selection of donor platelets (fresh vs frozen, pooled vs apheresed), production methodology and characterisation of the final product including potency have made interpretation of clinical efficacy difficult. Having said that, there is increasing evidence to suggest clinical effectiveness, although much of this remains anecdotal. As these are blood derived components, regulation has sometimes classed this together red cell and blood component transfusion. However, the more "experimental" nature of its use as well as its use in cell culture has opened new issues in these standard regulatory frameworks.

Immunobiology – Red Blood Cell Antigens

5A-S33-01

DISRUPTION OF A GATA-1 BINDING MOTIF 3.7 KB UPSTREAM OF THE XG/PBDX GENE ABOLISHES ERYTHROID XGA EXPRESSION AND ELUCIDATES THE LAST UNRESOLVED BLOOD GROUP SYSTEM

M Möller[1], Y Lee[1], K Vidovic[1], L Björkman[2], J Storry[1,2] and ML Olsson[1,2]
[1]Department of Laboratory Medicine, Lund University [2]Clinical Immunology and Transfusion Medicine, LabMedicine, Region Skåne, Lund, Sweden

Background: Anti-Xg^a was first described by Mann et al. (Lancet 1962). About 66% of men and ~90% of women express Xg^a on their erythrocytes. Due to its skewed gender distribution Xg became the first blood group system to be assigned to a specific chromosome, the X chromosome. The underlying gene, PBDX, now known as XG, was identified by Ellis et al. (Nat Genet 1994) but the molecular basis for the Xg^a antigen remains undefined. XG partly resides in the pseudo-autosomal region 1 (PAR1) on both sex chromosomes: the first three exons lie in PAR1, while the remaining seven exist only on the X chromosome. Thus, XG is disrupted on the Y chromosome and only produces a functional protein from the X chromosome.

Aims: Using an integrated bioinformatics approach, we aimed to establish the genetic basis underlying the Xg(a+) vs. Xg(a–) phenotypes. We hypothesized Xg^a expression to be transcriptionally regulated by a single SNP within the XG region, potentially disrupting an erythroid transcription factor binding site.

Methods: Calculated Xg^a allele frequencies in different populations were compiled from historical data. Comparisons were made with frequencies for multiple variants in the XG region as found in the 1000 Genomes Project. Expression quantitative trait loci (eQTLs) were analyzed in the GTEx portal (https://gtexportal.org). Transcription factor binding site analysis was made in JASPAR (http://jaspar.genereg.net). Blood samples from 120 blood donors anonymized other than for gender were phenotyped for Xg^a. Genomic DNA and mRNA were isolated, and genotyping for the candidate SNP and XG transcript quantification were performed by real-time PCR. Functionality of the detected SNP was ascertained by electrophoretic mobility shift assay (EMSA) and a luciferase reporter assay.

Results: Among 2,612 investigated variants in the XG region, rs311103G/C, located 3.7 kb upstream the transcription start site, was identified as the SNP with strongest correlation to the expected distribution. Furthermore, rs311103 was identified as the eQTL with the most significant impact on XG transcript levels in whole blood (P = 2.0 × 10^{-22}). JASPAR analysis identified a GATA-1 binding motif disrupted by rs311103C. These findings were corroborated by SNP genotyping: all female Xg(a–) samples (n = 8/59, 13.6%) were homozygous for rs311103C while all Xg(a+) samples regardless of gender carried at least one copy of the major allele (G). Of the male Xg (a–) samples identified (n = 15/60, 25.0%), all carried at least one C allele but in 7 of 15 samples (46.7%), this was accompanied by a G allele, presumably from the Y chromosome. As opposed to Xg(a+) individuals, Xg(a–) donors had low-to-undetectable mRNA levels, suggesting that disruption of the GATA-1 motif prevented transcription of XG. Strong binding of K562 nuclear extracts was observed by EMSA using a biotinylated oligonucleotide probe with rs311103G but not C. Addition of anti-GATA-1 resulted in a supershift. Finally, a luciferase reporter assay to determine if the GATA-1 motif is important for transcription showed a robust positive response with a vector containing rs311103G but only basal expression when substituted with rs311103C.

Summary / Conclusions: The Xg(a+) phenotype depends on an intact GATA-1 binding motif 3.7 kb upstream of the XG transcription start site. The Xg(a–) phenotype is due to impaired transcription, which in turn follows from disruption of the GATA-1 site at this locus. We have solved a longstanding conundrum by combining bioinformatics and molecular approaches. Genotyping to predict the Xg^a status of blood donors and transfusion recipients is now possible.

5A-S33-02

SEROLOGICAL AND MOLECULAR CHARACTERISATION OF A NOVEL HIGH FREQUENCY ANTIGEN IN THE YT BLOOD GROUP SYSTEM

V Karamatic Crew[1], R Laundy[1], P Walser[2], S Turnley[3], D Palmer[3], S Afzal[4], A Blackburn[4], R Mitha[5], T Trimble[5] and N Thornton[1]

[1]*International Blood Group Reference Laboratory* [2]*Clinical Biotechnology Centre, NHS Blood and Transplant, Bristol* [3]*Red Cell Immunohaematology, NHS Blood and Transplant, Liverpool* [4]*Transfusion Laboratory, Tameside General Hospital, Ashton-under-Lyne* [5]*Transfusion Laboratory, Manchester University Foundation Trust, Manchester, United Kingdom*

Background: The antigens of the Yt blood group system are located on the acetylcholinesterase (AChE) glycoprotein. AChE is a highly conserved enzyme crucial in cholinergic neurotransmission at synaptic junctions, whilst the erythroid isoform is a hydrophobic GPI-linked membrane enzyme with an unknown function. All isoforms are encoded by the single gene ACHE, located on 7q22.1. Since its discovery in 1956, the Yt system comprised two antithetical antigens Yta and Ytb, with a third antigen, YTEG, described in 2017.

Aims: To present serological and genetic evidence of two novel high frequency (HFA) Yt antigens, discovered during complex antibody investigations in two unrelated pregnant patients. In the first case, samples from a 29-year-old pregnant woman (S1) and her family were investigated. The patient had a history of transfusion and previous pregnancies and was known to have anti-Jka present in her plasma, together with an additional, unidentified antibody to a HFA. In the second case, a 26-year-old pregnant Sickle Cell Disease patient (S2) presented with a complex mixture of antibodies requiring extensive serological and molecular investigation to identify multiple antibodies, including one to a novel HFA in the Yt blood group system.

Methods: Serological investigations were performed by standard IAT (LISS tube and Bio-Rad gel) technique. Enzyme treated and chemically modified cells were utilised, including papain, trypsin, chymotrypsin, pronase and DTT treated cells. Plasma inhibition studies were completed with soluble recombinant Yt (srYt) protein. For S1, an eluate was prepared from Jk(a–) cells to isolate the antibody of interest. Genomic DNA from both patients and S1 family members was isolated from whole blood and the coding exons of the erythroid ACHE isoform were amplified by PCR and analysed by Sanger sequencing. The impact of the identified mutation on AChE structure was studied by molecular dynamics calculations.

Results: In S1, anti-Jka was confirmed to be present in the plasma, reacting by IAT with untreated and papain treated cells. S1 plasma reacted weak to moderate strength with all untreated Jk(a–) cells, except for autologous cells and cells from the patient's brother, which were negative. Reactivity with papain treated Jk(a–) cells was much weaker. Plasma inhibition studies using srYt showed complete inhibition with Jk(a–) cells, whereas Jk(a+) cells remained positive due to the anti-Jka. S1 cells were Yt(a + b–), YTEG+. Yt(a–) cells and YTEG– cells were positive with the patient's plasma and eluate, respectively. ACHE sequencing confirmed S1 to be YT*A/A. A novel homozygous mutation c.169G>A in exon 2 was revealed, encoding p.Gly57Arg change in AChE. Testing of family samples revealed the patient's mother and four siblings to be heterozygous YT*A/B. Both parents and two siblings were heterozygous for c.169G>A, whilst one sibling, the compatible brother, was homozygous for c.169G>A. Although a unit of red cells from the compatible brother was available at the time of delivery, no transfusions were required. The healthy newborn had a positive DAT, no clinical signs of HDFN, and only anti-Jka was detected in an eluate prepared from the newborn's cells. The baby was subsequently shown to be YT*A/A and heterozygous c.169G>A. In the second case, S2 plasma reacted with all "antigen matched" [C-, E-, Fy(a-b-), K-] cells by LISS IAT. Reactivity was variable, with some cells showing papain resistance and others showing weakened reactivity in papain tests. This serological picture indicated the possibility of at least two antibodies. A Yt-related antibody was suspected from results of enzyme studies and subsequently the antibody was successfully inhibited with soluble recombinant Yt protein. S2 cells were Yt(a+), YTEG+. Sequencing of ACHE confirmed S2 to be YT*A/A and identified a novel homozygous mutation c.101G>A in exon 2, encoding p.Arg34Gln change in AChE. Identification of the Yt-related antibody in S2 lead to larger scale inhibition studies with soluble recombinant Yt protein enabling the identification of underlying alloantibodies including anti-Fya and anti-Jsa. Despite elucidation of a novel Yt-related antibody in this complex mixture, at least one other antibody specificity remains unresolved. S1 and S2 were shown to be mutually incompatible. In both cases, molecular dynamics calculations suggested the amino acid changes to be located on a peripheral loop of AChE and although they may affect AChE conformation, they are unlikely to affect the enzymatic activity.

Summary/Conclusion: We present evidence for two new HFAs in the Yt blood group system, where lack of these antigens was a result of homozygous mutations c.169G>A (p.Gly57Arg) in S1, and c.101G>A (p.Arg34Gln) in S2. These cases also demonstrate the difficulties encountered when investigating complex antibody mixtures in multiply transfused patients and highlight the effectiveness of using soluble recombinant blood group proteins in these circumstances.

5A-S33-03

GBGT1 IS ALLELICALLY DIVERSE BUT DISPENSABLE IN HUMANS AND NATURALLY-OCCURRING ANTI-FORS1 SHOWS AN ABO-RESTRICTED PATTERN

A Hult[1,2], E McSherry[2], M Möller[2] and ML Olsson[1,2]

[1]*Department of Clinical Immunology and Transfusion Medicine, LabMedicine, Region Skåne* [2]*Department of Laboratory Medicine, Lund University, Lund, Sweden*

Background: The FORS histo-blood group system was described in 2013 and much remains to be investigated regarding its genetic and immunohematological characteristics, as well as its clinical importance. Whilst c.887G>A in the GBGT1 gene results in FORS1 glycosphingolipid expression on human erythrocytes, this phenotype is rare in the populations tested so far. Conversely, however, naturally-occurring anti-FORS1 in plasma appears common in FORS1-negative individuals.

Aims: The aim of this study was a) to characterize this new blood group system genetically, b) to select principally interesting allelic variants for further study, and c) to test for the presence of anti-FORS1 in plasma from donors of different ABO groups to gain further insight into this naturally-occurring antibody.

Methods: A recently reported database, Erythrogene (www.erythrogene.com), was utilized to probe genetic variation in GBGT1. We also screened 1,108 Swedish blood donors for three principally important GBGT1 SNPs: c.363C>A, c.886C>T and c.887G>A. Selected samples were analyzed further. GBGT1 transcript levels were examined by extracting mRNA from peripheral blood of two individuals homozygous for c.363C>A and two wild-type controls. Transfections into MEG-01 cells were performed to examine the effect of c.886C>T (p.Arg296Trp) on FORS1 antigen expression. Plasma enzyme activity assay in three different set-ups were tested and the outcome analysed by flow

cytometry. Screening for naturally-occurring anti-FORS1 in plasma from 100 donors of different ABO groups was done using human, ovine and canine red blood cells (RBCs) as well as kodecytes (RBCs artificially uploaded with the Forssman pentasaccharide).

Results: We identified 68 GBGT1 alleles in Erythrogene, of which only four were previously listed as blood group alleles by ISBT. Eight potential null alleles were observed based on three different nonsense mutations, of which the most common is present in ~8% of European donors. Four healthy Swedish donors were found homozygous for c.363C>A, which truncates the GBGT1-encoded Fs synthase prematurely. This is the first description of human knock-outs for GBGT1. Transcripts were readily detected in mRNA preparations from all samples and no apparent quantitative differences were noted between wild-type and c.363C>A. The rare c.886C>T (p.Arg296Trp) mutation that alters the same codon as c.887G>A (p.Arg296Gln) has been found in individuals of African descent. It was over-expressed to investigate if it induces a FORS1-positive phenotype, but in contrast to the c.887G>A mutation, c.886C>T did not result in synthesis of FORS1. Human plasma (wild-type and c.887G>A) as well as supernatant from a protein expression system showed no enzymatic activity, in contrast to the canine plasma tested. This indicates that the soluble human Fs-synthase may not be present in functional form in plasma. Of the 100 plasmas tested, 10% were positive when tested with human papain-treated FORS1-positive RBCs, of which none in the A$_1$ (n = 20) and A$_1$B (n = 10) group came up positive. However, 98% tested positive with kodecytes uploaded with a high concentration of the Forssman structure (FSL-FS5 50 μg/ml). Interestingly, a lower titer score was noted for the A$_1$ and A$_1$B plasmas tested.

Summary / Conclusions: We have extended the knowledge of GBGT1 variants and alleles and the characteristics of naturally-occurring antibodies in our newest carbohydrate blood group system, FORS. The frequency of antibody reactivity may suggest an ABO-restricted response and the finding of c.363C>A-homozygous blood donors indicates that GBGT1 is dispensable in humans.

5A-S33-04

REGULATION OF ABO BLOOD GROUP ANTIGEN EXPRESSION BY MIRNA–331-3P AND MIR-1908-5P

R Kronstein-Wiedemann[1], P Bugert[2] and T Tonn[1]

[1]Institute for Experimental Transfusion Medicine, DRK-Blutspendedienst Nord-Ost, Dresden [2]Institute for Transfusion Medicine and Immunology, Medical Faculty Mannheim, Heidelberg, Mannheim, Germany

Background: The ABO blood group system is unequivocally the most important in clinical transfusion medicine. Furthermore ABO is implicated in the development of a number of human diseases. The ABO antigens are not confined to RBC's but are widely expressed in a variety of human cells and tissues. Aberrant A and B oligosaccharide expression levels are common and in many – but not all – cases can be explained by more than 100 reported genetic variations in the respective glycosyltransferase.

Aims: The role of miRNAs in the regulation of blood group antigens during erythropoiesis has not been addressed so far. MicroRNAs are small noncoding RNAs that bind to the 3′ untranslated region (UTR) of target mRNAs resulting in translation repression or mRNA degradation. Here, we show that miR-331-3p and miR-1908-5p directly target glycosyltransferase A and B mRNA.

Methods: By distinct complementary approaches, including gene array analysis and overexpression of glycosyltransferase specific miRNAs in primary hematopoietic stem cells (HSC's), we identified that miR-331-3p and -1908-5p directly target glycosyltransferase A and B. Using microRNA target prediction tools we also identified Sp1 as a potential target gene for miR-331-3p. Therefore we treated HSCs with an inhibitor of SP1 and analyzed blood group A expression by flow cytometry and ID-Card gel method.

Results: Expression levels of miR-1908-5p and miR-331-3p were found to inversely correlate with the amount of blood group A antigen. Interestingly, this is already the case in hematopoietic stem cells (HSC's) and remains stabilized in mature red blood cells (RBC's). Overexpression of miR-331 and -1908 in HSC's leads to a significant reduction in the number of blood group A antigens per RBC. The effects are further enhanced by simultaneous targeting transcription factor Sp1 by miR-331-3p, rendering Sp1 incapable of binding to the promoter of the ABO gene, thereby downregulating blood group A antigen expression by up to 70%. Further approaches with the Sp1 inhibitor, mithramycin A, revealed similar results.

Summary / Conclusions: While expression changes in miRNA's may account for rare cases of weak A/B phenotypes which cannot be explained by genetic variations, it may play an important role in disappearance of glycan antigens in carcinogenesis.

5A-S33-05

LACK OF THE NUCLEOSIDE TRANSPORTER ENT1 IN INDIVIDUALS WITH THE RARE AUGUSTINE–NULL BLOOD GROUP IS ASSOCIATED WITH AN ABNORMAL ERYTHROPOIESIS AND MACROCYTOSIS

M Mikdar[1,2,3], C Le Van Kim[2,3,4], S Kinet[3,5,6], N Taylor[3,5,6], Y Colin[2,3,4], S Azouzi[1,2,3] and T Peyrard[1,2,3]

[1]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine [2]UMR_S1134 Inserm Université Paris Diderot [3]Laboratoire d'Excellence GR-Ex [4]Institut National de la Transfusion Sanguine, Paris [5]Institut de Génétique Moléculaire de Montpellier [6]Centre National de la Recherche Scientifique UMR5535, Université de Montpellier, Montpellier, France

Background: The Augustine blood group system consists of two antigens (AUG1 and AUG2, abbreviated as At^a) that are located on the equilibrative nucleoside transporter ENT1. The null phenotype (AUG: -1,-2) results from a homozygous splice site mutation in the SLC29A1 gene, c.589 + 1G>C. At^a (AUG2) is a high-frequency red blood cell (RBC) antigen and to date, all individuals with a negative phenotype (At (a−)) are of African origin. Our team has recently shown that the lack of ENT1 in humans (AUG:-1-2 phenotype) is associated with ectopic calcification, suggesting that ENT1 is an important factor in the regulation of bone metabolism.

Aims: Given the absence of ENT1 on red cells of At(a−) individuals, we analyzed the properties of their RBCs as well as the erythroid differentiation potential of their hematopoietic progenitors.

Methods: RBC deformability and osmoscan data were determined by laser diffraction analysis (ecktacytometry), using the Laser-assisted Optical Rotational Cell Analyser (LORCA, RR Mechatronics, Hoorn, the Netherlands). In vitro erythropoiesis was performed in 2 phases. Briefly, isolated peripheral blood CD34+ progenitors from the 3 ENT1-null patients as well as healthy donors, were expanded for 7 days in the presence of cytokines (IL-3, IL-6, and SCF) and then differentiated in the presence of erythropoietin (IL-3, SCF, and Erythropoietin (2U/ml)) at a density of 10^5 cells/ml.

Results: The haematological properties of ENT1null individuals showed no abnormalities as assessed by CCMH, reticulocyte count and Hb levels. However, all ENT1null RBCs displayed macrocytosis (103–105 fL) and abnormal morphologies, characterized by the presence of anisopoikilocytosis/target cells. In addition, all 3 patients exhibited hyperhydrated RBCs and rheological experiments showed an altered deformability in one patient. Furthermore, upon erythroid differentiation of CD34+ progenitors from ENT1null donors (n = 2), we detected a decreased level of proliferation and a delayed erythroblast maturation. Interestingly, differentiating reticulocytes showed an increased volume as compared to control reticulocytes, consistent with the macrocytosis observed in ENT1null individuals. To assess whether these phenotypic alterations were due to changes in nucleoside transport, we evaluated the effects of exogenous adenosine (50 μM) on the erythroid differentiation of healthy CD34+ progenitors. Notably, exogenous adenosine attenuated progenitor cell proliferation but the differentiation of progenitors to the reticulocyte stage was accelerated. Moreover, differentiated reticulocytes exhibited an increased volume, suggesting that the macrocytosis observed in ENT1null patients may be due to higher intracellular adenosine levels. Intriguingly, these effects were specific to adenosine as neither guanosine, uridine nor cytidine affected the erythroid commitment and differentiation of healthy HSCs.

Summary / Conclusions: Studies of null phenotype blood group systems will promote our understanding of the roles of the proteins carrying their antigens, on both the erythroid differentiation process and mature RBC physiology. Our results strongly suggest a significant role for ENT1-mediated adenosine transport in erythroid differentiation and macrocytosis in ENT1null patients.

5A-S33-06

CHARACTERIZATION OF A NOVEL HIGH-PREVALENCE RED BLOOD CELL ANTIGEN IN THE AUGUSTINE BLOOD GROUP SYSTEM

C Vrignaud[1,2,3], M Mikdar[1,2,3], A Raneri[1], O Hermine[3,4], Y Colin[3,5], C Le Van Kim[3,5], S Azouzi[1,2,3] and T Peyrard[1,2,3]

[1]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine [2]UMR_S1134 Inserm Université Paris Diderot [3]Laboratoire d'Excellence GR-Ex [4]Institut Imagine, UMR_S1163 Université Paris Descartes [5]UMR_S1134 Inserm Université Paris Diderot Institut National de la Transfusion Sanguine, Paris, France

Background: The Augustine blood group system consists of two antigens (AUG1 and AUG2) located on the equilibrative nucleoside transporter ENT1. Of note, a

provisional high-prevalence antigen, AUG3 (c.1159A>C, p.Thr387Pro), was recently proposed. The null phenotype (AUG:-1) results from homozygosity for a splice site mutation in the SLC29A1 gene, c.589 + 1 g>c. At[a] (AUG2) is a high-prevalence red blood cell (RBC) antigen. The molecular basis of the rare At(a−) phenotype, specifically encountered in people of African descent, corresponds to a homozygous c.1171G>A mutation in exon 12 of SLC29A1, predicted to cause a p.Glu391Lys amino acid change.

Aims: We investigated an antibody to a high-prevalence antigen of unknown specificity in a proband of Caucasian ancestry.

Methods: Antibody identification and RBC typing were performed by IAT (gel-test/Bio-Rad). Exome sequencing and data analysis were performed on genomic DNA. Expression level of ENT1 was analyzed by flow cytometry and western blot testing.

Results: An alloantibody against a high-prevalence RBC antigen was detected in 1995 in a 67-year-old female patient, group A_1, D-C-E-c + e+, K-. She had one pregnancy and a RBC transfusion in 1983. The antibody was found again in 1999 prior to a gastric surgery. All efforts towards determining the specificity of this antibody were unsuccessful. To identify the gene responsible for the rare blood phenotype of the proband, we implemented a next-generation sequencing (NGS) approach using whole-exome sequencing (WES). Variant filtering strategies using an in house software package (PolyWeb) led to the identification of a homozygous missense variations in the SLC29A1 gene, encoding the ENT1 protein. The proband was homozygous for the allele rs72555353 (SLC29A1 NM_001078177: c.242A>G). The c.242A>G (p.Asn81Ser) variant has been reported with a frequency of 127/120,302 (0.106%) in the Exome Aggregation Consortium (ExAC) database. This variant, however, had not been reported in the homozygous state. The c.242A>G mutation is predicted as being nonpathogenic by the PolyPhen and SIFT tools, suggesting that p.Asn81Ser probably does not cause a null Augustine phenotype. To further characterize the Augustine phenotype of this proband, we performed a crossmatch test using anti-AUG1 and anti-AUG2 antisera. The proband's RBCs were reactive with anti-AUG1 and anti-AUG2, confirming the presence of ENT1 on his RBCs. The proband's eluate reacted with standard and AUG:-2 RBCs but not with AUG:-1 RBCs, confirming that this antibody was directed against the ENT1 protein. In addition, flow cytometry and immunoblotting analyses indicated that the expression level of ENT1 in the proband's RBCs was significantly decreased (approximately 30%), suggesting that the p.Asn81Ser mutation probably affects ENT1 expression on the RBC surface.

Summary / Conclusions: This case provides an illustrative example of the benefits of genomic methods in resolving complex cases in immunohematology. Serological and molecular studies have provided evidence here for a novel antigen in the Augustine blood group system. Since this system currently comprises three antigens, we suggest to provisionally assign the names AUG4 and AYMA (after the proband's name) for the new high-prevalence antigen described here, subject to the agreement of the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology.

Blood Products: Red Cells

5A-S34-01
AUTOMATED BLOOD COMPONENT PRODUCTION

J Cid and M Lozano

Apheresis & Cellular Therapy Unit, Department of Hemotherapy and Hemostasis, Hospital Clínic, Barcelona, Spain

Automation of blood component preparation (BCP) from whole blood (WB) collections can help to optimize the BCP process, and it is increasingly being widespread implemented. This presentation summarizes the quality of blood components obtained with new automated devices developed in the 2000s. The quality of blood components obtained with these new automated devices reported in the available literature shows that blood components obtained with the new devices met European standards. It is important to point out that, compared with platelet concentrates obtained with manual methods, automation of BCP improved the consistency of the final platelet products. In conclusion, the complete automation of BCP from WB collections is still in development, and it represents a huge change in paradigm.

5A-S34-02
PROCESSING METHODS AND QUALITY MARKERS IN THE PRODUCTION OF RED BLOOD CELL UNITS

AW Shih[1,2], N Heddle[3], R Barty[4], N Li[4], J Acker[5,6] and Q MIP Investigators on behalf of BEST Collaborative[7]

[1]*Pathology and Laboratory Medicine, Vancouver Coastal Health Authority* [2]*Pathology and Laboratory Medicine, University of British Columbia, Vancouver* [3]*Medicine* [4]*McMaster Centre for Transfusion Research, McMaster University, Hamilton* [5]*Centre for Innovation, Canadian Blood Services* [6]*Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada* [7]*Transfusion Medicine, NHSBT, Oxford, United Kingdom*

Background: Recent publications have shown that there are in vitro qualitative differences in red blood cell (RBC) units processed from whole blood (WB) depending on the method of processing. Differences in blood production factors such as hold before processing, leukoreduction, centrifugation speed, and materials used lead to differences in quality markers such as hemolysis, residual plasma, and 2,3-DPG. As clinical information emerges regarding variability in patient outcomes depending on different types of RBC products transfused, it is essential to understand differences in processing methods which may contribute to differences in quality characteristics.

Aims: To collect information from key blood manufacturers in different countries regarding 1) details of WB processing to produce RBCs; and 2) quality parameters that are used to test RBCs as part of routine quality control testing.

Methods: A web-based survey was refined which submitted data to a REDCap database stored on a secure server, refined after performing pilot data collection from three participating sites. Blood center representatives from different jurisdictions were approached to participate and provided a unique login to the survey for completion.

Results: As of January 2018, data from nine blood operators in eight countries (Australia, Canada, France, Germany, the Netherlands, Norway, Sweden, and the United Kingdom) have been collected. Two primary methods of RBC processing were the top-and-top (TAT) method which produces RBCs and plasma used by six blood operators (67%); and the bottom-and-top (BAT) which additionally produces buffy coat platelets used by eight blood operators (89%). Of the six operators using both methods, three favor BAT processing. The blood operator surveyed in Norway utilizes the Reveos system.

All jurisdictions surveyed universally leukoreduced blood products, use CPD as an anticoagulant, and SAGM as an additive solution (except the German Red Cross; PAGGSM). Canada, the Netherlands, Norway, and Sweden actively cool whole blood before processing. Other processing parameters demonstrated variability amongst respondents: including length of hold before processing, donor hemoglobin limits, acceptable collection weights, concentrations of anticoagulant, collection sets, time to leukoreduction, centrifugation speeds, and extraction devices. RBC shelf life for most jurisdictions was 42 days, except for Germany (Red Cross; 49 days), and the Netherlands, Norway, and the United Kingdom (35 days). In Canada and the United Kingdom, higher centrifugation speeds were recorded in the TAT methods compared to BAT methods.

Quality marker testing also differed; with unit volume, hematocrit, hemolysis, and residual white blood cell (WBC) concentration being common markers tested in jurisdictions surveyed. Unit volume for the BAT methods were similar, though Canada had a higher hematocrit. Significantly lower hemolysis (mean difference: −0.18; 95% CI −0.22, −0.14) and a trend of lower residual WBC concentrations were in BAT processing across jurisdictions compared to TAT.

Summary / Conclusions: Methods and parameters of WB processing of RBCs differ amongst blood producers worldwide. Quality differences between BAT and TAT methods may be important in understanding and evaluating emerging clinical data. As blood is a therapeutic biologic, further studies are needed to elucidate effects of differences to clinical outcomes associated with variations in WB processing; and the potential harmonization of methods.

5A-S34-03

APPLICATION OF IMAGE FLOW CYTOMETRY ON THE CHARACTERIZATION OF RED BLOOD CELL MORPHOLOGY: VALIDATION AGAINST THE CONVENTIONAL TECHNIQUE AND TRENDS OBSERVED DUE TO DONOR VARIABILITY

JA Sebastian[1,2], R Pinto[2,3], T Turner[4], M Parsons[5], J Acker[4,6] and M Kolios[2,3]

[1]*Department of Electrical and Computer Engineering, Ryerson University* [2]*Institute of Biomedical Engineering, Science, and Technology (iBEST)* [3]*Department of Physics, Ryerson University, Toronto* [4]*Centre for Innovation, Canadian Blood Services, Edmonton* [5]*Lunenfeld-Tanenbaum Research Institute (LTRI), Sinai Health System, Toronto* [6]*Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada*

Background: For RBC transfusions, red cell concentrate (RCC) units are produced by separating RBCs from donated blood and suspending them in a preservative solution. During storage, the characteristic biconcavity exhibited in regular functioning RBCs (termed smooth discs) is gradually lost in the following sequence: formation of membrane crenations (crenated discs); spicule formation resulting in budding vesicles (crenated discoids); loss of cell membrane, intracellular content and central pallor (crenated spheroids); complete loss of biconcavity and adoption of a spherical shape (crenated spheres) and; complete loss of all spicules (smooth spheres). Conventional morphology indices (MI) are laborious, inherently subjective and use a relatively small data set for analysis. The potential application of image flow cytometry (IFC), a branch of flow cytometry that captures images of cells flowing in suspension, for characterization of RBC morphology has been recently published. The technique rapidly captures and characterizes tens of thousands of RBC images in minutes, overcoming the limitations outlined with light microscopy and allowing for more robust statistical analysis.

Aims: The study includes a validation of the IFC technique against light microscopy using the MI method and, using the IFC technique, we investigate the effects of storage duration and donor variability on the temporal behaviour of the morphological distribution.

Methods: Laboratories at Canadian Blood Services (Edmonton, CA) and iBEST (St. Michael's Hospital, Toronto, CA) carried out the light microscopy and IFC techniques, respectively, to morphologically characterize 11 LR, SAGM (Top / bottom) RCC units from 5 female and 6 male donors during storage. Each RCC unit was shared between the two facilities and the mean MI measure was calculated using triplicate measurements on a weekly ($\pm$24 h.) basis until expiration at 6 weeks postdonation. IFC datasets of each morphology class were used for trend analysis based on donor variability.

Results: A strong correlation ($0.842 \le r^2 \le 0.996$) was exhibited in the MI obtained with both techniques. Bland Altman plots of all data showed a mean difference (IFC - light microscopy) of +4.06 units, which is attributed to the current limitation of the IFC technique in capturing the smooth sphere morphology. We found a higher amount of variation in the trends exhibited by infrequent donors (<3 donations / yr.) and found sharper temporal changes in the morphological distribution of younger female donors (<30 yrs.) during weeks 2–3 of storage.

Summary / Conclusions: The MI comparison study provides confidence in the ability of IFC technique to morphologically characterize RBCs at similar precision to the conventional method. Further work on IFC technique will be required, particularly at capturing smooth sphere images, in order to reduce the overestimate of ~4%. The IFC technique shows promise in demonstrating the effects of donor variability on the morphological distribution of RCC units.

5A-S34-04

SOLUBLE FACTORS IN PACKED RED BLOOD CELLS MODULATE INFLAMMASOMES: POTENTIAL MECHANISM ASSOCIATED WITH TRANSFUSION-RELATED IMMUNOMODULATION

M Dean[1,2], K Rooks[1], F Chong[1] and R Flower[1,2]

[1]*Research and Development, Australian Red Cross Blood Service, Kelvin Grove* [2]*Faculty of Health, School of Biomedical Science, Queensland University of Technology, Brisbane, Australia*

Background: Packed red blood cell (PRBC) transfusion has been associated with modulation of recipient immune responses contributing to increased rates of infection, higher patient mortality and longer hospital stays, however, the mechanism behind this modulation is largely unknown. Interleukin (IL)-1β is an important mediator of the inflammatory response and is involved in several cellular processes

including proliferation, differentiation and apoptosis. The maturation and release of IL-1β is dependent on inflammasome activation. Inflammasomes are important innate immune multiproteins that when activated by pathogens, damage signals or particulate matter, trigger a proteolytic cascade to cleave pro-IL-1β to form mature IL-1β, regulated by caspase-1. While there are many biologically active proteins, lipids and enzymes in PRBC that could modulate the inflammasome there has been no specific assessment of the potential for PRBC transfusion to modulate processes involved with IL-1β dependent inflammation, including inflammasome activation.

Aims: To investigate whether soluble factors in PRBC modulate inflammasome activation.

Methods: PRBC were obtained from the processing department of the Australian Red Cross Blood Service. At Day(D) 2 and D42 of routine storage an aliquot was aseptically removed from each unit and centrifuged (1800 g, 15 min) to obtain the supernatant (PRBC-SN). We developed an in-vitro model of transfusion and concurrent infection. Briefly, monocytes were isolated from healthy volunteers and cultured (4 h, 37°C, 5% CO_2) without stimulation, or stimulated with lipopolysaccharide (LPS, 1 μg/ml), LPS + D2-PRBC-SN, LPS + D42-PRBC-SN or LPS + ATP. Inflammasome activation was assessed by quantification of IL-1β (via cytometric bead array) and caspase-1 (via ELISA) in culture supernatants. IL-1β, caspase-1 and macrophage migration inhibitory factor (MIF) were also quantified in the PRBC-SN. LPS alone was used as the comparator treatment for all other treatments (Paired T-test, n = 18, P < 0.05 considered significant).

Results: IL-1β and caspase-1 were not detectable in PRBC-SNs regardless of storage duration. MIF, a known modulator of inflammasome activation was detected in both D2- and D42-PRBC-SN. In the monocyte culture model, IL-1β was at the limits of detection in unstimulated monocytes. As expected, exposure to LPS alone and LPS + ATP resulted in release of IL-1β from cultured monocytes. Levels of IL-1β were significantly increased by both D2-PRBC-SN and D42-PRBC-SN in our model of concurrent infection (LPS) and transfusion demonstrating that soluble mediators present in PRBC augments IL-1β maturation and release indicating modulation of the inflammasome. In addition, there was a significant increase in caspase-1 in the model of concurrent infection and transfusion, providing further evidence that PRBC-SN modulates inflammasome activation.

Summary / Conclusions: Inflammasomes play a critical role in regulating inflammation, auto-immune diseases and cancer. We provide the first evidence that soluble mediators present in PRBC can modulate inflammation and the immune response through the activation of the inflammasome pathway and the release of IL-1β. It is likely that modulation of inflammasome activation and IL-1β inflammation is mediated through a multitude of factors in PRBC-SN including reactive oxygen species (ROS), microparticles and MIF signalling. Further characterisation of how blood transfusion modulates inflammasome activation is warranted.

5A-S34-05

TRANSFUSIONS OF PACKED RED BLOOD CELLS AT THE END OF SHELF LIFE ARE ASSOCIATED WITH INCREASED CIRCULATING MICROPARTICLES UNDER FLOW CONDITIONS

MS Ng[1,2], J Suen[1], K Rooks[2], J Tung[2] and J Fraser[1]

[1]*Critical Care Research Group, Faculty of Medicine, University of Queensland* [2]*Research and Development, Australian Red Cross Blood Service, Brisbane, Australia*

Background: During ex vivo storage, packed red blood cell (PRBCs) accumulate biochemical and functional changes which have been associated with adverse transfusion outcomes. Microparticles are submicron particles that are formed during cellular stress and activation. These particles have been postulated as a potential mediators of adverse transfusion outcomes as they can interact with cells to disrupt immune and thrombosis processes. Stored PRBC constituents such as red blood cells, cytokines, microparticles, lipids and non-transferrin bound iron activate recipient endothelial and immune cells – potentially altering circulating bioactive microparticle populations post-transfusion.

Aims: This study aimed to detect changes in microparticle concentration after stored PRBC circulation with whole blood using a novel in vitro vascular flow model.

Methods: Whole blood was diluted 1:1 in PBS to simulate recipient blood. PRBC units were added to recipient blood at 1:9 dilution to simulate transfusion. PRBC transfusions experiments were performed when the PRBC unit was <7 days old (fresh) and 42 days old (stored at 4°C). Lipopolysaccharide (LPS) was combined with recipient blood to a final concentration of 100 ng/ml to simulate endotoxaemia. Nine replicates were conducted for each treatment. Blood mixtures (no transfusion, PRBC transfusion, LPS) were perfused through an endothelialised vascular model for 4 h at 37°C. Microparticle concentration and cytokine concentration in the perfusant were measured using flow cytometry and nanoparticle tracking analysis.

Results: Stored PRBC transfusion increased microparticle formation compared to fresh PRBC transfusion on flow cytometry (147% vs. 215%, P = 0.05) and nanoparticle tracking analysis (172% vs 262%, P = 0.05). PRBC transfusion and LPS treatment led to different microparticle and cytokine responses.

Summary / Conclusions: Perfusion of PRBCs with whole blood in an endothelialised vascular model led to increased microparticle formation.

Donors and Donation – Building a Safe and Sustainable Donor Base

5A-S35-01

AN OVERVIEW OF DONOR BASE MODELS IN SUB-SAHARAN AFRICA: CHALLENGES AND SUCCESSES

I Bates

Public Health, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

The aim of this presentation is to provide an overview of the challenges and successes associated with different donor base models in sub-Saharan Africa (SSA). Information was derived from multiple sources including primary data, published literature, consultations and personal experience.

Blood supply is inadequate to meet global needs and availability and accessibility is highly inequitable. Low-middle income countries (LMIC) have 24% of the global blood supply for 48% of the world's population with 4.6 donations/1000 people compared to 33.1 donations/1000 in high-income countries. Using a conservative target for blood donations of 10 donations/1000 population), the shortfall in blood in SSA (excluding South Africa) is about 5.3 million units.

There are three types of blood donors recognised in SSA: voluntary non-remunerated donors (VNRD); family/replacement donors (FRD) and paid/professional donors. VNRD donate blood without coercion or payment in cash or 'in kind'. FRD donate blood in response to need by a family member or friend either in advance of the transfusion, or to replace blood used. Paid donors receive money for their donation and emerge wherever demand for blood exceeds supply; a situation which pertains across much of SSA. Many countries in SSA are struggling to achieve the WHO goal to ensure all donors are VNRD. For example, in 15 countries in Africa, accounting for 45% of the regions' population, only 25–50% of blood was from VNRD.

Outreach services to recruit VNRD are one of the costliest components of the blood system and are unaffordable by many poorer SSA countries, hence the reliance in many countries on the sustainable but inadequate, FRD system. Although a few SSA countries have managed to set up a nationwide VNRD system, others run a hybrid system with VNRD recruitment in large cities and FRD in less accessible peripheral, rural areas. The safest type of donor is one who is unpaid and donates regularly, irrespective of whether they were originally a VNRD or FRD. With better availability of quality health reviews and infection screening tests in SSA, there is now an increasing focus on converting FRDs into repeat, voluntary donors. This has advantages in that FRD do not require expensive outreach recruitment services, and they have already overcome initial barriers to donating blood. Furthermore there is evidence that FRD often perceive themselves to be voluntary donors, expressing their main reasons for donating as altruism, the wish to save lives and donating blood for family or community members.

Summary/conclusions: A paradigm shift is required to increase blood donations in SSA and prevent the many needless deaths of pregnant women and children that result from critical, chronic blood shortages. This will involve a new focus on encouraging and retaining repeat donors, including those who were originally FRD, and re-aligning motivational messages to be more culturally sensitive and focused on donating for families and communities.

5A-S35-02

BUILDING A BLOOD SYSTEM: THE VIEW FROM SAUDI ARABIA

M Badawi

Hematology, King Abdulaziz University, JEDDAH, Saudi Arabia

Despite the significant advances in the transfusion medicine field, maintaining an adequate and safe blood supply remains challenging for some areas of the world. Data from the World Health Organization reveal that many developing countries continue to have low rates of blood collections per capita, and many suffer from chronic shortage of blood and components. An effective way to improve the status of transfusion services in various countries is the establishment of effective blood systems. Various models of these systems exist, including national blood systems, institution-based blood centers, and hybrids of the two models. Currently, Saudi Arabia continues to operate on an institution-based model, with a blood collection and processing center affiliated with almost all individual hospitals. Given the high number of sectors that hospitals belong to, challenges are faced in communication and collaboration among blood centers including those in geographic proximity from each other. Building a national blood system is expected to result in positive outcomes in many aspects, including donor recruitment efforts and strategies, standardization of policies and processes, and effective utilization of resources and supplies. A hybrid model is proposed as a suitable approach for the country. Recruitment efforts, management of financial resources, creation of policies and standards can be established on a national level. In the same time, blood collection, processing, testing and storage may be performed in multiple satellite sites to allow for easier access and minimize transportation difficulties. Steps are being taken towards achieving this goal in the Kingdom.

5A-S35-03

FIRST TIME VOLUNTARY BLOOD DONORS RETURN RATE AND DETERMINANTS IN ETHIOPIAN NATIONAL BLOOD BANK SERVICE

DF Adamu[1], M Addissie[2] and W Haileselassie[2]

[1]Donor Service Directorate, Ethiopian National Blood Bank Service [2]Health System Management, Addis Ababa University, Addis Ababa, Ethiopia

Background: Accessibility of a safe and adequate blood transfusion is a challenge worldwide and even more critical in sub Saharan Africa. According to the World Health Organization recommendation, in order to meet a nation's most basic blood needs, the number of the blood donors of the nation should be 2%>3% of the total population. Contrary to the recommendation, in Ethiopia less than 0.5% of the population donates blood.

Aims: The study aimed to identify first time voluntary blood donors return rate and return determinants in Ethiopian National Blood Bank Service (ENBBS)

Methods: To evaluate the return rate secondary data review on 24,684 first time voluntary blood donors was done.

To investigate return determinants, facility based unmatched case control study design was implemented. The cases were first time voluntary blood donors returned for donation within two years since their index donation whereas controls were those who didn't return. Structured questioner was used to collect data from randomly selected 438 samples from the ENBBS donor record through telephonic interview from March –April 2017. Logistic regression analysis were implemented to assess relevant determinants

Results: First time voluntary blood donors return rate: Among the 24,684 first time voluntary blood donors, 9,307 were returned within two years period from their index donation making the return rate to be 37.7% per two years.

First time voluntary blood donors return determinants: A total of 207 cases and 207 controls have participated in the study. First time voluntary blood donor return was found more likely to be determined by positive perceived donation capability (AOR = 3.3, 95% CI: 1.5 - 7.03) and larger volume blood donation (AOR = 2.8, 95% CI: 1.09 - 7.30). Furthermore compared to donors who donated blood for the reason of self interest those who donated out of altruism were 2 times more likely to return (AOR = 1.98, 95% CI: 1.00–3.54).

Summary / Conclusions: The study findings have showed that less than half of first time voluntary blood donors returned for successive blood donations. In order to increase donors' return rate, it is recommended to have a timely scheduled mobile campaign at blood collection sites and also increase the number of fixed donation sites so as to make donation services more convenient and available.

The return of first time voluntary blood donors' was found to be positively associated with altruism, perceived donation capability and donating larger blood volume.

Therefore working on promotional and marketing service of the ENBBS could sensitize the community's altruism for a regular blood donation. In addition making donors to be aware about the requirements, screening procedures and the benefit of donated blood could avoid the feeling of perceived incapability and enhance the urge of donating blood regularly.

5A-S35-04

VOLUNTARY BLOOD DONATION- THE CHALLENGES AND PRACTICES AND FEASIBILITY IN DEVELOPING COUNTRIES

JD Jeyakumar[1,2], C Subash[3], R Krishnamoorthy[4] and P Muddegowda[5]

[1]Transfusion Medicine, Chennai [2]Transfusion Medicine [3]Hemato Oncology, MIOT International Hospitals [4]Transfusion Medicine, Ramachandra Medical College and Hospital, Chennai [5]Transfusion Medicine, Vinayaka Mission Medical College and Hospital, Salem, India

Background: World Health Organisation fact sheet 2017 on blood safety and availability states that 71 countries collect more than 50% of their blood supply from family/replacement or paid donors. National AIDS control Organisation state that more than 50% of the blood banks in India are operated by private sector and most of them depend on replacement donation as their main source of blood supply. This study analyses the challenges to voluntary blood donation among these replacement/ family blood donors in India.
Aims: To understand the challenges faced towards voluntary blood donation and look into possibilities to convert these motivated replacement/family blood donors into repeat regular voluntary blood donors.
Methods: This study was conducted between 1st April 2017 and 24th December 2017 in 4 major corporate /medical college hospitals in Tamilnadu in India. All motivated replacement / family donors were interviewed using standard questionnaire. The questions include; have you donated blood before for any patient or voluntarily in any blood camps. Are you aware if the continuous need for blood in hospitals? Are you willing to be regular voluntary blood donor?. What is the reason for you to not donate blood? Are you exposed to blood donation camp at your work place or during your college days? Are you aware of blood donation camps and places where you can donate blood before coming for this donation?
Results: A total of 11784 replacement/ family donors were interviewed with standard questionnaire during the study. Among the 11,784 Replacement Donors, 95.35% (11235) were males and 549 (4.65%) were females. 53% (6245) were first time donors, 13% (1532) donors had donated more than 10 times. 34% (4007) of the donors have donated more than 3 times at varied intervals. 67.2%(4197) of the 1st time replacement donors are not aware of the need of blood and had never been exposed to blood donation either during their education or at work place. And 32.8% (2048) of them had no opportunities to donate blood though they are aware of blood donation.
Summary / Conclusions: Lack of awareness towards voluntary blood donation stands the most important cause for decreased voluntary blood donation in developing countries. Knowledge and accessibility to blood camps and places to donate blood is the second biggest challenge faced by most of the donors who are otherwise willing to donate blood. More than 50% of the healthy adults neither have access to blood camps nor aware about the places where they can donate blood. Only donors who are attached to big educational institutions, IT- parks or industries get the awareness or opportunity to donate blood. Most of the healthy common population like farmers, people running small scale business, pizza/ delivery boys, are not aware about the need of blood. These catchment population gets first idea about blood donation mostly during replacement/ family donation. Systems should be adopted to motivate these replacement donors towards repeat voluntary donation through proper counselling. This would improve the voluntary blood donation in developing world.

Blood Safety – Viruses

5A-S36-01

SPLENIC MACROPHAGE SUBSETS AND THEIR FUNCTION DURING BLOOD-BORNE INFECTIONS

R D' Imperio Lima, H Borges da Silva, R Fonseca, A Cassado and J Alvarez Mosig
Department of Immunology, University of São Paulo, Sao Paulo, Brazil

The spleen is particularly shaped for maintaining blood homeostasis. Microanatomically, the spleen is divided into the white pulp and the red pulp (Rp), separated by the marginal zone (MZ). Rp and MZ have a complex macrophage (MΦ) network with distinct origins and functions, which contribute in complimentary ways to control blood-borne infections. To properly execute these functions, they are provided with a large variety of pattern-recognition receptors (PRRs) that recognize pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). Marginal metallophilic macrophages (MMMΦs) and marginal zone macrophages (MZMΦs) are cells with great ability to internalize blood-borne pathogens such as virus or bacteria. Their localization adjacent to T- and B-cell-rich splenic areas favors the rapid contact between these macrophages and cells from adaptive immunity. Indeed, MMMΦs and MZMΦs are considered important bridges between innate and adaptive immunity. Rp macrophages (RpMΦs) play important roles in the uptake of apoptotic cells, oxidized LDL, or senescent red blood cells from the circulation. Venous cords and sinuses render the splenic Rp bloodstream in a slow pace. This characteristic allows for the filtering function of the spleen and favors elimination of aberrant red blood cells. RpMΦs are also important for iron homeostasis, and conversely, iron homeostasis seems to control their development. Beyond the task of maintaining blood homeostasis in steady state conditions, RpMΦs contribute to control blood-borne infections such as malaria, bacterial and viral infections, as well as in the induction of innate and adaptive immunity. Interestingly, a proportion of Rp phagocytes exhibit strong labeling for F4/80 and CD11c, a phenotype shared by RpMΦs and dendritic cells. This population participates in the early clearance of Plasmodium parasites, but it sharply declines at the parasitemia peak. RpMΦs have a slow turnover rate and possibly undergo cell death after ingesting Plasmodium-infected RBCs due to the toxic effects of hemozoin. Of note, there are many T cells scattered in Rp, and this population interacts with F4/80^{+}CD11c^{+} cells in acute immune responses to Plasmodium infection. RpMΦs involvement in controlling excessive immune responses is suggested by studies on autoimmune syndromes, while a similar participation in infectious diseases remains to be established. In several aspects, splenic MΦs shape splenic structure and/or microenvironment. The development of splenomegaly is typical in blood-borne infections, and it is characterized by profound changes in splenic microarchitecture, including remodeling of Rp. Given this, splenic MΦs are expected to play a prominent role in the recruitment of different cell types during acute immune responses. Conversely, the splenic structure and its microenvironment seem to play pivotal roles in MΦ homing and function. For instance, arrangement of sinusoidal endothelial cells inside Rp hampers the circulation of aging and/or Plasmodium-infected RBCs, facilitating their trapping inside Rp and posterior phagocytosis by RpMΦs. This study addresses the roles of each one of these MΦ subsets, with special focus on how they recognize and help eliminate blood-borne pathogens, and, in turn, how the splenic microarchitecture and microenvironment influence macrophage function and survival in different phases of infection (acute, chronic, and after pathogen clearance).

5A-S36-02

HBV INFECTION RATES IN SOUTH AFRICAN NATIONAL BLOOD SERVICE (SANBS) DONORS BORN BEFORE AND AFTER THE IMPLEMENTATION OF UNIVERSAL HBV VACCINATION

WA Sykes[1], M Vermeulen[2], C Coleman[2] and K van den Berg[3]
[1]Donation Testing, SANBS, Durban [2]Donation Testing, SANBS, Johanessburg [3]Medical, SANBS, Port Elizabeth, South Africa

Background: Hepatitis B (HBV) is endemic in South Africa (SA) with more than 70% of the population exposed. Even though it is a vaccine preventable disease, it remains one of the main causes of liver related disease. In April 1995, SA introduced universal hepatitis B vaccination for newborns as part of the Expanded Programme of Immunisation. Infants vaccinated in 1995 became eligible to donate blood in 2011 at the age of 16.

Aims: To compare HBV rates in first time blood donors <20 years of age in 2015 and 2010 to determine whether the introduction of universal HBV vaccination translated to a decrease in the observed HBV rate among blood donors.

Methods: All donations were screened for HBsAg (Abbott Prism) and HBV DNA (Procleix TIGRIS Hologic). The Ultrio assay was used in 2010 and the Ultrio Plus assay (with improved HBV sensitivity) in 2015. HBV positive rates were analysed by age, gender and population group in first time donations from 2010 (probable non-vaccinated) and 2015 (probable vaccinated). Significance was determined using Chi square statistics.

Results: Of 91,540 donations from first time donors <20 years of age in 2010 and 2015, 223 (0.24%) tested HBV positive; 201 were confirmed positive, 18 NAT yields (NY - HBV DNA+/HBsAg−) and four serology yields (HBV DNA-/HBsAg+). HBV rate decreased by 69% from 0.377% in 2010 to 0.117% in 2015 (P < 0.0005). HBV rate decreased by 71% in males (0.471% to 0.134%) (P < 0.0005) and 64% in females (0.285% to 0.103%) (P = 0.00001). There was a 5-fold insignificant decrease in HBV rate in White donors (0.032% to 0.006%) (P = 0.21) and a 4 fold significant decrease in both Black (0.787% to 0.201%) (P < 0.0005) and Coloured donors (0.467% to 0.110%) (P = 0.031). Occult HBV Infection (OBI) accounted for 57% of NYs in 2010 but only 18% in 2015 (P = 0.23). While there were no vaccine breakthroughs in first time donors <20 years old in 2010, 45% of HBV NYs in 2015 were attributed to vaccine breakthrough (P = 0.12). Only 1.8% (4 of 223) HBV positive donors were also HIV positive.

Summary / Conclusions: HBV rates in first time blood donors <20 years of age decreased significantly from 2010 (probable non-vaccinated) to 2015 (probable vaccinated). The decrease in HBV rate in male donors was greater than in female donors, which could indicate that the program had a higher impact on male donors for reasons that are not yet apparent. The decrease was slightly greater in White donors as compared to Black and Coloured donors however insignificant due to small sample size. An increase in vaccine breakthroughs was observed in donors who had probably been vaccinated (2015) while OBI decreased in these donors even when a more sensitive assay for OBI was used.

More work in the area is required including performing anti-HBs titre and anti-HBc testing on HBsAg and HBV DNA negative donors to conclude that the decline in HBV rates in young blood donors is related to the implementation of universal HBV vaccination in SA.

5A-S36-03

FIRST CASE OF HIV–NAT NEGATIVE DONATION COLLECTED DURING ECLIPSE PHASE SINCE IMPLEMENTATION OF HIGHLY SENSITIVE INDIVIDUAL NAT IN FRANCE

P Cappy[1], V Barlet[2], Q Lucas[1], X Tinard[3], J Pillonel[4], S Gross[5] and S Laperche[1]

[1]Département des Agents Transmissibles par le sang, INTS, PARIS [2]Laboratoire de Qualification Biologique des dons, Etablissement Français du Sang, ETS Auvergne-Rhône-Alpes, Metz-Tessy [3]Pôle des vigilances, Etablissement Français du Sang, ETS Grand Est, Nancy [4]Direction des maladies Infectieuses, Santé Publique France, Saint-Maurice [5]Siège national, Etablissement Français du Sang, Saint-Denis, France

Background: In France, the risk of transmission of HIV infection by blood was reduced by implementing nucleic acid testing (NAT) in pool in 2001 and individual testing (ID-NAT) in 2010. Nevertheless, two situations can lead to false-negative results, even with highly sensitive ID-NAT: polymorphisms in the genomic regions targeted by the assay, and donation collected in the early phase of infection.

Aims: We report here the first case of blood donation identified in eclipse phase that tested ID-NAT negative.

Methods: Blood donations are currently screened for HIV antibodies (Ab) (PRISM, Abbott) and HIV RNA (Ultrio Procleix, Grifols, LOD 95%: 39 UI/ml). Upon seroconversion of a repeat donor, a repository sample from donation N-1 is retested with the Roche Cobas Taqman assay (LOD 95% = 29 UI/ml).

Results: In August 2017, a 57-year-old male repeat donor without declared risk factor was screened positive for HIV Ab and RNA (donation N; VL = 19,787 UI/ml, subtype B). Donation N-1 had tested negative with Ultrio in March 2017, but was positive when retested with Cobas Taqman, with a VL below the quantification limit (58 UI/ml). A 539-nt sequence from gp41 was 99.8% identical between donation N-1 and a control sample collected two weeks after donation N, confirming the strain identity. In addition, full-length sequencing of the strain showed no mismatch between the primers/probes used in Ultrio and the target sequence. A look-back study allowed identifying the recipients of the blood components from donation N-1. Red blood cells (residual volume of plasma [RVP]: 20 ml) had been transfused to a 23-year-old bone marrow transplant recipient who died of graft-versus-host disease six days after transfusion. A sample gathered five days post-transfusion tested

negative for HIV RNA. The platelets (RVP: 20 ml) had been pooled with other donations, inactivated by amotosalen/UVA and transfused to a 62-year-old woman with acute myeloblastic leukaemia who was HIV Ab negative seven months after transfusion, ruling out transmission. Lastly, the plasma yielded from donation N-1 had been fractionated. No measure of withdrawal of blood-derived products was initiated given the efficacy of pathogen inactivation on such a low level of viremia.

Summary / Conclusions: This case underlines that false-negative results of ID-NAT remain exceptional but demonstrates that the risk of contaminated donations due to early HIV infection phase going undetected is real. Our report is in agreement with HIV residual risk, estimated in France at 1/4.8 million donations or one donation every 1.5 year (2014–2016). The absence of detection of HIV RNA in the red blood cells recipient does not formally exclude a transmission given his early death. Lastly, the absence of transmission to the platelets recipient could be due to the very low viral inoculum (20 ml RVP x 29–39 UI/ml = 580–780 UI) and/or to the efficacy of the viral inactivation used on pools of platelets. This case also highlights the additional value of a systematic donation archiving (3 years in France) for lookback studies.

5A-S36-04

IMPLEMENTATION OF HEPATITIS E VIRUS RNA TESTING IN BLOOD DONORS IN ENGLAND – MOVING FROM PARTIAL TO UNIVERSAL SCREENING

I Ushiro-Lumb[1,2], K Tettmar[1], B Haywood[2], S Ijaz[2] and R Tedder[1,2]

[1]Microbiology Services, NHS Blood and Transplant [2]National Infection Services, Public Health England, London, United Kingdom

Background: In February 2016, the English blood services introduced partial HEV RNA screening of blood donors in order to minimise risks of transfusion-associated HEV infection in certain groups of vulnerable patients; it was initially predicted that 27% of the donor pool would have to be tested but numbers raised significantly in order to meet needs of hospital inventories. In April 2017, this was extended to universal screening, in accordance with recommendations made by the UK Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO). This was followed by the introduction of universal screening of donors of stem cells, tissues and organs in October 2017.

Aims: To describe the incidence of acute HEV infection in the English blood donor population since implementation of universal screening.

Methods: Donors were screened in pools of 24 samples, using the Roche Cobas MPx Taqscreen; reactive pools were resolved to single donation and confirmation with the Procleix HEV Assay. All HEV RNA confirmed positive samples were tested with the Wantai IgG and IgM assays (Fortress Diagnostics). Where viral load permitted, strains were sequenced for genotype and sub genotype assignment based on partial Open Reading Frame 2 sequences.

Results: During the partial screening period, NHSBT screened 662713 donors and observed a positivity rate of 0.04%. Between April and December 2017, 1,151583 donors were screened and 241 donor samples were found to be initially reactive. All samples tested positive with the second assay at the reference laboratory. Many samples had a viral load that was too low to allow sequencing. To date, 127 strains have been sequenced, all belonging to genotype 3 and distributed as follows: 26 clade 1 (sub genotype 3e = 18, 3f = 8) and 101 clade 2 (sub genotype 3a = 1, 3c = 81, 3c* = 16, 3i = 1).

During the first phase following the introduction of screening, sequential monitoring of HEV RNA, IgG and IgM was performed before and after donor reinstatement to panel. They all had serology compatible with different stages of acute HEV infection at pick up; where initially seronegative, seroconversion was demonstrated in all donors bar one. This whole blood donor was seronegative when found to be viraemic and only returned 1 year later, when HEV IgG was undetectable; presence of HEV RNA was confirmed in the plasma pack and it is possible that antibody levels had peaked and declined during this period, as we have observed in other donors from whom we tested serial samples. All reactive pick-ups were therefore true infections.

Summary / Conclusions: HEV RNA prevalence in our blood donors has declined when compared to the 2012–2013 period, from around 1:2858 to 1:4778; this is in keeping with HEV activity observed in the general UK population (Public Health England data), and it does varies periodically. As for the sub genotype distribution of genotype 3 virus, clade 2 continues to predominate over clade 1, also mimicking the distribution seen in clinical cases presenting in the community. We will continue to monitor changes in epidemiology and clinical impact of infection in vulnerable groups, which will help inform blood, tissue, cells and organ safety strategies.

5A-S36-05

HEV IGG LEVELS DECLINE FOLLOWING ASYMPTOMATIC
INFECTION: LONGITUDINAL LONG-TERM FOLLOW UP OF
BLOOD DONORS IN ENGLAND

I Ushiro-Lumb[1,2], M Madhaparia[1], K Tettmar[1], S Ijaz[2] and R Tedder[2]

[1]Microbiology Services, NHS Blood and Transplant [2]National Infection Services,
Public Health England, London, United Kingdom

Background: Partial blood donor screening for HEV RNA was implemented by the
UK blood services in 2016, with universal screening from April 2017. In order to
monitor NAT performance, collect data and inform our donor reinstatement criteria,
we followed up donors by testing them for HEV RNA, IgG and IgM. Whole blood
donors were deferred for 6 months and apheresis donors could return to panel once
HEV RNA became undetectable and IgG sample/cut off ratio was greater than 10.
This criterion was later modified and relaxed.

Aims: To describe a small subset of prospective data collected from blood donors
found to be HEV viraemic at the time of donation. Longitudinal HEV IgG values
were monitored for documentation of seroconversion and trends in antibody levels
over time.

Methods: Screening is performed using pools of 24 samples in the Roche
Cobas®HEV assay. Pool reactivity is resolved to single donations, which undergoes
individual NAT in the Procleix® HEV (Grifols Diagnostic Solutions) or AmpliCu-
be®HEV (Mikrogen Diagnostik) assays. Serology is performed using the Wantai®
HEV IgG and IgM assays (Fortress Diagnostics). Follow up samples are tested by
individual NAT in the Procleix or AmpliCube assays. Returning donors had longitu-
dinal serology performed, with samples tested up to 20 months after initial HEV
RNA positive pick up donation.

Results: In 2016–2017, 1,814286 donors were screened, with 480 confirmed HEV
RNA positive cases (0.03% positivity rate, 1 in 3779 donors). Longest follow up time
was 20 months. Donors who were seronegative at pick up had demonstrable sero-
conversion, with no false-positive HEV RNA screening results. Following seroconver-
sion, most donors maintained good levels of HEV IgG, with sample/cut off ratios in
the 10 to 20 range. A small number of donors had a different serological pattern;
longitudinal follow up revealed variation in the ability to sustain levels of specific
IgG. Five donors had clear decline in anti-HEV levels of whom two went on to lose
detectable HEV antibodies.

Significant drop in IgG levels in the range of 50 to 86% was seen at 2, 4 and
15 months in four donors, and sero-reversion was documented in two donors by 14
and 15 months. One donor was seronegative at pick up and again when they
returned to donate 1 year later. It is possible that this donor reached peak antibody
levels which went on to became undetectable in this time interval.

Summary / Conclusions: It is unclear why some donors had a significant decline in
HEV IgG levels during the observation period, the longest interval being 20 months.
Samples were not obtained at the same intervals as we only tested samples collected
for the purpose of apheresis donor re-instatement and samples taken when donors
returned to donate. Donors did not report overt acute hepatitic illness post index
donation, so symptomatic disease alone does not account for the strength or dura-
tion of specific antibody response; viral and host factors may have played a role.
This observation may have significance for future blood safety strategy planning
and understanding of host responses to HEV and should be explored further.

Clinical – Transfusion in Haemato-oncology

5A-S37-01

LOWERING TRANSFUSION THRESHOLDS IN
HAEMATOPOIETIC STEM CELL TRANSPLANTATION

A. Tinmouth

No abstract available

5A-S37-02

EFFICACY AND AVAILABILITY OF HLA-MATCHED PLATELET
TRANSFUSIONS FOR PLATELET REFRACTORY PATIENTS IN
THE NETHERLANDS

A Kreuger[1,2], A Mäkelburg[3,4], J Somers[3,5], B Tomson[3], L van de Watering[3],
J van der Bom[1,2], M van Kraaij[1,3,6] and C Weller[3]

[1]Center for Clinical Transfusion Research, Sanquin Research [2]Department of Clinical
Epidemiology, Leiden University Medical Center, Leiden [3]Unit Transfusion Medicine,
Sanquin Blood Bank, Amsterdam [4]Department of Hematology, University Medical
Center Groningen, Groningen [5]Department of Hematology, Erasmus MC-Daniel Den
Hoed Cancer Center, Rotterdam [6]Unit Donor Affairs, Sanquin Blood Bank,
Amsterdam, Netherlands

Background: Patients are defined refractory for platelet transfusions when the one
hour corrected count increment (1hCCI) is ≤7.5 on two subsequent AB0-compatible
transfusions with random platelet concentrates. These patients may benefit from pla-
telet transfusions matched for HLA-A and -B antigens, for which a large panel of
donors has been HLA-typed. Patients receive single-donor products that are either
split-matched or partially matched containing up to four HLA-mismatches. If feasi-
ble, AB0-compatibility is taken into account.

Aims: We aimed to evaluate our HLA-matched donor program and to quantify the
efficacy of split-matched and partially mismatched platelet transfusions by means of
1hCCI after transfusion.

Methods: A cohort study was performed among recipients of HLA-matched platelets
in the Netherlands between 1994 and 2017. The number of available split-matched
donors per patient was determined. The ethnic background of patients with five or
less donors was compared with that of a random sample of 100 patients with at least
30 donors. Since ethnicity is not registered in the Netherlands, we used Haplostats to
estimate the most likely ethnic background.

Next, we selected the first transfusion with exposition to a new mismatch. The 1hCCI
after mismatched transfusions was compared with 1hCCI after matched transfusions
using mixed model linear regression, adjusted for within patient variation. Next,
subgroup analyses were performed for patients with positive and negative HLA-anti-
body screens, as this is not necessarily known upon request of the first HLA-
matched product. Lastly, the effect of AB0-mismatches was investigated.

Results: During the study period, 1,206 patients received a total of 12,350 HLA-
matched transfusions. In September 2017, 19,478 HLA-typed donors were registered.
Median 83 (interquartile range 18; 266) matched donors were available per patient.
For 95 (10.3%) patients, five or less donors were available. Of these, 23 (29%)
patients were estimated to be Caucasian, 18 (23%) Asian-Pacific, 16 (21%) African
American. For a random sample of 100 patients, with a median of 155 donors (IQR
86 to 365), the most likely ethnicities according to HaploStats were Caucasian
(74%), Native American (15%), and Hispanic (6%).

The 1hCCI was available for 427 first HLA-matched transfusions and 641 unique
mismatched transfusions. The average 1hCCI after a matched transfusion was 14.09
(95% reference interval 1.13; 29.89). This decreased with 1.94 (95% confidence inter-
val (CI) −3.15; −0.74) after an HLA-mismatched transfusion. In patients with a posi-
tive HLA-antibody screen, the 1hCCI decreased with 3.09 (−4.68; −1.50) after a
mismatched transfusions, regardless antibody specificity, whereas in patients with
negative HLA-antibody screens, the degree of HLA-matching did not influence the
1hCCI. Conditional on HLA-matching, 1hCCI decreased 3.70 (CI −5.22; −2.18) after
a major AB0 mismatched transfusion.

Summary / Conclusions: HLA-matched platelet support could be offered to the
majority of refractory patients. The number of patients from ethnic minorities is dis-
proportionally large in the group of patients with less than five donors. HLA-
matched platelet concentrates yielded the highest 1hCCI, but partially matched trans-
fusions can still result in increments larger than 7.5. We would recommend to have
a more diverse HLA-typed donor population in order to meet patients' needs.

5A-S37-03

EFFECT OF STORAGE AND PATHOGEN REDUCTION ON
ALLOIMMUNIZATION AFTER PLATELET TRANSFUSIONS

A Saris[1], J Kerkhoffs[2], P Norris[3], I Peyron[4], T Stuge[5], S van Ham[4], P van der Meer[2],
J Zwaginga[6] and A ten Brinke[4]

[1]Immunopathology, Sanquin, Amsterdam [2]Sanquin, Leiden, Netherlands [3]Blood
Systems Research Institute, San Francisco, United States [4]Sanquin, Amsterdam,
Netherlands [5]University of Tromsø, Tromso, Norway [6]Leiden University Medical
Center, Leiden, Netherlands

Background: Platelet transfusion can elicit alloimmune responses leading to alloan-
tibody formation against donor-specific polymorphic residues on HLA class I,

ultimately resulting in platelet transfusion refractoriness. It is, however, unknown if the risk for alloimmunization is caused by white blood cells remaining after leukoreduction or if alloimmunization can even be induced by platelets themselves.

Aims: This study first investigated the capacity of platelets to induce alloimmunization and subsequently determined the effect of storage and pathogen reduction on alloimmunization after platelet transfusions.

Methods: Platelet were either isolated from untreated or pathogen reduced platelet concentrates that were stored under routine blood bank conditions or freshly isolated and subsequently incubated with monocyte-derived dendritic cells at 37°C. After 4 h, DCs were harvested and platelet internalization was determined using confocal microscopy and quantified with imaging flow cytometry. In addition, presentation of platelet-derived peptides in HLA class II was determined using mass spectrometry after immunoprecipitation of HLA class II/peptide complexes. Alternatively, DCs were subsequently incubated with human platelet antigen 1a-specific CD4 T cells after which IFNγ production was measured to determine platelet-specific T cells responses. The effect of pathogen reduction on alloimmunization was further investigated in vivo. Hemato-oncological patients (n = 397) were randomized to receive either untreated (n = 205) or Mirasol pathogen reduced (n = 192) platelet transfusions (as part of the PREPAReS trial). In weekly blood samples, the presence of HLA class I and class II antibodies was determined using a Luminex assay. Patients were analyzed according to per protocol analysis.

Results: Allogeneic platelets were phagocytosed and platelet-derived peptides were presented by dendritic cells (DCs). Furthermore, platelet-loaded DCs induced platelet-specific CD4 T cell responses. Altogether, this indicates a platelet-specific ability to induce alloimmunization. Phagocytosis of stored platelets was enhanced compared to fresh platelets. Storage-induced apoptosis and accompanied phosphatidylserine exposure seemed to be instrumental for the increased phagocytosis. Mirasol pathogen reduction enhanced the storage-mediated phagocytosis of platelets.

At enrollment, 37 (9.3%) patients were HLA class I and 25 (6.3%) HLA class II positive. In these patients no differences were observed in antibody titers or broadness of immunization after receiving either untreated or pathogen reduced platelet concentrates. In patients that were antibody negative at enrollment, 25 (13.0%) developed anti-HLA class I antibodies after receiving pathogen reduced platelet concentrates compared to 11 (5.4%) after receiving untreated PCs (P = 0.006). No apparent differences in antibody titers or panel reactivity were observed after receiving untreated vs pathogen reduced platelets. HLA class II antibody formation was similar in both study arms (P = 0.98).

Summary / Conclusions: This study shows the capacity of platelets to induce platelet-specific alloimmune responses. Moreover, storage-induced apoptosis of platelets is identified as potential risk factor for alloimmunization after platelet transfusions. Furthermore, in vivo, platelet concentrates treated with Mirasol pathogen reduction enhanced HLA class I alloimmunization, which may be due to enhancement of storage-induced apoptosis by pathogen reduction.

5A-S37-04

COMPARISON OF CORRECTED COUNT INCREMENT (CCI) AND ABSOLUTE PLATELET COUNT INCREMENT (API) IN ABO-COMPATIBLE VERSUS ABO-INCOMPATIBLE PLATELET TRANSFUSIONS IN NON-CANCER RECIPIENTS

R Chandrabhan Dara, R Sharma, H Bhardwaj and V Tak

Transfusion Medicine, Manipal Hospitals Jaipur, Jaipur, India

Background: Platelets due to its short shelf life always remain in limited supply and because of this platelets are often transfused across ABO blood groups. ABO major compatibility is essential requisite in red cell transfusion but not in platelet transfusion. There is some evidence from published literature that transfusion efficacy of ABO incompatible platelet transfusion is inferior or comparable with ABO-compatible transfusions. However, most studies have involved cancer, hematology and transplant recipients

Aims: To assess the response to PLT transfusions in a cohort of non–cancer recipients and to study the relationship of ABO compatibility to PLT count increments after PLT transfusion

Methods: In this study, we conducted an observational study in primarily non-cancer recipients to determine the efficacy of ABO- compatible versus ABO incompatible platelet transfusions. Data was collected on all non-cancer recipients receiving a platelet transfusion during 12-month period (August 2016- July 2017). Collected variables were gender, age at the time of transfusion, height and weight, diagnosis, ABO group, number of platelet units transfused, type of platelet unit transfused, platelet count, ABO group, volume of the platelet, pre-transfusion and post-transfusion platelet counts with their time. Corrected Count Increment (CCI) and Absolute

Platelet Count Increment (API) were calculated and compared in ABO-compatible versus incompatible platelet transfusions. Uni-variate models and Multi-variate models were applied to all potential explanatory variables of interest. p values of less than 0.05 were considered significant.

Results: A total of 1856 platelet units (1518 random donor platelets and 338 single donor platelets) were transfused in non-cancer recipients in 741 transfusion episodes during the study period. Total of 1804 platelet units were included in final analysis, 52 were excluded. Median age of the patients was 54 years and males contributed 76.2%. Compatibility status of the PLT transfusions included 51.3% being ABO identical (925/1804), 23.4% having minor incompatibility (422/1804) and 25.3% having an ABO major incompatibility (457/1804). For ABO-identical transfusions, the median API was 37, ABO minor incompatible transfusions, the median API value was 36 and for ABO-incompatible transfusions, the median API value was 34 (P = 0.238). The median post-transfusion CCI was 19.7 for identical transfusions, 19.5 for minor incompatible transfusions versus 19.2 for incompatible transfusions (P = 0.459).

Limitations: 1. First, it's an observational study and lacks randomization.

2. We analysed only changes in the platelet count using API and CCI rather than clinical criteria (bleeding, length of hospital stay and/or mortality).

3. Since the data was initially collected and planned as a quality improvement study to monitor count increments after transfusion a formal sample size calculation was not performed

Summary / Conclusions: ABO-compatible platelet transfusions lead to higher post-transfusion absolute increment compared with ABO-incompatible platelet transfusions (based on median APIs of 37 and 34, respectively). But when comparing ABO compatible versus ABO major incompatible platelet transfusions, no significant difference was observed between the median CCI.

5A-S37-05

ESTABLISHMENT AND VALIDATION OF A LABORATORY ASSAY FOR MONITORING SURVIVAL OF TRANSFUSED PLATELETS: TRACKING HLA MISMATCH BETWEEN DONOR AND RECIPIENT

M Kjær[1,2], E Fleck[3], J Kjeldsen-Kragh[2,4], A Vetlesen[5] and C Geisen[3] Funded by EU's Seventh Framework Programme for Research (FP7)

[1]University Hospital North Norway [2]Prophylix Pharma AS, Tromsø, Norway [3]German Red Cross, Frankfurt, Germany [4]University and Regional Laboratories, Lund, Sweden [5]Oslo University Hospital, Oslo, Norway

Background: The large European collaborate study (PROFNAIT) is in the process of developing Hyperimmune anti-HPA-1a IgG (NAITgam) for the prevention of HPA-1a immunization and fetal and neonatal alloimmune thrombocytopenia (FNAIT) in HPA-1a positive children born by HPA-1a negative women. The ability of NAITgam to eliminate HPA-1a positive platelets transfused to HPA-1a negative healthy individuals will be tested in a phase 1/2 trial.

Traditionally, in vivo monitoring the survival of transfused platelets has been carried out by measuring radioisotope-labeled platelets. This labeling procedure requires significant manipulation of platelets and it is questionable if these platelets are comparable with un-manipulated platelets. Hence, establishment and validation of a high sensitive method for studying survival of un-manipulated transfused platelets would allow for measurement of a more true platelet survival kinetic for use in clinical settings.

Aims: The aim was to establish, optimize and validate a high sensitive flow cytometric method that allowed the detection of minor amounts (<0.015%) of transfused platelets. The established method will be used in the PROFNAIT phase 0 and phase 1/2 clinical trials for measurement of in vivo platelet survival.

Methods: The established flow cytometric assay was based on the method published by Vetlesen et. al (Transfusion, 2012) using HLA-A2 or HLA-A9 mismatch between donor and recipient. Standards and quality control samples were prepared by adding small amounts of HLA A2 or HLA A9 positive platelets (0.015–1%) to different batches of platelet rich plasma (PRP) from HLA A2 or HLA A9 negative donors. A total of 10E6 platelets, at a flow rate of 10 μl/min, were collected and isolated in a FCS/CD41 (PERpCy5.5, Beckman Coulter) dot plot. Further, the targeted populations of HLA A2 or HLA A9 positive platelets were identified in a SSC/FL1 dot plot using FITC conjugated anti-HLA A2, 28 IgG2a or anti-HLA A9 IgG2b monoclonal antibodies (One Lamda Inc). Parameters to be validated were; selectivity, carry-over, lower limit of detection (LLOQ), calibration curve, accuracy, precision, and robustness.

Results: HLA-A2 and HLA-A9 positive platelets exhibited strong signals (FL1) that allowed for discrimination of 0.015% positive platelets among 99,985% negative platelets. The validation confirmed the acceptance criteria of an accuracy and precision within 15% (respectively 20% for LLOQ), a linearity (R^2) of >0.97 and a LLOQ of 0.015%.

Summary / Conclusions: We successfully established a high sensitive method for measurement of the natural clearance of transfused platelets. The method validation was according to EMAS guidelines and fulfilled the requirement of Good Laboratory Practice (GLP).

Working Party Session on Clinical – Paediatric Sub Group

5A-S38-01
STRATEGIC 'BIG DATA' INITIATIVES IN PEDIATRIC TRANSFUSION MEDICINE

R Goel

Laboratory Medicine, Pathology and Pediatrics, New York-Presbyterian Hospital, Weill Cornell Medical College, New York, United States

Pediatric/neonatal transfusion and blood management practices remain relatively understudied and underrepresented areas of transfusion medicine, despite being a highly transfused population. Still, nearly two decades into the 21st century, a majority of clinical practices continue to extrapolate results from adult studies and apply them to neonates and children. There remains a critical need for not only compelling tangible, evidence-based opportunities in neonates and pediatric populations for filling the identified gaps in knowledge, but also the eventual dissemination of research results directly applicable to these vulnerable populations; thus ensuring translation and integration of the evidence into routine practice of pediatric and neonatal transfusion medicine. Transfusions of red blood cell (RBCs), platelets, and plasma are critical therapies for pediatric populations ranging from intrauterine transfusions, to transfusing preterm neonates in the neonatal Intensive care unit (NICU), to treating the critically ill child in the pediatric intensive care unit (PICU), on extracorporeal membrane oxygenation, to the child/adolescent/young adult in need of a solid organ or hematopoietic cell transplant. Those involved in clinical care for neonatal and pediatric patients recognize that significant physiological adaptations intrinsic to the transition from fetus to neonates to childhood and adolescence are the context in which these therapies are administered. Other important considerations to treat these patients include the maternal-fetal pair; changing body weight; blood and plasma volumes, developing renal, hepatic, hematologic, and immune systems; in addition to the effects of drug-related toxicants and environmental factors on the developmentally evolving neonate and child. 'BIG DATA' in PTM may be the answer to some of the problems identified in the NHLBI seminars; such as small sample size, difficulty in getting IRB approvals and consent and difficulties in RCTs in neonates and children due to very slow enrollment and thus remaining underpowered to study various outcomes. Alternatively, utilizing some large databases and registries which allow retrospective as well as longitudinal analyses while employing robust statistical tools is a very attractive and feasible option while appropriately acknowledging the multiple inherent limitations of such study designs. Some of the nationally representative databases e.g. KID, PED NSQIP, PHIS and the Vermont-Oxford Neonatal Database are key potential treasure troves and robust tools that may help to answer some vital PTM questions.

5A-S38-02
EPIDEMIOLOGY, PRACTICE PATTERNS AND OUTCOMES FOR CHILDREN TRANSFUSED FOR LIFE THREATENING HAEMORRHAGE

P Spinella

No abstract available

5A-S38-03
WHAT HAVE WE LEARNED FROM NEONATAL AND PAEDIATRIC HAEMOVIGILANCE?

H New[1,2]

[1]Clinical, NHS Blood and Transplant [2]Haematology, Imperial College, London, United Kingdom

Haemovigilance collects information on adverse outcomes of transfusion: reactions and errors. This is part of the risk-benefit decision to transfuse, which also takes into account the clinical situation, transfusion 'threshold', and possible alternatives. Information on adverse outcomes aids development of transfusion guidelines and optimal patient blood management.

Neonates and children should be considered a distinct group when assessing transfusion adverse outcomes. Several countries have haemovigilance schemes which identify paediatric patients, including the Netherlands (TRIP) and Héma-Québec. The UK Serious Hazards of Transfusion Scheme (SHOT) has provided separate analysis of paediatric reports since 2007. From 2008–16, paediatric reports (<18 years) to SHOT were 1,075 out of the total 13,934 (7.7%). Of these, 63% were error-related, most commonly the 'incorrect blood component transfused', including failure to provide correct specific requirements.

There are many specific sources of error for paediatric transfusion, leading to disproportionate reporting particularly for neonates. Many countries provide special components, which may be incorrectly selected/requested by the laboratory/clinicians. Neonatal pre-transfusion compatibility testing includes maternal blood group/serology, increasing the chance of laboratory errors. Administration of blood components to neonates and small children requires specific giving sets and pumps, a source of technical errors. Miscalculation and prescription of transfusion volumes by inexperienced staff can result in significant over or under transfusion. Errors in communication between shared care centres can lead to missed special requirements such as irradiation. A focus on paediatric transfusion education is important for both laboratory and clinical staff.

Although preterm neonates are vulnerable recipients and likely to be susceptible to transfusion reactions such as transfusion-associated cardiac overload (TACO), there are relatively fewer reports of acute transfusion reactions to SHOT in this group, possibly due to under-recognition or to more subtle signs. Research is contributing to understanding potential adverse transfusion reactions in neonates and children, e.g. for transfusion associated necrotising enterocolitis (TANEC), transfusion-related acute lung injury (TRALI) and TACO. A UK prospective observational study has shown cardiorespiratory changes following neonatal red cell transfusion. The number of patients on paediatric intensive care with TACO has been shown to vary significantly depending on the diagnostic criteria used (De Cloedt et al, Transfusion 2018 https://doi.org/10.1111/trf.14504). The studies emphasise the need for clinical awareness of paediatric transfusion reactions, further research into their true incidence, and the development of appropriate definitions for this age group.

Reports to SHOT have also highlighted specific areas of risk in complex specialised situations including fatal transfusion associated graft vs host disease following intrauterine transfusion with maternal blood (SHOT 2012 report), morbidity and delays to neonatal exchange transfusions, and unusually high supernatant potassium levels in red cell units from donors with a mutation which increases potassium leakage on cold storage (SHOT 2013 report; Bawazir et al, Transfusion 2014;54:3043–3050). Lessons learned have been incorporated into recommendations in the recent British Society for Haematology fetal, neonatal and paediatric transfusion guidelines (New et al, B J Haem 2016;175:784–828).

Plenary Session on Platelets

PL4-01
IN VITRO PRODUCTION OF PLATELETS

B Dykstra, J Valdez, C Peters, L Beaulieu and J Thon

Platelet BioGenesis, Cambridge, United States

Platelets are the principal blood cells responsible for clot formation and blood vessel repair at sites of active bleeding. Platelet transfusion units (3x10ˆ11 platelets per 200–400 ml) are presently derived exclusively from human volunteers, for which mounting demand exceeds supply by ~20%. We are developing scalable, cost-competitive, human induced pluripotent stem cell (hiPSC)-derived platelets from an FDA-approved, cGMP-compliant hiPSC line to meet this clinical need.

We have established a serum and feeder-free megakaryocyte differentiation process (Feng et al. Stem Cell Reports, 2014), and have since identified a primary and

backup cGMP-compliant hiPSC line from which we are generating proplatelet-producing megakaryocytes and platelet. We are beginning to translate our megakaryocyte differentiation protocol into industrial scale bioreactors to increase overall yield and decrease platelet unit cost. hiPSC-megakaryocytes and resulting platelets express relevant biomarkers, size, and ploidy (by flow cytometry), morphology and ultrastructure (by microscopy), and growth factor, cytokine, and chemokine composition (by Luminex array).

To further increase our overall platelet yield we developed a millifluidic platelet bioreactor that exposes megakaryocytes to physiologic shear stresses of flowing blood (Thon et al. Blood, 2014). We have since begun industrially manufacturing our devices from cGMP-compatible thermoplastics, scaled our platelet bioreactor to support larger volumes, defined the pressure and shear forces triggering platelet production, improved the separation/concentration of our platelets from progenitor cells, and have begun automating bioreactor operation. Functionally, our bioreactor-derived platelets are resting and express activation biomarkers upon agonist exposure in vitro. Studies are presently being extended into mice.

Platelet production is poised to become among the first stem cell-derived tissue engineering platforms advanced for clinical use and represents a major first step toward a sustainable, donor-free blood system.

PL4–02
NOVEL ROLES FOR PLATELETS IN HEALTH AND DISEASE

MT Rondina

Molecular Medicine, University Of Utah, Salt Lake City, United States

Platelets are one of the few eukaryotic cells that live and function without a nucleus. Because they are anucleate, platelets have long been categorized as simple cells that inherit a predictable and fixed hemostatic toolset from their parent megakaryocytes. Emerging evidence, however, demonstrates that platelets are far more dynamic and complex than previously considered. It is now well accepted that platelets regulate thrombo-inflammation and are critically involved in the development, progression, and evolution of numerous human diseases including arthritis, atherosclerosis, cancer, diabetes, and inflammatory syndromes. As new roles for platelets have emerged, there has been a parallel appreciation that these anucleate cells possess complex molecular machinery that governs their behavior. This machinery includes an extensive repertoire of mRNAs and non-coding RNAs (ncRNAs). Using emerging technologies such as Ribosomal Footprinting to profile the transcriptional and translational landscape of human platelets in health and disease, coupled with in vitro and in vivo validation and functional determination, novel roles for previously unknown proteins in platelets and megakaryocytes have been discovered. This State-of-the-Art lecture will discuss how inflammatory stressors alter the regulation of gene expression in platelets and megakaryocytes and the functional responses that follow.

PL4–03
PREVENTION OF HLA ALLOIMMUNE PLATELET REFRACTORINESS

K Pavenski[1,2]

[1]*Laboratory Medicine, St. Michael's Hospital and University of Toronto* [2]*Medicine, St. Michael's Hospital and University of Toronto, Toronto, Canada*

Platelet refractoriness refers to lack of appropriate platelet increment following transfusion of platelets. Platelet refractoriness is associated with increased bleeding and increased health resource utilization. Most cases of refractoriness are due to non-immune factors such as splenomegaly, infection, medications, bleeding among others. Less than 20% of cases of platelet refractoriness are thought to be caused by alloimmunization against HLA Class I and/or HPA antigens which are present on the platelet surface. Alloimmune platelet refractoriness is managed by provision of matched platelet transfusions. A few methods of HLA selection as well as platelet crossmatching are available and usually lead to improved post transfusion increments. However, none of these methods were shown to affect any clinically significant outcomes. Furthermore, these methods are generally expensive as well as time and resource intensive. Prevention of alloimmune refractoriness therefore should be the goal. Both product and recipient factors play a role in pathogenesis of alloimmune refractoriness. There does not appear to be a dose response relationship and only about 30% of alloimmunized patients are refractory. In murine models, alloimmunization occurs most efficiently when a platelet product contains both platelets and white cells. MHC molecules (free or platelet associated) in platelet product are

taken up by RES allowing antigen presenting cells to stimulate the recipient's immune response and produce IgG anti-donor antibodies. These IgG antibodies can effectively bind donor platelets and cause their premature destruction. Furthermore, to enhance immunity against donor MHC Class I molecules, direct allorecognition of donor antigen presenting cells is necessary. This means that the reduced numbers of donor white cells in the platelet product will result in less robust immune response in a recipient. Therefore, it is not surprising that multiple studies have shown that leukoreduction significantly reduces the rates of alloimmunization and alloimmune platelet refractoriness. In a recent study involving a canine model, leukoreduction in combination with Mirasol pathogen reduction technology resulted in further, significant reduction in alloimmunization suggesting that alloimmunization can be effectively prevented. The mechanism for this salutary effect of PRT has not yet been elucidated.

Blood Products – The Relationship Between Donor Characteristics and Transfusion Outcome

5C-S39-01
EFFECT OF BLOOD DONOR SEX AND PARITY ON THE OUTCOME OF TRANSFUSED PATIENTS – THE SCANDAT EXPERIENCE

G Edgren[1,2] and H Hjalgrim[3,4]

[1]*Medical Epidemiology and Biostatistics, Karolinska Institutet* [2]*Department of Cardiology, Södersjukhuset, Stockholm, Sweden* [3]*Department of Epidemiology Research, Statens Serum Institut* [4]*Department of Hematology, Rigshospitalet, Copenhagen, Denmark*

Background: Several recent studies have investigated whether different characteristics of blood donors, such as demographic variables and parity status, affect the survival of transfused patients. However results have, been variable, with at least two studies finding that patients who are transfused with red-cell units from female donors have an increased mortality, but larger studies unable to replicate such effects.

Aims: Recognizing methodological inconsistencies and problems with missing data in previous studies, we investigated the effect of blood donor sex and parity on the short- and long-term survival of transfused patients, using data from the Scandinavian Donations and Transfusions (SCANDAT) database, with nationwide, complete data from Sweden and Denmark.

Methods: We set up a retrospective cohort study of all patients transfused in Sweden and Denmark between 2003 and 2012. Patients were followed for short- and long-term mortality, starting from their first transfusion in the period. The effect of number of red-cell transfusions from female donors or from parous female donors, on the risk of death was estimated in separate models using Cox regression with time dependent covariates. Adjustment was made for total number of red-cell transfusions using flexible methods, and other key confounding factors. We also investigated the risk of additional transfusions in relation to the sex of the contributing donor, with adjustment for donor hemoglobin concentration.

Results: A total of 923,732 patients were included. Among these, we observed 468,501 deaths. Neither number of red-cell units from female donors (hazard ratio [HR], 1.00; 95% confidence interval [CI], 0.99–1.00), nor number of red-cell units from previously pregnant donors (HR, 1.00; 95% CI, 1.00–1.01) were associated with recipient mortality. Analyses restricted to male recipients younger than 50 years, yielded virtually identical results (HR, 1.01; 95% CI, 0.96–1.07). No conspicuous pattern emerged when the number of units from female donors or previously pregnant donors was categorized. Patients who received ³10 units from previously pregnant donors had an identical risk of death (HR, 1.05; 95% CI, 0.98–1.12) as patients who received no such unit. Analyses of 30-day mortality showed virtually identical results, but with wider confidence intervals on account of fewer deaths. In analysis of risk of re-transfusion, blood units from female donors resulted in a 7% higher risk of needing additional units (HR, 1.07; 95% CI, 1.06–1.08). Adjustment for donor hemoglobin concentration removed this association (HR, 1.01; 95% CI, 1.00–1.02), indicating that blood units from female donors have a poorer efficacy on account of their lower hemoglobin concentration.

Conclusions: In this large-scale analysis of donor demographics and parity status on the outcomes of transfused patients we find no effect on mortality overall, nor in selected sub-groups which have been implicated in previous studies. Due to the completeness of the data and large sample size, these results should provide reassurance to the transfusion medicine community.

5C-S39-02

THE EFFECT OF SEX OF THE DONOR ON THE SURVIVAL OF TRANSFUSION RECIPIENTS

RA Middelburg[1,2]

[1]Clinical Transfusion Research, Sanquin Research [2]Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

The first discussions about the effect of sex of the donor on the survival of transfusion recipients appeared in the literature during the late 1940's. During the 1950s, reports of transfusion reactions associated with "leuko-agglutinins" (i.e. leukocyte agglutinating antibodies) were published. It was soon shown these leukocyte-antibodies were more common among multi-parous donors (i.e. donors with several previous pregnancies). In the 1980's and 1990's transfusion-related acute lung injury (TRALI) was reported to be the main transfusion reaction associated with these leukocyte-antibodies. Subsequent research confirmed the role of plasma rich blood products from female donors in the etiology of TRALI. As a corollary plasma from female donors was also shown to be associated with increased mortality, especially of pulmonary causes.

However, modern red blood cells contain so little plasma that any possible association of female blood donors with an increased incidence of TRALI was shown to be immeasurably weak. Therefore, it came as somewhat of a surprise when in 2011 we observed an association between sex of the donor and mortality of transfusion recipients. The association was especially strong for young male recipients of red blood cells from female donors (hazard ratio (HR): 1.8 (95% confidence interval (CI), 1.2 to 2.7)). Subsequently, several other groups have confirmed increased mortality of male recipients of female blood products (pooled HR from 5 studies: 1.4 (CI: 1.1 to 1.6)). Meanwhile, we also performed a confirmation study which showed two things.

First, the association of transfusions from female donors with increased mortality was limited to male recipients under 50 years of age and female donors with previous pregnancies.

Second, ignoring these two important effect modifiers resulted in a dilution of the effect to the point of near undetectability.

For recipients under 50 years of age the difference in cumulative mortality between recipients of a single transfusion from a male donor and from an ever-pregnant donor was: 6.1% (CI: 1.7 to 10%) for male recipients, while the negative control group (i.e. female recipients) showed no relevant difference (−0.9% (CI: −3.8 to 1.9%)). For the alternative negative control group (i.e. male recipients but never pregnant female donor) the difference in cumulative mortality was −0.005 (CI: −0.029 to 0.019).

The interpolated HR for male recipients under 50 years of age of transfusions from ever-pregnant donors was 2.2 (CI: 1.3 to 3.8), while for the negative control group (i.e. female recipients) it was 0.6 (CI: 0.2 to 1.5). For the alternative negative control group (i.e. male recipients of transfusions from never pregnant female donors) the HR was 0.8 (CI: 0.4 to 1.9).

In conclusion, in some populations it might seem like there is little to no effect of sex of the donor on the survival of transfusion recipients. This could be explained by the relative contributions of males under 50 years of age to the population of transfusion recipients and of previously pregnant donors to the population of female donors. The biological mechanism still needs to be elucidated and could lead to other contributing explanations, potentially including product preparation and storage time.

5C-S39-03

UNTARGETED METABOLOMICS ANALYSES OF REDS-III RECALLED DONORS IDENTIFY METABOLIC MARKERS OF OSMOTIC AND OXIDATIVE HEMOLYSIS BASED ON DONOR GENDER, AGE, ETHNICITY AND STORAGE ADDITIVES

A D'Alessandro[1], J Reisz[1], R Culp-Hill[1], T Nemkov[1], S Gehrke[1], X Fu[2], T Kanias[3], M Gladwin[3], G Page[4], S Kleinman[5], M Busch[6] and J Zimring[7,8]

[1]Biochemistry and Molecular Genetics, University of Colorado Denver, Aurora [2]1551 Eastlake Avenue E, Suite 100, Bloodworks Northwest, Seattle [3]Vascular Medical Institute, University of Pittsburgh, Pittsburgh [4]RTI International, Atlanta, United States [5]1281 Rockcrest Avenue, Center for Blood Research, Victoria, Canada [6]Blood Systems Research Institute, San Francisco [7]1281 Rockcrest Avenue, Blood Systems Research Institute, Seattle [8]for the National Heart, Lung, and Blood Institute Recipient Epidemiology Donor Evaluation Study III Program, REDS III, United States

Background: Background Spontaneous hemolysis is one of the gold standards to determine storage quality of packed red blood cells (RBCs) per Food and Drug Administration criteria. Once transfused into the recipient, RBCs are also exposed to oxidative and osmotic stressors, which may aggravate hemolysis and impact transfusion efficacy and safety by compromising vasodilation, and promoting pro-inflammatory or septic complications. In the light of these considerations, the National Heart, Lung, and Blood Institute Recipient Epidemiology Donor Evaluation Study III (REDS-III) program launched the Red Blood Cell-Omics (RBC-Omics) study. One aim of the RBC-Omics study is to define genetic and metabolomic bases for donor-specific differences in RBC storage stability.

Aims: Aims To identify small molecule markers of oxidative and osmotic hemolysis in donors characterized by extreme values of spontaneous, oxidative and osmotic hemolysis.

Methods: Methods High throughput hemolysis assays were developed and used to evaluate stored RBC samples from 13,770 African American, Asian, white, and Hispanic blood donors from 4 geographically diverse regions in the United States. Leukocyte-reduced RBC concentrate-derived samples were stored for 39 to 42 days (1–6°C) either in additive solution 1 (AS-1) or AS-3 and then evaluated for storage, osmotic, and oxidative hemolysis. Six hundred and sixty-four donors showing extremes in spontaneous, oxidative or osmotic hemolysis were recalled for a second donation, and stored LR-RBC component-derived samples were evaluated for spontaneous and stress hemolysis at storage days 10, 23 and 42 and aliquots processed for metabolomics were stored in LN2; serial samples from 200 recalled donors were selected for untargeted metabolomics analyses via Ultra-High-Pressure Liquid Chromatography-Mass Spectrometry at the University of Colorado Denver.

Results: Results Untargeted metabolomics and lipidomics analyses confirmed and expanded upon the previously identified small molecule markers of the metabolic age of stored packed RBCs. Quantitation of these markers (including hypoxanthine, lactate, 5-oxoproline and reduced glutathione) through spiked in stable isotope-labeled internal standards identified ranges predictive of oxidative and osmotic hemolysis. Unsupervised data analysis through Compound Discoverer identified >600,000 total features, >5,000 putative metabolites. Preliminary statistical analyses of these data revealed >4,133 candidate small molecule markers of oxidative and osmotic hemolysis on the basis of donor gender, age, ethnicity and additive solution. High oxidative hemolyzers were characterized by significantly higher levels of adenosine triphosphate, as well as reduced and oxidized glutathione at all tested time point (P < 0.01 ANOVA).

Summary / Conclusions: Summary Unbalance of the energy-redox homeostasis axis (ATP/glutathione ratios) significantly correlates with donor-specific propensity to oxidative hemolysis. Ongoing mechanistic analyses including linkage to detailed genetic data from these donors will expand on the relevance of the observational findings reported here.

5C-S39-04

THE ASSOCIATION BETWEEN DONOR SEX AND AGE AND MORTALITY IN BLOOD TRANSFUSION RECIPIENTS: AN EXPLORATORY ANALYSIS

NM Heddle[1], R Cook[2], Y Liu[3], M Zeller[1], R Barty[4], J Acker[5], J Eikelboom[1] and D Arnold[1]

[1]Medicine, McMaster University, Hamilton [2]Statistics and Actuarial Sciences, University of Waterloo, Waterloo [3]McMaster Centre for Transfusion Research, McMaster University [4]McMaster Centre for Transfusion Research, McMaster University, Hamilton [5]Centre for Innovation, Canadian Blood Services, Edmonton, Canada

Background: There are conflicting reports as to an association between blood donor sex and/or age and mortality in transfused recipients. A Canadian study found that

recipient mortality was increased after exposure to red blood cells (RBCs) from female donors and younger donors. Analysis from Scandinavian countries found no associations.

Aims: We analysed data from a large transfusion registry to further explore the association between donor characteristics (sex and age) and in-hospital mortality in transfused adults.

Methods: This exploratory retrospective analysis used clinical and transfusion registry data (adults transfused between 2008 and 2014) with linkage to donor sex and age information from the blood supplier. Cox regression models were used controlling for risk variables and confounding variables as either covariates or using stratification. Variables were either fixed or time dependent. Fixed covariates included: recipient age, sex, and ABO group. Time dependent covariates included: exposure to an intervention during hospitalization; exposure based on the method of blood processing; and, exposure to fresh RBCs (stored ≤ 7 days). Fixed stratification variables included: diagnosis and fiscal year of admission. Time dependent stratification variables included: cumulative number of RBCs transfused; hemoglobin; creatinine; exposure to ABO non-identical RBCs; exposure to platelets; and, exposure to plasma. Time dependent variables were updated in the model as new information became available. A series of models were fitted exploring recipient outcome with donor sex exposure (female and male); donor age exposure (≤ 45 years and > 45 years); and, exposure to donor/recipient sex-mismatched RBC transfusions and donor age in one model. Exposures for each model were defined by mutually exclusive categories, and the outcome was in-hospital mortality.

Results: There were 25,219 patients who received 97,886 RBC units with 70% of the patients in the diagnostic categories of: cardiovascular (28.8%); neoplasms (15.6%); injuries (15.4%) and gastrointestinal (10.5%). 56.3% of transfused RBC units came from male donors: median age (all donors) was 45 years (IQR30-54). The risk of death was increased for females exposed to male RBCs (Hazard Ratio (HR) 1.31: 95% CI 1.02–1.69; P = 0.038); but not for males exposed to female RBCs (HR 1.13: 95% CI 0.92–1.39; P = 0.252). Risk of death for female recipients exposed to RBCs from donors ≤ 45 years was not different compared to exclusive exposure to donors >45 years of age (HR 1.10; 95% CI 0.87–1.39; P = 0.433); however, the risk of death for males exposed to RBCs from donors ≤ 45 years was higher compared to exclusive exposure to RBCs from donors >45 years (HR 1.32: 95% CI 1.06–1.66; P = 0.015). The interaction term indicated no difference between male and female recipients (P = 0.236), and when the interaction was removed from the model the HR for male and female recipients exposed to RBC from donors ≤ 45 years was 1.21: 95% CI 1.02–1.44; P = 0.026. The final model which included sex-mismatched RBC exposure and donor age showed that both variables were associated with increased mortality (sex mismatch HR 1.23: 95% CI 1.04–1.45; P = 0.017; donors ≤ 45 years HR 1.21: 95% CI 1.02–1.43; P = 0.031).

Summary / Conclusions: Donor/recipient sex mismatched RBC transfusions and transfusions of RBCs from donors ≤45 years were both associated with increased in-hospital recipient mortality. We did not find a statistically significant increased risk of in-hospital mortality with exposure to female RBCs, but a significantly increased risk was observed when females were exposed to male RBCs.

Management and Organisation – Clinical Audit and Education

5C-S40-01

ENHANCED EFFICACY OF AUDIT AND FEEDBACK TO IMPROVE TRANSFUSION PRACTICE: DESIGNING AND TESTING NOVEL FEEDBACK INTERVENTIONS IN A NATIONAL CLUSTER RANDOMISED TRIAL

S Stanworth[1] and F Lorencatto[2]
[1]Haematology/Transfusion, NHSBT/OUH, Oxford [2]Centre for Behaviour Change, UCL, London, United Kingdom

Background: Audit and feedback (A&F), defined as 'a summary of the clinical performance of healthcare providers over a specified time period', is a very widely used quality improvement strategy in transfusion practice. However, the effects of A&F are modest and highly variable. Evidence for continuing use of blood outside evidence-based recommendations raises questions regarding the efficacy of current transfusion A&F strategies and how to improve.

Aims: The AFFINITIE (Development & Evaluation of Audit and Feedback INterventions to Increase evidence-based Transfusion practIcE) research programme (funder NIHR) aims to apply behavioural theory and evidence related to A&F to develop and evaluate two theoretically-enhanced feedback interventions within the NHSBT National Comparative Audit (NCA) programme for blood transfusion.

Methods: The AFFINITIE programme described four interrelated workstreams:

1). Intervention development- a) analysis of existing feedback reports to identify discrepancies between the content and format of current NCA feedback reports and A&F theory and evidence, and b) observations of hospital meetings where transfusion feedback is discussed plus semi-structured interviews based on behavioural theory with staff from transfusion-related roles to identify barriers/enablers to hospitals responding to feedback.

2). Two linked 2x2 cluster-randomised trials embedded in NCA's to evaluate the (cost-) effectiveness of two enhanced interventions against standard NCA practice. Trial 1 audited surgical patient blood management; and trial 2 use of transfusions in haematology. The primary outcome was whether a transfusion was categorised as necessary or not (binary measure) and was measured at the patient level based on NCA follow-up audit data.

3). Parallel process evaluation to investigate intervention fidelity and 'how/why' the interventions achieved observed outcomes.

4). Exploring generalisability of AFFINITIE's findings to other national audit programmes beyond transfusion

Results:

1a). Current feedback reports were found to make limited use of theory-based behaviour change techniques or feedback characteristics likely to increase their effectiveness (e.g. goal-setting, action planning, multiple modalities, comparators). Intervention 1 ('enhanced content') was therefore developed to include specific guidance for audit-writing groups on how to prepare feedback reports for hospital staff that includes theory- and evidence-based content.

1b). Hospital's response to feedback was found to vary widely in terms of extent of localised planning, and depended upon supportive infrastructures and role clarity. Feedback often did not reach key individuals involved in transfusion, and had to be amended for local use. Intervention 2 ('enhanced follow-on') therefore was designed to consist of practical web-based tools to support dissemination planning and strategic decision-making (e.g. action planning around local response to feedback), plus telephone support to encourage engagement with tools by transfusion staff.

2). Recruitment to the national cluster trial was very good, and nearly all hospitals in England participated in the national audit of surgery and haematology (e.g. 135 clusters with data from 2714 patients for surgery). Analysis of outcomes is currently underway.

Summary / Conclusions: AFFINITIE describes a pragmatic research programme to enhancing and testing the effectiveness of A&F strategies, using the rigour of a randomised trial design. It provides a framework for implementation research to address the often poor and slow uptake of research into patient blood management practice.

5C-S40-02

IMPROVING BLOOD COMPONENT ORDERING PRACTICES IN A DEVELOPING COUNTRY BY INTRODUCING COMPUTER PHYSICIAN ORDER ENTRY [CPOE] SYSTEM

F Karim
Pathology and laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

Background: Ordering blood components is one of the most critical steps in transfusion safety. To facilitate physicians in ordering blood components and aid in decision making, computer physician order entry systems (CPOE) are used worldwide. The system helps physicians make appropriate requests and avoid unnecessary transfusions.

Aims: To improve blood component ordering practices in a developing country by introducing computer physician order entry system.

Methods: This quality project was initiated at blood bank of Aga Khan University Hospital, Karachi, Pakistan. PDSA [Plan, Do, Study, Act] was used as a methodology tool. In the planning phase, an audit was conducted on one thousand randomly selected blood component orders. The orders were reviewed for completeness and legibility. Deficiencies identified in audit were noted down. A team comprising of transfusion medicine consultants, blood bank manager and information technology personnel was formulated. In the Do phase, an in-house CPOE was designed after multiple meetings between the stakeholders. A clinical decision support option to promote evidence based transfusion practice was incorporated. The indications for transfusion were based on British committee for standards in Hematology (BCSH)

guidelines. The CPOE was linked to laboratory information system and to medical health record so information about treating physician, clinical diagnosis and lab results was automatically captured by system. The project was first piloted in medical unit in February 2016. Feedback was taken from end-users and from blood bank. Minor issues were rectified. Once the CPOE was validated, it was gradually implemented in all areas of hospital. Before implementation, awareness was created and presentations were given to end-users on how to use CPOE. A gradual shift was made from manual requests to online orders. By July 2016, the project was completed and successfully implemented across the hospital. In Study phase, post audit on blood component orders was done from March 2017 to November 2017 to evaluate blood ordering practices. In Act (A), CPOE use is continued.

Results: In the planning phase audit, completeness and legibility of orders was poor. Only the type and number of blood components were mentioned in 100% of slips. The information missing in orders included primary consultant's name in 76.1% (n = 761), the ordering physician's name in 53.8% (n = 538), clinical diagnosis in 97.5% (n = 975) and the reason for transfusion was missing in 99.4% (n = 994) blood orders. After identifying these deficiencies, CPOE was carefully designed and implemented. In the post CPOE implementation audit, total of 30,156 blood component orders were reviewed. [Packed red cells 56% (n = 16841), platelets 24% (n = 7227), FFP 18% (n = 5540) and cryoprecipitate 2% (n = 548)]. All blood orders (100%) gave complete information about clinical diagnosis, treating physician and ordering physician's name. Reason for transfusion was selected from the provided list in 55.7% (n = 16803) orders.

Summary / Conclusions: CPOE with clinical decision support was successfully implemented at our institution to improve ordering practices and to promote evidence-based transfusion practice. Development of in-house CPOE significantly improved the quality of orders in terms of legibility and completeness. It is a step forward to enhance transfusion safety in a developing country.

5C-S40-03

TRANSFUSION CAMP: A PROSPECTIVE EVALUATION OF A TRANSFUSION MEDICINE EDUCATION FIVE-DAY PROGRAM ON MULTI-SPECIALTY POSTGRADUATE TRAINEE ATTITUDES, KNOWLEDGE AND SELF-REPORTED BEHAVIOUR

Y Lin[1,2], A Alam[2], S Charge[3], C Cserti-Gazdewich[2], W Lau[2], C Lee[2], L Lieberman[2], P Nixon[2], W Owens[4], K Pavenski[2], J Pendergrast[2], E Saidenberg[5], N Shehata[2], R Skeate[6], E Tilokee[3] and J Callum[1,2]

[1]Department of Laboratory Medicine & Molecular Diagnostics, Sunnybrook Health Sciences Centre [2]University of Toronto, Toronto [3]Centre for Innovation, Canadian Blood Services [4]Ontario Regional Blood Coordinating Network [5]The Ottawa Hospital, Ottawa [6]Canadian Blood Services, Toronto, Canada

Background: Transfusion is the most common procedure administered in hospitals and prescribed by physicians of almost every specialty. The optimal method of postgraduate transfusion medicine (TM) education has not yet been determined. Transfusion camp is a novel approach to TM education with a centralized curriculum for postgraduate trainees from various specialties delivered locally and off-site to multiple universities.

Aims: To evaluate the Transfusion Camp education program on postgraduate trainee attitudes, knowledge acquisition and self-reported behaviour.

Methods: Transfusion camp was established in 2012 at the University of Toronto as a centralized local TM education curriculum delivered over five days across the academic year. Its target audience is non-hematology specialty based postgraduate trainees. Starting in 2016, in collaboration with Canadian Blood Services, Transfusion Camp was expanded to 6 Canadian and 1 United Kingdom university site. Didactic lectures given in Toronto were webcast to five sites for remote live-attendance and recorded for later viewing by the remaining two sites. Team-based learning seminars were delivered by local faculty at each site. Knowledge assessment using a validated 20 multiple choice question exam was conducted pre- and post-transfusion camp. Attitudes and self-reported impact on transfusion behaviour were collected through trainee surveys.

Results: In the 2016–2017 academic year, 160 postgraduate trainees attended at least one day; 143 attended at least 2 days; 113 attended at least 3 days; 94 attended at least 4 days; and 54 attended all 5 days. On each day, there was an average of 113 trainees attending (range 97–132). Trainees from 12 different specialty programs were represented. The top 5 specialties were anesthesia (43%); hematology (16%); pathology (13%); critical care medicine (7%) and obstetrics (7%). The average score on the pre-camp exam was 10.2 ($\pm$2.9) (N = 128) compared with the post-camp average score of 12.9 ($\pm$3.0) (N = 96) (P < 0.0001; mean difference 2.7; 95% CI 1.9–3.5). Of the 83 trainees who wrote both the pre-camp and post-camp

exam, 63 (76%) improved their scores, 6 (7%) had no change and 14 (17%) had worse scores. Improved scores were also seen at non-Toronto sites. At the end of transfusion camp, 92% rated their ability to obtain consent as good/very good /excellent; 77% rated their overall ability in managing transfusion related patient issues as good/very good/excellent; and 96% rated TM knowledge as very or extremely important in providing patient care. On the final evaluation survey of transfusion camp (N = 32),75% of respondents indicated that Transfusion Camp had impacted on their clinical practice. Examples included: minimizing unnecessary transfusion; transfuse one unit at a time; consider furosemide to prevent TACO; always give vitamin K for warfarin reversal; how to obtain transfusion consent; and how to manage transfusion reactions. 100% of respondents indicated that they would recommend transfusion camp to their colleagues.

Summary / Conclusions: Transfusion camp is a novel approach to the delivery of high quality TM education to postgraduate trainees. It is an example of a scalable intervention that has now expanded to 7 additional university sites. Transfusion camp has demonstrated a modest increase in TM knowledge, fostered a positive attitude towards TM and enabled a self-reported positive impact on transfusion practice.

5C-S40-04

TAILOR-MADE TRANSFUSION EDUCATION FOR AUSTRALIAN JUNIOR DOCTORS

C Flores[1], B Quested[2], T Spigiel[2], A Thomson[3], J Little[4] and B Saxon[2]

[1]Transfusion Policy and Education, Australian Red Cross Blood Service, West Melbourne [2]Transfusion Policy and Education, Australian Red Cross Blood Service, Adelaide [3]Transfusion Policy and Education, Australian Red Cross Blood Service, Sydney [4]Transfusion Policy and Education, Australian Red Cross Blood Service, Brisbane, Australia

Background: Early postgraduate training is a critical period for influencing junior doctors' current and future clinical transfusion practice. Within the Australian blood sector, there are multiple providers of online education to support best transfusion practice. The relevance or usefulness of the resources for junior doctors is unknown. Little is understood about Australian junior doctors' existing transfusion knowledge and its application in patient care.

Aims: To understand junior doctors' transfusion practice support and education preferences by: (1) determining and developing learner-defined practice support tools; and, (2) implementing and evaluating the utility of these tools.

Methods: The study was conducted in two phases from April 2016 to March 2017. Participation was voluntary.

Phase 1 involved focus group sessions in six hospitals. Transcripts of audio recordings were analysed using thematic analysis.

Findings were considered when developing the suite of transfusion practice support tools, presented as a Transfusion Orientation Pack. The pack addressed all priority transfusion topics identified by junior doctors in both print and online formats. Tools included practical advice on how to prescribe a transfusion (lanyard card); an infographic about patient blood management (PBM); a transfusion checklist; a transfusion practice flow chart; and adverse event recognition and management lanyard card and poster.

Phase 2 surveyed junior doctors' response to the tools provided during orientation in five hospitals.

Results: Fifty-two junior doctors participated in the focus groups. Their priority was to be able to practise safely, appropriately and confidently. Preferred format for transfusion learning included expert-led face-to-face education; printed tools e.g. lanyard cards; and, one app that covers essential aspects of transfusion practice. Adverse events management and practical transfusion prescribing were topics of most importance. An infographic to promote understanding of PBM was the least valued item.

Thirty-nine survey respondents found the transfusion practice support tools useful to assist their decision-making in everyday practice, particularly the transfusion overview poster and three lanyard cards. The majority of respondents would recommend use of the tools to complement clinical practice. Junior doctors reported that the support tools impacted their practice by learning something new and feeling reassured about their transfusion knowledge.

Summary / Conclusions: There is a need for improved education to ensure best transfusion practice. Australian junior doctors want immediate, practical, reliable transfusion information from credible sources to support them in practicing safely and confidently. Their educational needs are driven by real time patient management. Tailor-made transfusion practice support tools were developed after user input and assessed by junior doctors. These had high acceptance, were seen as valuable, easy to use and met expectations as a simple but comprehensive and authoritative

practice support tool. With 3,399 predicted interns for 2018 intake, 4,398 transfusion orientation packs, modified by the results of this study, were provided to hospitals across Australia. Promotion of the available resources and tools provided by the blood sector is important, and may translate into other institutions internationally.

5C-S40-05

THE EXPERIENCE OF THE INTERNATIONAL COLLABORATION FOR TRANSFUSION MEDICINE GUIDELINES (ICTMG) IN GUIDELINE DISSEMINATION

M Fung[1], H Hume[2], K Pavenski[3], S Nahirniak[4], R Kaufman[5], T Viner[6], S Torrance[6], D Landry[6] and N Shehata[7] on behalf of the International Collaboration for Transfusion Medicine Guidelines (ICTMG)

[1]The University of Vermont Health Network and University of Vermont, Burlington, United States [2]University of Montreal, Montreal [3]Department of Laboratory Medicine and Pathobiology, St. Michael's Hospital, Toronto [4]University of Alberta, Edmonton, Canada [5]Brigham and Women's Hospital and Harvard University, Boston, United States [6]Centre for Innovation, Canadian Blood Services, Ottawa [7]Departments of Medicine and Laboratory Medicine and Pathobiology, Institute of Health Policy Management and Evaluation, Mount Sinai Hospital, and Canadian Blood Services, Toronto, Canada

Background: The International Collaboration for Transfusion Medicine Guidelines (ICTMG) establishes evidence based transfusion medicine guidelines to optimize transfusion care. The intent of this international group is to increase the credibility of guideline development for transfusion medicine by using a widely collaborative effort leveraging consistent up-to-date methodology to enable timely and cost-effective creation of transfusion medicine guidelines. The ICTMG consists of hematologists, hematopathologists, and methodologists from 8 countries. In addition to publishing guidelines, and to facilitate guideline dissemination, the ICTMG has created a website and podcasts for its guidelines.

Aims: The aim of this assessment is to determine the impact of the ICMTG guideline on platelet transfusion in patients with hypoproliferative thrombocytopenia, as well as the impact of the ICTMG website and podcast as modalities for dissemination of guideline recommendations.

Methods: The ICTMG assembled an expert panel to conduct a systematic review and develop recommendations for platelet transfusion for patients with hypoproliferative thrombocytopenia that included recommendations for prophylactic platelet transfusion triggers, platelet dose, the use of apheresis compared to whole blood derived platelets, the use of ABO compatible platelets, the need for Rh immune globulin for patients for patients who are RhD negative and receive RhD positive platelets and management of platelet refractoriness. The ICTMG partnered with the AABB to produce a podcast for platelet transfusion - Platelets Unplugged

The Sticky Truth as the guideline developed by the AABB complemented the guideline developed by the ICTMG. The 43 min podcast was divided into three segments to enhance use. The guideline and podcast were made available at ICTMG.org, and the podcast was also posted at AABB.org. The ICTMG developed a POWERPOINT presentation of the methods for guideline development and a summary of the recommendations for aiding implementation for guideline users. Podcast downloads; website access and guideline citations were monitored to assess guideline dissemination.

Results: The platelet guideline was published in 2014. The guideline has been cited by 22 articles and read by 274. Podcasts were accessed on 234 occasions from October 2017 to January 2018 from the ICTMG website. The AABB website has received 1969 page views for all its podcasts including the podcast for platelet transfusion. ICTMG.org has received 1,662 page views from April 2017 to January 2018. There were 276 visits to the education and resources page containing the guideline and presentation. Page views were predominantly from Canadian sites (51%), but also included the United States (18%), Australia (3%), United Kingdom (3%), India (2%), Netherlands (2%), Brazil (2%), Italy (2%), Philippines (1%) and 35 other countries (<1% each).

Summary / Conclusions: Dissemination of guideline using web tools and podcasts appears to be effective in circulating guideline information. Future studies are needed to determine whether these modalities can improve implementation of guideline recommendations.

Donor Recruitment and Retention

5C-S41-01

STRATEGIES TO PROMOTE REPEAT DONATION IN FIRST-TIME BLOOD DONORS IN GHANA

L Asamoah-Akuoko[1], H Ullum[2], O Hassall[1] and I Bates[1]

[1]Liverpool School of Tropical Medicine, Liverpool, United Kingdom [2]Department of Clinical Immunology, Copenhagen University Hospital, Copenhagen, Denmark

In Ghana, there is shortage of blood for transfusion all year round, with a deficit of about 35% of the annual national requirement of 250,000 units. Voluntary non-remunerated blood donors (VNRBDs) are uncommon and contribute only 36% of the donated blood. Repeat donations constituted 38.2% of donations by VNRBDs at the Southern Area Blood Centre of the National Blood Service, Ghana in 2016.

Aims: To identify the perceptions about blood and blood donation; motivators for, and deterrents to blood donation; and intention to return to donate blood among first-time VNRBD and family replacement blood donors (FRDs); and recommend interventions to increase repeat donations among first time donors.

Methods: A cross-sectional survey of 250 first time VNRBDs and 255 first-time FRDs selected from the SABC was conducted. A questionnaire, designed to determine perceptions, motivators and deterrents to blood donation and intention to return to donate among first time donors, was used for data collection from 24th June to 12th October 2015.

Results: Of 540 persons who accepted to respond, 505 completed the survey. Respondents were aged 18–58 years (median, 25 years; interquartile range 21–31 years). Most respondents were below 35 years (87.4%), male (72.5%) single (73.3%), Christian (93.7%); employed (58.8%), had at least a basic education (98%), and lived with parents/family (54.3%). VNRBD were younger (median, 23 years; interquartile range 20–29 years) than FRD (median, 28 years; interquartile range 23–33 years). Factors that positively predicted intention to return to donate were: convenient access to donation sessions (OR = 2.6, 95% CI 1.5–4.6; P = 0.001); if Ghana needs blood (OR = 2.5, 95% CI 1.1–6.0; P = 0.033); if it makes one feel good about himself/herself (OR = 1.8, 95% CI 1.0–3.2; P = 0.040); SMS/email reminders (OR = 2.7, 95% CI 1.54–4.8; P = 0.001); TV, radio or newspaper advertisement (OR = 2.9, 95% CI 1.6–5.1; P).

5C-S41-02

RECEIVING A TEMPORARY DEFERRAL: DO DONORS' KNOWLEDGE AND EMOTIONAL REACTIONS IMPACT ON THEIR INTENTION TO RE-DONATE?

N Van Dyke, C Gemelli, A Thijsen, N Van Dyke and T Davison
Clinical Services & Research, Australian Red Cross Blood Service, Melbourne, Australia

Background: Temporary deferrals negatively impact on donor retention. Research has found that the type of deferral, donor status and duration of the deferral are predictors of donor return post deferral; however, these aspects are not amenable to interventions. Areas that require further investigation are the donor's level of knowledge regarding the deferral and their emotional response to being temporarily deferred. Anecdotal evidence from the Australian Red Cross Blood Service (Blood Service) blood collection staff involved in applying deferrals suggested that some donors display feelings of anger, disappointment or rejection when receiving a deferral, and many are unclear about the reason for the deferral; however, we lack information from the donor's perspective. If poor knowledge and negative reactions to receiving a deferral are present and associated with intention to re-donate, it may be possible to develop tailored strategies to improve donor retention.

Aims: The aim of this study was to investigate donor knowledge about the deferral and their emotional reactions to receiving a deferral and to identify whether these aspects impact on their intentions to re-donate.

Methods: A survey was sent to 1,613 donors who had recently received a temporary deferral during a pre-donation telephone call or within the donation centre when attending to donate. The survey focused on the information received at the time of the deferral, the donor's understanding of the deferral, degree to which the donor experienced a number of emotions, and intention to re-donate.

Results: A total of 435 donors completed the survey (Response rate of 27%), with 80% of donors receiving a deferral during a pre-donation telephone call and 20% while attending a donation centre to donate.

Compared to those deferred via telephone, donors deferred while attending their donation appointment were less satisfied with the quantity and quality of information they

received about their deferral and felt less knowledgeable about why they were deferred. Only 63% of donors in the study could correctly identify they were currently ineligible to donate, while 14% reported they were currently eligible and 23% reported being unsure. Emotional responses impacted negatively on intention to return. Key emotions included anger, sadness and disappointment. These negative emotions were reported more strongly by donors deferred in centre while donors deferred via the telephone reporting higher levels of calmness

Summary / Conclusions: This study provides insights that can assist blood collection agencies in developing potential strategies to prevent the future lapse of donors who are temporarily deferred from donation. It would be beneficial to increase the number of donors who are notified of their ineligibility prior to attending the donation centre. Ensuring that donors understand the reasons why they were deferred at the time of the deferral and when they are eligible to return also appears important. The study findings demonstrate the impact of emotions experienced when receiving a deferral on intention to re-donate. The development and evaluation of strategies to address these emotions at the time of the deferral, is worth consideration.

5C-S41-03

MOBILE BLOOD COLLECTION AND ITS ROLE IN INCREASING VOLUNTARY UNPAID BLOOD COLLECTIONS: AN 8-YEAR GHANA EXPERIENCE

EN Dei[1], L Asamoah-Akuoko[1,2] and J Ansah[3]

[1]Research and Development, National Blood Service Ghana, Accra, Ghana [2]Liverpool School of Tropical Medicine, Liverpool, United Kingdom [3]National Blood Service Ghana, Accra, Ghana

Background: Blood donation rates in some African countries are generally very low. Ghana has not been able to meet its blood requirements, leaving a deficit of 31–42% from 2009 to 2016 and a blood collection per 1000 population of 6. The National Blood Service, Ghana (NBSG) applies the best accessible evidenced-based strategies to increase blood collections from voluntary unpaid blood donors (VUBDs). In 2013, the NBSG instituted a strategy within the catchment area of its Southern Area Blood Centre (SABC) to increase blood collections from VUBDs. An analysis of donor recruitment activities informed the development of the strategy, aimed at boosting the performance of Donor Services staff. Key components of the strategy included formation of permanent mobile blood collection teams, zoning the catchment area and setting targets for the teams.

Aims: To analyze the effectiveness of the strategy in increasing voluntary unpaid blood donations, using data on blood collections by the SABC from 2009 to 2016.

Methods: Based on blood needs, four blood collection teams were formed. Each team comprised a minimum of six members including a blood donor recruitment officer (BDRO), donor care nurses and assistants, orderlies and a driver. The catchment area was divided into four zones based on population, organized donor panels (educational and religious institutions, workplaces, organized groups), and distance from the Blood Centre. Each team was assigned a zone and given blood collection targets to meet. BDROs were encouraged to stop concentrating all their activities on weekend days, and to utilized weekdays for educational talks and blood donation activities for their zones, based on the target groups' calendar of activities such as schools holidays or exams, religious activities and festivities. The blood collection teams also increased the number of blood collections sessions in educational institutions. An analysis of the trend of total blood collections and the percentage of blood collections from VUBDs versus family replacement donors (FRDs) pre and post implementation was conducted.

Results: Prior to the implementation, 289 mobile sessions were conducted in 2012. After the implementation, mobile blood donation sessions increased by 23% to 355 in 2013. Blood collection increased from 24,600 in 2009 to 27,653 in 2012, prior to implementation, as compared to an increase from 32,894 in 2013 to 34,274 in 2016. This shows a gradual increase (2–6%) from 2009 to 2012, compared to a sharp increase (19%) right after the implementation in 2013. Blood collections from VUBDs was always lower than collections from FRDs (37–44%) before the implementation. Two years after the implementation, collections from VUBDs was higher than collections from FRDs (51% and 53% in 2015 and 2016 respectively).

Summary / Conclusions: Our findings show that blood collections by the SABC, and percentage of blood collections from VUBDs, after the implementation of the strategy was significantly higher as compared to before implementation.

5C-S41-04

BLOOD DONATION WILLINGNESS, MOTIVATORS AND BARRIERS IN BLOOD DONORS AND THE GENERAL POPULATION IN SURINAME

EM Huis In 'T Veld[1], M Adhin[2], G Jalink[3], E Burleson[3] and M Smid[4]

[1]Donor Studies, Sanquin Blood Supply, Amsterdam, Netherlands [2]Faculty of Medical Sciences, Anton de Kom University [3]Nationale Bloed Bank Rode Kruis, Paramaribo, Suriname [4]Sanquin Consultancy Services, Sanquin Blood Supply, Amsterdam, Netherlands

Background: The choice to become a donor is personal but can be influenced by external factors (e.g. opening times) or personal factors (e.g. attitudes towards the donation procedure). In Suriname, the need to recruit new donors is high. As part of the collaborative Twinning Project Capacity Building Surinam Red Cross – Blood Bank (NBB-RK), and Sanquin in the Netherlands, the main author visited the Blood Bank in Paramaribo to train staff to improve donor recruitment and to perform retention research.

Aims: To assess willingness to donate blood and key barriers and motivators in the general, non-donor population of Suriname. Furthermore, we compared these aspects to the attitudes of existing blood donors.

Methods: Two studies were developed; a "Donor Satisfaction" survey (N = 194 blood donors), and a "Donor Motivation" survey (N = 254 non-donors from the general population). The donor sample was recruited among donors who attempted to donate in Paramaribo and Nickerie during a two week window, and filled out the questionnaire on location. The non-donor sample was recruited online, using snowball sampling among existing donors. Participants were asked to rate to what extent they agree with 7 motivators and 16 reasons to become a donor (on a 5-point Likert scale). Attitudes towards blood donation were rated (on a bipolar 7-point scale), as well as the intention to donate in the coming year (on a 5-point Likert scale). Further, the non-donor sample was asked to rate how much 23 donation barriers stopped them from becoming a donor and what their preferred method of communication would be.

Results: Donation attitudes were significantly more negative among non-donors, who especially thought donating was more repulsive, unpleasant, annoying and scary. Non-donors indicated that more information about the procedure, better use of social media, and the ability to donate together with family or friends might motivate them to donate. Furthermore, being asked by a religious leader was related to a higher donation willingness. Donors were more likely to believe that donating is good for their health and the right thing to do, whereas non-donors were more likely to say that they would donate to show others that they are a good person. However, only non-donors who indicated that they thought donating might be good for their health showed a higher donation intention.

Donation barriers among non-donors could be clustered into three main types of barriers, relating to fear, lack of knowledge, and health concerns. Knowledge (e.g. about the procedure) positively, whereas fears (e.g. needles) negatively impacted donation intention. Most non-donors would prefer to be recruited via WhatsApp (37,4%), social media (39%) and e-mail (42,9%).

Summary / Conclusions: Future recruitment campaigns in Suriname could benefit by involving religious leaders and better use of social media, WhatsApp and email, and also by a focus on educational aspects regarding the whole procedure and its consequences, in addition to the appeal to "help people". Furthermore, interventions aimed at helping people to cope with certain fears (of needles, adverse reactions, or pain) could benefit donor recruitment and retention.

5C-S41-05

SOCIAL MEDIA AND BLOOD DONOR BEHAVIOR: NEW WAYS OF RESEARCH AND COMMUNICATION

E Merz[1,2] and P Kerkhof[3]

[1]Donor Studies, Sanquin Blood Supply [2]Sociology [3]Communication Science, Vrije Universiteit, Amsterdam, Netherlands

Background: Various studies have examined stopping reasons for blood donors, mostly using survey designs. Such studies provide important input for developing effective retention strategies. Until now, to our best knowledge, social media data have not been used as data source for research and retention. Analysis of social media data can supplement current knowledge on stopping motives. This adds to existing databases such as the donor data base or cohort studies (e.g., Donor InSight, Danish Blood Donor Study), with the benefit that social media provide information about what donors think and do when not present at the blood bank, and not participating in research. Social media communication goes beyond factual and campaign information and often entails (positive and negative) opinions and experiences. The large scale use

of social media, with over 10 million active Facebook users in the Netherlands alone, makes social media an important context and tool for blood banks to both learn about and influence how donors and the general public think, feel and behave with regard to blood donation. Hundreds of thousands social media messages provide blood banks with a big data source of rich information about donor motivation and behavior.

Aims: This study explored who (actors) communicates what, when and how about blood donation on social media platforms. We focused on motives related to stopping with blood donation that appear in online messages on Facebook and Twitter. Besides, we also focused on dissatisfaction (anger and disappointment) around blood bank and blood donation as unfavorable experience.

Methods: Online messages between January 2012 and December 2016 were collected through a social media monitoring tool (Coosto) by applying a search string related to blood donations and blood bank. A content analysis of all Dutch posts related to blood donation on Facebook and Twitter was performed to find relevant messages in the dataset. Messages were clustered into categories, including actors and topics. Associations between keywords were measured and then visualized.

Results: The final dataset contained 96.408 messages on blood donation and the blood bank, of which 11.796 (~12%), contained words related to stopping, either voluntarily or involuntarily, and dissatisfaction, i.e. anger and disappointment. Stopping reasons were categorized into physical reactions, medical reasons, pregnancy, traveling, lifestyle (e.g., lack of time), opening and waiting times, (sexual) risk behavior, blood bank policy. Stopping involuntarily associated most strongly with medical reasons and sexual risk behavior. Stopping voluntarily associated most strongly with top management salaries and medical reasons. Posts including anger associated most strongly with sexual risk behavior, posts including disappointment most strongly with medical reasons.

Summary / Conclusions: Our study gives insight into prominent stopping motives and dissatisfaction regarding blood donation and blood bank in social media messages. The most often discussed stopping motives in social media differ from those obtained from survey research. Such results may indicate that social desirability and selection bias play a role in survey research. Combining data sources, including social media data and observational (survey) studies may paint a fuller picture of stopping motives for blood donors in the future.

Clinical – Problems in Transfusion Medicine

5C-S42-01

THE SIGNIFICANCE OF ALTERED IGG-GLYCOSYLATION IN TRANSFUSION MEDICINE

G Vidarsson

Experimental Immunohematology, Sanquin Research, Amsterdam, Netherlands

Alloimmune diseases against blood cells can occur in pregnancy and after blood transfusions, when antibodies are formed, targeting foreign cells and tissues for destruction by myeloid cells through IgG Fc-receptors (FcγR) in particular. In pregnancy, antibodies against human platelet or red cell antigens (RBC), can cause life-threatening anaemia or thrombocytopenia in the developing foetus. A peculiar feature of many of these antibodies, especially clinically important antigens, is that antibody titer does not correlate well with diseases severity. This is true of both antibodies induced in pregnancy and after transfusion. Work from our own laboratory and others have shown that antigens on these cell types can in many cases induce immune response characterized by altered IgG-Fc glycosylation that is stable in time (also found years after induction, irrespective of intermittent boosting events). These changes are in particular low level of core-fucose, but also increased galactosylation. In a series of biochemical analysis, we and others have found that these features affect binding to FcγRIII (low level of Fc-fucosylation which is boosted by additional high galactose), with elevated galactose increasing binding to C1q as well, resulting in increased downstream complement activity. The degree of these changes are also in agreement with the level of anemia seen for example in pregnancies affected by anti-D, anti-K, and thrombocytopenia in pregnancies affected by anti-human platelet-antigen 1a. In agreement with their clinical importance, other RBC antigens such as anti-c and anti-E do newer show altered glycosylation. This work collectively shows that IgG-glycosylation in transfusion medicine and pregnancy-related features can be extremely important, culminating in elevated disease pathology, and provides an evidence based platform to screen for antibodies in patients at risk.

5C-S42-02

TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD (TACO): TIME TO SHED LIGHT ON THE PATHOPHYSIOLOGY

R Kapur

Lund University, Lund, Sweden

Transfusion-associated circulatory overload (TACO) is the most frequent pulmonary complication of transfusion and the second leading cause of transfusion-related fatalities (as reported to the Food and Drug Administration in 2015). TACO is characterized by new or worsening hydrostatic pulmonary edema which occurs within 6 h of blood transfusion and results in respiratory distress. TACO is underdiagnosed and underreported, with an increased incidence in a mixed intensive care unit population making TACO an independent risk factor for in-hospital morbidity and mortality.

A retrospective cohort study of 66 patients diagnosed with TACO identified cardiac failure, renal failure, and degree of positive fluid balance as risk factors for TACO (Bosboom et al, Transfusion 2018). Another study prospectively enrolled 200 patients with TACO and found congestive heart failure, cardiomegaly on chest X-ray, pre-transfusion diuretic use, elevated blood pressure, chronic kidney disease, acute kidney injury, plasma transfusion and emergency surgery to be risk factors associated with TACO (Roubinian et al, Crit Care Med 2018). A retrospective review of 98 TACO cases also identified congestive heart failure and renal dysfunction as common features in TACO, in addition to an age of over 70 years (Lieberman et al, Transfus Med Rev 2013). This study also described frequent suboptimal fluid management and inappropriate infusion practices (such as rapid infusion rates).

Unfortunately, the pathophysiology of TACO is poorly understood. It can be hypothesized that the pathophysiology of TACO may be generally reflected by a 2-hit model. The first hit in TACO may be represented by the poor adaptability for volume overload in the transfusion recipient, which is supported by the identification of cardiovascular and renal risk factors for the onset of TACO. The second hit may subsequently be conveyed by the transfused blood product. Interestingly, it was recently found that the degree of positive fluid balance is associated less with the development of TACO than with the development of circulatory overload in the absence of transfusion (Bosboom et al, Transfusion 2018). This may be due to the increased colloid-osmotic pressure of a blood product, stimulating fluids from the extravascular space into the intravascular space, contributing to a more effective circulating volume. Alternatively, it may indicate that other factors in the transfused blood product, besides the transfusion volume, could perhaps play a role in the development of TACO. These factors may possibly contribute to inflammation and capillary leakage. Of interest, interleukin (IL)-10 levels have been described to be increased in TACO patients (Roubinian et al, Transfusion 2015). Secretion of IL-10 is known to require specific stimulation, such as by microbial products or specific antibodies. It could therefore be hypothesized that factors in the transfused blood product may perhaps be responsible for this effect. To obtain more insight into the TACO pathophysiology, however, it will be important to assess and validate potential biomarkers in TACO. In addition, development of currently unavailable TACO-animal models will provide a useful tool for dissecting the pathophysiologic mechanisms. Collectively, this will aid in improving diagnostic approaches and shed light on possible therapeutic interventions.

5C-S42-03

ASSOCIATION AND TIMING OF DEATH IN REACTIONS CLASSIFIED AS TRANSFUSION ASSOCIATED CIRCULATORY OVERLOAD

C Cserti-Gazdewich[1], A Escorcia[2], F Tasmin[2], J Pendergrast[1], L Lieberman[3], Y Lin[4], H Ross[5] and J Callum[4]

[1]*Blood Transfusion Laboratory & Division of Hematology, University Health Network/ University of Toronto* [2]*Blood Transfusion Laboratory, University Health Network* [3]*Blood Transfusion Laboratory, University Health Network/University of Toronto* [4]*Blood Transfusion Laboratory & Division of Hematology, Sunnybrook Health Sciences Centre/University of Toronto* [5]*Peter Munk Cardiac Centre, University Health Network/University of Toronto, Toronto, Canada*

Background: Transfusion Associated Circulatory Overload (TACO) is common, and is assumed to be reversible with diuretics. However, it is often severe and is nevertheless rising in rank as the commonest cause of transfusion-related death. The extent to which TACO mortality reflects direct effects of the injury (as a driver), or selection of the sick (as a passenger), is not known. More fundamentally, whether the associated mortality rate and time-to-death are different in TACO compared with other reactions is unknown.

Aims: In consecutively reported transfusion reactions (TR), we sought to determine whether TACO (vs non-TACO reactions [NTR]) exhibited a higher proportion of death at discharge, and whether the time to death occurred any sooner.

Methods: In the hemovigilance database of an urban-academic adult healthcare institution (comprising 3 sites transfusing a total of 55,000–65,000 components/year), consecutive TR (in outpatients and inpatients) were retrospectively analyzed for the final diagnosis, be it TACO (possible to definite [± other disturbances]), vs NTR (all other TR, including one or more of the following: unrelated, allergic, febrile non-hemolytic, serologic ± hemolytic, transfusion-associated dyspnea, transfusion-related acute lung injury, bacterial contamination, pain/inflammation-ischemia, citrate toxicity, cold [product refrigeration-related], and not otherwise specified). Vital status at discharge (dead or alive) was compared for TACO vs NTR. Among decedents, the TR-to-death intervals were characterized. Results used applicable summary statistics (proportions and Fisher's exact test for 2x2 comparisons; medians with interquartile range [IQR]; t-tests for distributions; non-significance [NS] defined as p > 0.05). Review of early deaths (defined as death within 3 days of TR) was also undertaken.

Results: Over 8.5 years (10/05/2009 - 23/12/2017), 2723 TR were assessed, with median patient age 57.5 (44.8–68.7) years, males: females 51%/49%. Vital status at discharge was recorded in 2698 (99%) of TR, with 279 cases of TACO (10.3% of TR), leaving 2419 NTR. A higher proportion of TACO cases died (47, 16.7%), versus 247 of NTR (10.2%), $P = 0.0015$. Among TR with death at discharge, the time between TR and death was similar at 16 (6–37) days for TACO and 14 (6–38) days for NTR, $P = 0.10$, NS. Furthermore, a similar proportion had died within 3 days in TACO (6 of 47 or 12.8%) as in NTR (46 of 247 or 18.6%), $P = 0.41$, NS. For the 6 TACO cases with death within 3 days, TACO was not deemed to be singularly attributable in any case, but was thought to have contributed in part and/or to have accelerated the demise in four, versus inevitable death in two (intracranial hemorrhage, metastatic terminal cancer). None of the deaths occurred within 24 h, but rather at 1–2 days amid TACO-related interventions; locations for TACO-associated deaths were both medical and surgical.

Summary / Conclusions: Patients with TACO exhibit a higher mortality rate than NTR, although time to demise or the proportion dying within three days is similar. TACO contributed in part (but not exclusively) to the death in early decedents. An untransfused cohort with matched casemix morbidity would serve as a valuable comparator to better distinguish cause from effect. Although neither typically nor immediately fatal, TACO persists as an important form of transfusion-related harm and may be prognostic in transfusion recipients.

5C-S42-04

THE PRO- INFLAMMATORY AND PRO- COAGULANT MICROPARTICLES FROM STORED RED BLOOD CELL CONCENTRATES ARE IMPLICATED IN ONSET OF TRANSFUSION RELATIVE LUNG INJURY (TRALI)

R Xie[1], J Yang[1], Y Yang[1], L Gao[1], Y Zhu[2] and K Qian[1]

[1]Shanghai Blood Center, Shanghai [2]The first Affiliated Hospital of Anhui Medical University, He Fei, China

Background: Researches have indicated systemic and pulmonary inflammation and coagulopathy are important characters of transfusion relative lung injury (TRALI). Red blood cell microparticles (RMPs) accumulated in stored red blood cell concentrates (RBCs) has pro- inflammatory and pro- coagulant potential, but it has little known how RMP play a role in developing TRALI. We hypothesized that RMP improve intrinsic pathway of blood coagulation, induce human pulmonary microvascular endothelial cells (HMVEC) activation and damage may contribute to TRALI.

Aims: To investigate the effects of red cell microparticles on thrombin generation, HMVECs activation and damage

Methods: RMPs were obtained from 35 days stored RBCs. The amounts of MPs were counted using flow cytometric and nanoparticle tracking analysis. RMPs promoting thrombin generation and intrinsic pathway of blood coagulation was assayed by Calibrated Automated Thrombogram assay(CAT) and activated partial thromboplastin time (APTT) respectively. The expression of ICAM-1 and releasing of cytokine by endothelial cells were determined with flow cytometric analysis. HMVEC damage was determined by incubation of Lipopolysaccharide (LPS) treated endothelial cells with RMPs. The activity of NADPH oxidase in neutrophils was inhibited by apocynin treatment.

Results: Microparticles from stored RBCs were a heterogeneous vesicle population with diameter of 100~300 nm. The RMPs was in majority. Remainders are platelet, leukocyte and other microparticles. RMPs improved thrombin generation in a dose dependent manner. APTT was shortened by adding RMPs to MPs depleted plasma. Depletion of microparticles in 35 days stored RBCs supernatant either by 0.1 μm filtration or by 20,000 × g centrifugation reduced the amount of RMPs, meanwhile decreased promoting thrombin generation ability of the RBCs supernatant significantly. Expression of adhesive molecule ICAM-1 on HMVEC was increased significantly by incubating the endothelial cell with RMPs for 6 h, and continuously increased until 24 h of incubation. Meanwhile RMPs induced the endothelial cell releasing inflammatory cytokine IL-6 and IL-8 after 12 h of incubation. RMPs were

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able to induced LPS activated HMVEC damage, but were prevented by inhibiting of PMN respiratory burst with apocynin.

Summary / Conclusions: RMPs in stored RBCs may improve the systemic coagulopathy, induce pulmonary endothelial cell activation and prime LPS treated HMVEC damage. All of them were relative to the onset of TRALI. The role of RMPs which are implicated in onset of TRALI need to be further explored.

Blood Safety – Emerging Infectious Diseases

5C-S43-01

EMERGING INFECTIOUS DISEASES

C Erikstrup[1] and H Ullum[2]

[1]Department of Clinical Immunology, Aarhus University Hospital, Aarhus
[2]Department of Clinical Immunology, Copenhagen University Hospital, Copenhagen, Denmark

Emerging infectious diseases (EID) is a special group of infections defined by their increasing incidence in humans during the last two decades either as a new infection or a known infection introduced in new populations. EIDs pose a threat to blood safety if the pathogen: 1) has an asymptomatic phase where it is present in the blood, 2) can survive blood processing and storage, and 3) can establish a clinically relevant infection in the recipient. The threat to patients may be exaggerated by the fact that many transfused patients are immunocompromised.

Since the HIV epidemic in the 1980s the world has experienced many other emerging infections, e.g. variable Creutzfeldt-Jakob disease, severe acute respiratory syndrome (SARS), West Nile Virus infection, Chikungunya virus infection, dengue virus infection, Zika virus infection, Ebola virus infection, babesiosis and infections with Methicillin-resistant Staphylococcus aureus (MRSA). The number of new threats is increasing due to population growth and globalization with extensive exchange of people and goods within and between countries leading to the very effective spread of both person-to-person transmitted and vector-borne infections. The spread of diseases is facilitated by climate changes and the subsequent introduction of vectors into new areas. Fortunately, our tools to recognize and handle EIDs have improved with newly developed screening tests (e.g. for Zika virus, Babesia microti) and better surveillance.

With the recognition of EIDs posing a threat to the blood supply we face the challenge to choose the correct intervention, which may include the spectrum from no intervention to pre-donation screening and e.g. travel deferral to testing for the pathogen or pathogen inactivation. It is of paramount importance that these decisions are based on risk assessments using the available knowledge about the disease and e.g. travel patterns and appropriate tools such as The European Up-Front Risk Assessment Tool (EUFRAT). We must mitigate the risk for our recipients and on the same time avoid taking unnecessary, often costly, measures. However, several features of a newly discovered pathogen or epidemic are often not known.

Moreover, there are also inherent challenges with all interventions. Deferral of at risk donors may be thought of as cheap interventions but temporarily deferring donors decreases the donor return rate. There has been too little focus on the accumulated costs associated with deferrals not based on evidence. Screening donations for pathogens is costly, take time to implement, and may not be available. Pathogen inactivation (PI) may soon be available for the treatment of not only plasma and platelet components but also red blood cell components, however PI is costly, and we still need larger studies assessing the quality of the PI treated components especially for use in areas with low infectious pressure.

The presentation will include a review of new threats to the blood supply and the dilemmas posed by requirements to reduce residual risk to negligible levels in a context of ever growing demands for efficiency. However, the blood banks have the potential to provide new knowledge on EIDs using our access to a large percentage of the population.

5C-S43-02

COST–EFFECTIVENESS OF SCREENING THE BLOOD SUPPLY FOR ZIKA VIRUS IN PUERTO RICO AND THE FIFTY US STATES

W Russell[1], S Stramer[2] and B Custer[3,4]

[1]Management Science and Engineering, Stanford University, Palo Alto [2]Scientific Support Office, American Red Cross, Gaithersburg [3]Epidemiology and Policy Science, Blood Systems Research Institute [4]Department of Laboratory Medicine, University of California San Francisco, San Francisco, United States

Background: The spread of Zika virus (ZIKV) throughout the Americas prompted the United States FDA to require individual donation nucleic acid testing (ID-NAT) for all units of donated blood in US states and territories in 2016. The health-related and economic consequences of screening the blood supply for ZIKV have not been systematically evaluated.

Aims: To assess the effectiveness and cost-effectiveness of universal ID-NAT for the 50 US states and separately for Puerto Rico (PR) in the first year of implementation as compared to alternative screening options.

Methods: Policies were evaluated by a microsimulation model that captured the expected lifetime health consequences and costs that accrue over a one-year period. ZIKV-related adverse health events experienced by transfusion recipients, sexual partners, and infants born to recipients or sexual partners were captured. For both the US and PR we compared universal ID-NAT, universal mini-pooled (MP) NAT, and ID-NAT for units transfused to women of child-bearing age only. For PR we also considered seasonally-adapted strategies, and for the 50 states we considered strategies that target donors based on residence in or travel to an area of known local transmission.

Results: Preliminarily, with no ZIKV screening, the estimated number of transfusion-transmissions in PR in a year was 242.4, with 44.7 symptomatic cases, 0.06 cases of Guillain-Barre Syndrome, and 0.03 cases of congenital Zika syndrome. With no screening in the 50 US states, the estimated number of transfusion-transmissions was 46.3, with 8.2 symptomatic cases, 0.012 cases of Guillain-Barre Syndrome, and 0.006 cases of congenital Zika syndrome. The estimated annual test-related costs for ID-NAT screening were $807,000 in Puerto Rico and $126 million in the 50 States. Compared to no screening, the cost-effectiveness ratio for ID-NAT was $339,000 per QALY in PR and $341 million per QALY in the 50 states and District of Columbia. When compared against other potential interventions, exclusive use of ID-NAT had an incremental cost-effectiveness ratio of $15 million per additional QALY gained in PR and $78.4 billion per additional QALY gained in the 50 states and District of Columbia. At a willingness-to-pay of $1 million per quality adjusted life year (QALY), use of MP-NAT only during high mosquito season was cost-effective in PR at $81,000 per additional QALY gained. No intervention was cost-effective in the 50 states. However, using MP-NAT exclusively in areas experiencing a known local transmission had the lowest cost-effectiveness ratio in the 50 states at $10 million per QALY

Summary / Conclusions: In its first year, ID-NAT screening was not cost-effective in the 50 US states and District of Columbia. When compared to no screening ID-NAT was cost-effective in PR at a $1 million per QALY willingness-to-pay, but compared to other interventions, including seasonal testing and use of MP-NAT, it was not. Moreover, in periods of lower ZIKV prevalence such as 2017 all interventions will be less cost-effective than reported here.

5C-S43-03

CHARACTERIZATION OF EVOLVING VIRAL AND SEROLOGICAL STAGES OF ZIKV RNA POSITIVE BLOOD DONORS AND ESTIMATION OF POPULATION INCIDENCE OF INFECTIONS DURING THE PUERTO RICO ZIKA EPIDEMIC, 2016

P Williamson[1], G Simmons[2], B Biggerstaff[3], M Stone[2], V Winkelman[1], G Latoni[4], J Alsina[4], A Powers[3], S Bakkour[2], L Pate[5], S Galel[5] and M Busch[2]

[1]Creative Testing Solutions, Tempe [2]Blood Systems Research Institute, San Francisco [3]United States Centers for Disease Control, Fort Collins, United States [4]Banco de Sangre Servicios Mutuos, San Juan, Puerto Rico [5]Roche Molecular Systems, Inc., Pleasanton, United States

Background: The US territory of Puerto Rico (PR) began screening blood donations for Zika virus (ZIKV) RNA using nucleic acid amplification technology (NAT) on April 3, 2016 as a result of FDA guidance. Analyses of NAT-positive index donations and follow-up of positive donors were used to assess the viral and serologic dynamics through the early stages of ZIKV infection and to estimate the incidence of infections in the PR population in 2016.

Aims: To analyze NAT-positive blood donations from Puerto Rico during the 2016 ZIKV epidemic in order to assess the viral and serologic dynamics through early infection and to estimate incidence in the Puerto Rican population.

Methods: Individual donation (ID) aliquots of plasma from volunteer blood donors were screened for the presence of ZIKV using NAT (Roche cobas® Zika). ID-NAT reactive samples were further tested to confirm infection, estimate viral load (VL), and identify ZIKV-specific antibodies by monoclonal antibody capture (MAC) ZIKV IgM and IgG ELISAs. Simulated minipools (MP) of 6 were tested by cobas® Zika to discriminate ID-NAT-only detectable vs MP-NAT-detectable donations and stage them according to VL and by ZIKV IgM reactivity over the course of the 2016 Puerto Rico epidemic. A novel analytic process was used to estimate the NAT detection period and time to IgM seroconversion in acutely infected donors: First the viral load in 90 pre-seroconversion (IgM-negative) index donations and the RNA doubling time in 18 acutely infected macaques (5.35 h; Standard Error 0.36 h) were used to back-extrapolate to the first date of NAT-detectable infection for each donor. This date was then used to evaluate duration of NAT detectability and time to IgM seroconversion based on results on follow-up samples collected 5 to 77 days post-index donation. The NAT detection period and yield of NAT-positive donors in 2016 were used to project the number of infections and incidence of ZIKV in PR in 2016.

Results: Between April 3 and December 31, 2016, 52,942 donations in PR were screened at CTS for the presence of ZIKV. 339 confirmed infected (NAT+) donations were detected through December 2016. Index donations that tested IgM-negative had significantly higher VLs (mean of 1.1 x 10^6 [IgM-negative] vs 8.3 x 10^4 [IgM-positive] International Units/ml) and higher proportions of simulated MP-detectable results (93% vs 13%, respectively) than IgM-positive donations. The distribution by stage of infection (proportions of NAT reactive donations) that were ID-NAT-only detectable and IgM-positive donations increased significantly as the epidemic season evolved. The mean duration of NAT-detectability was estimated at 11.7 (95% CI: 10.0–14.5) days. Time from initial NAT-detectability to IgM-seroconversion was estimated at 7.45 (95% CI: 5.4–9.9) days. Applying the NAT detection period to 2016 NAT yield data resulted in an estimate for 595,938 (95% CI: 512,859–682,167) ZIKV infections, and seasonal incidence of 16.4% (95% CI 14.1%>18.7%) in PR in 2016.

Summary / Conclusions: Characterization of early ZIKV infection dynamics is important for blood safety considerations, since infectivity and utility of MP vs ID NAT screening likely correlate with VL and serological stages of infection. Our findings also have important implications for diagnostic testing, public health surveillance and epidemiology, including estimating that <20% of the PR population was infected during the 2016 outbreak.

5C-S43-04

ZIKA RNA AND ANTIBODY PERSISTENCE IN BLOOD AND BODY FLUIDS AND CLINICAL OUTCOMES IN INFECTED BLOOD DONORS

M Stone[1], S Bakkour[1], M Lanteri[1], G Simmons[1], D Brambilla[2], P Williamson[3], T Lee[1], J Orlando Alsina[4], R Reik[5], S Galel[6], J Linnen[7], S Kleinman[8] and M Busch[1] for the NHLBI Recipient Epidemiology and Donor Evaluation Study-III (REDS-III)

[1]Blood Systems Research Institute, San Francisco [2]RTI International, Rockville [3]Creative Testing Solutions, Tempe [4]Banco de Sangre de Servicios Mutuos, Puerto Rico [5]OneBlood, Ft. Lauderdale [6]Roche Molecular Systems, Pleasanton [7]Hologic, Inc, Jeff.Linnen@hologic.com San Diego, United States [8]Department of Pathology, University of British Columbia University of British Columbia, Victoria, Canada

Background: Zika virus (ZIKV) is associated with severe neurological consequences in fetuses and adults and potential transfusion transmission (TT), which prompted nucleic-acid amplification test (NAT) screening of plasma from U.S. blood donors in 2016. RNA persistence has been reported in whole blood (WB) long after clearance of viremia in plasma. Characterization of the dynamics of ZIKV persistence following acute infection is needed to inform donor NAT and diagnostic testing policies and to understand the natural history of ZIKV infection.

Aims: We sought to characterize the dynamics of infection and estimate durations of RNA and serological persistence through prospective study of ZIKV RNA+ blood donors.

Methods: Donors identified through investigational ZIKV NAT screening and confirmed by Zika quantitative RT-PCR (qRT-PCR) and serology were enrolled into longitudinal follow-up and assessed for viral and serological persistence and clinical outcomes. Plasma and RBC were obtained from index donations and blood, urine, saliva and semen were collected prospectively at weeks 1, 3, 6, 12, 24, 36 and 1 year following index donations; detailed symptom questionnaires were administered at each visit. Follow-up blood compartment and body fluid samples were tested for ZIKV RNA by qRT-PCR (calibrated against WHO International Standard) and follow-up plasma, urine and WB were also tested by a donor NAT/diagnostic assay (Grifols Zika Procleix/ Hologic Aptima) in replicates (8 for plasma; 2 for urine and WB). Plasma samples were tested for ZIKV-specific IgM, IgG and dengue virus (DENV) IgG antibodies.

Results: The duration of detection of ZIKV RNA for each assay/sample type relative to estimated dates of infection (derived from qRT-PCR viral load at index donation and RNA doubling time during ramp-up viremia from macaque infection studies) was calculated from follow-up testing of 53 enrolled donors. Plasma viremia was detectable by qRT-PCR for 11.4 days (95% CI: 8.2–16.5) whereas RBC- and WB-associated viral RNA persisted for 89.9 days (95%CI: 53.9–128.9) and 80.5 days (95%CI: 51.0–107.8), respectively. When tested by the Grifols NAT assay in replicates, plasma detection (1/8 positive results) was extended to 42.1 days (95%CI: 18.8–100.2) and WB (1/2 positive results to 102.2 days (95%CI: 88.7–117.9). Urine and saliva were reactive by qRT-PCR up to 25.9 (95%CI: 17.1–43.9) and 22.5 days (95%CI: 16.5–31.1), respectively. ZIKV IgM persisted for 233.3 days (95%CI: 160.4–361.6) following index donation. A reduction in ZIKV RNA and IgM persistence was observed in the 44 dengue IgG seropositive donors. Of donors identified in the acute pre-seroconversion stage of infection 65% (15/23) developed multiple ZIKV-related symptoms by 1 week after index donation, compared to 30% (7/27) in donors detected post-seroconversion.

Summary / Conclusions: RBC-associated ZIKV RNA persists for several months following clearance from plasma and body fluids. Highly sensitive NAT testing extends the period of detection in all compartments when performed with replicate testing. Higher rates of incident ZIKV symptoms were observed than previously reported. The persistence of ZIKV RNA in RBCs has unknown implications for blood screening, which currently relies on plasma testing; infectivity studies are in progress. WB testing may be of value to extend detection of acute infection for diagnostics and monitoring of pregnant women and sexual partners.

5C-S43-05

TRANSFUSION-TRANSMISSION OF ZIKA VIRUS IN NON-HUMAN PRIMATE AND MOUSE MODELS

G Simmons[1], K Van Rompay[2], L Coffey[3], K Lu[1], J Yee[2], S Bakkour[1], M Stone[1], P Williamson[4], M Muench[1] and M Busch[1]

[1]Blood Systems Research Institute, San Francisco [2]California National Primate Research Center [3]Department of Pathology, Microbiology and Immunology, University of California, Davis [4]Creative Testing Solutions, Tempe, United States

Background: Demonstration of Zika virus (ZIKV) transfusion-transmission (TT) led to the rapid introduction of sensitive individual donation (ID) nucleic acid amplification testing (NAT) in the US in 2016. However, following the resolution of the recent large-scale epidemics in the Americas important questions remain concerning the efficiency of NAT and ZIKV infectivity. In particular, whether donor screening can safely switch from routine ID- to minipool (MP)-NAT with triggering to ID-NAT when autochthonous outbreaks are identified, similar to well established NAT screening algorithms for West Nile virus.

Aims: Define the minimal infectious dose for ZIKV TT using murine and macaque models.

Methods: We used susceptible cell lines, and immunodeficient mice and immunocompetent rhesus macaque transfusion models to calculate the infectivity of ZIKV using acutely infected human and macaque plasma samples. We performed titration and dose-escalation studies by producing half-log dilution panels using uninfected macaque plasma as diluent and ZIKV RNA reactive/seronegative plasma samples - two derived from NAT+ humans and one from an acutely infected macaque – as the intravenous inocula. Serostatus of the input plasma was characterized by ELISA assays for IgM and IgG against ZIKV and dengue virus, as well as neutralization assays. Infections were monitored by ZIKV specific RT-PCR.

Results: Using ZIKV amplified in tissue culture and titrated in cell lines or in mice, one infectious unit corresponded to between 1,000 and 2,500 viral RNA copies. In comparison, using RNA reactive/seronegative plasma one infectious unit corresponded to only 50 to 500 viral RNA copies, with mice being significantly more sensitive to infection than in vitro culture. In macaques we observed variable infectivity with ZIKV NAT-reactive seronegative plasma. Plasma from a ZIKV RNA reactive Brazilian blood donor infected 3 macaques at doses ranging from 3,000 to 9,000 RNA copies. Performing back titrations this equated to doses of between 21 and 64 plaque-forming units (pfu) of infectivity in tissue culture. A second plasma from a ZIKV RNA reactive Puerto Rican blood donor infected a macaque at a dose of only 200 RNA copies (and approximately 0.75 pfu). Finally, macaque plasma collected at day 4 post-infection from one of the macaques infected with the Brazilian plasma was not infectious at a dose of 500 RNA copies, but was at 1,000 copies (<1 pfu). Interestingly, the kinetics of viral load development in these animals with low dose infection was considerably retarded compared to macaques infected with high (10,000 pfu) ZIKV doses.

Summary / Conclusions: Using tissue culture amplified ZIKV we found similar ratios of infectivity to RNA (~1:1000) as has been reported for other viruses. Also in

line with other viral systems, we found uncultured virus from donors or experimentally infected animals was significantly more infectious (as low as 1:50). Immunodeficient mice proved to be the most sensitive model for detecting infectious ZIKV, while we found in a more relevant macaque model of plasma transfusion between 200 and 9,000 RNA copies was required for infectivity. We are currently testing seropositive plasma from the same macaque to demonstrate the effect of specific anti-ZIKV antibodies on TT.

Working Party Session on Platelets

5C-S44-01

NEW DISCOVERIES IN IMMUNE-MEDIATED THROMBOCYTOPENIAS: IMPLICATIONS FOR DIAGNOSIS AND THERAPY

H Ni[1,2,3,4,5]

[1]Laboratory Medicine and Pathobiology, University of Toronto [2]Centre for Innovation, Canadian Blood Services [3]Laboratory Medicine, St. Michael's Hospital [4]Medicine [5]Physiology, University of Toronto, Toronto, Canada

Immune-mediated thrombocytopenias include both auto- and alloimmune thrombocytopenias. Most of the platelet destruction is mediated by antibody opsonization, although T cell-mediated platelet clearance may be also involved in the pathogenesis. The major target antigens are platelet surface glycoprotein (GP) IIbIIIa (integrin αIIbβ3) and GPIb complex. Earlier studies from Dr. Nieswandt's and our group demonstrated that anti-GPIb antibody-mediated thrombocytopenia can occur in an Fc-independent manner, whereas anti-αIIbβ3 antibodies need the antibody Fc portion to induce platelet clearance. We subsequently found that anti-GPIb-mediated thrombocytopenia is more resistant to intravenous IgG (IVIG) treatment, which is consistent with several clinical studies. We also found ITP patients with anti-GPIb antibodies (irrespective of presence of anti-αIIbβ3 antibodies) are 2–3 times more resistant to steroid therapy. Recently, we found anti-GPIbα, but not anti-αIIbβ3 antibodies, induce platelet activation, sialidase neuraminidase-1 translocation, and platelet desialylation in mice. This leads to platelet clearance in the liver, which is significantly different from the classical Fc-FcγR-dependent macrophage phagocytosis mechanism. Importantly, sialidase inhibitors ameliorated anti-GPIbα-mediated thrombocytopenia in mice. These animal data have been partially confirmed in human ITP patients. Interestingly, maternal anti-GPIb antibody-induced platelet activation can lead to thrombosis in the placenta in a murine model of fetal and neonatal alloimmune thrombocytopenia (FNAIT), while anti-β3 integrin antibodies may cross-react with αVβ3 integrin on angiogenic vessels and trophoblasts, leading to intracranial hemorrhage, placental pathology, intrauterine growth restriction and miscarriage. This presentation will discuss the significance of these studies and their implications for diagnosis and therapy in ITP and FNAIT.

5C-S44-02

PLATELET SEROLOGY FOR ALLO AND AUTOANTIBODIES: PIVOTAL OR JUST NICE TO HAVE?

UJ Sachs

Institute for Clinical Immunology and Transfusion Medicine, Justus Liebig University, Giessen, Germany

Background: The identification of platelet antibodies is generally considered pivotal for the diagnosis of fetal/maternal alloimmune thrombocytopenia (FNAIT), drug-induced thrombocytopenias (DITP), and platelet transfusion refractoriness (PTR). The relevance of platelet serology in diagnosing immune thrombocytopenia (ITP), in contrast, is often questioned. ISBT has not issued guidance so far.

Aim: This review aims to analyze the relevance of platelet serology in establishing a diagnosis of antibody-mediated thrombocytopenia, and in guiding therapeutic and/or prophylactic strategies in thrombocytopenic patients.

Methods: Current literature and available guidelines were reviewed for platelet serology test method characteristics and their clinical utility in FNAIT, DITP, and ITP.

Results: In FNAIT, identification of the antibody's specificity is generally considered relevant with respect to a current or any subsequent pregnancy. It is also considered

partially relevant for the treatment of the affected newborn. Sensitive, specific methods are available and are rigorously controlled in external quality assessment (EQA) schemes. Genotyping of family members is insufficient to establish a diagnosis and/or to guide clinical decisions. Whether sub-specification of HPA-1a antibodies or antibody titration are useful diagnostic add-ons is currently under discussion.

In DITP, the relevance of serological testing is less clear. Available tests lack standardization, sensitivity and specificity are not well defined, and established EQA schemes could not be identified. Positive test results for a specific drug may have clinical relevance, especially in patients under multiple drug therapy. The clinical relevance of negative test results is not well established.

In ITP, clear evidence for the clinical utility of antibody tests is available. Assays are highly specific, but lack sensitivity. Surprisingly, specific EQA schemes were not identified. Positive test results can be useful since additional, extensive testing to exclude other disorders may become unnecessary. They may also shorten the time to treatment in some patients. Negative test results are of no clinical value. Preliminary evidence indicates that sub-specification of autoantibodies may have relevance in predicting disease severity and/or in selecting appropriate treatment options.

Conclusions: For FNAIT and ITP, robust and specific test methods are available. Test results contribute substantially to the initial diagnosis; and facilitate clinical guidance in FNAIT families and ITP patients. No substantial evidence was identified why platelet serology is disregarded in some ITP guidelines.

For DITP testing, there is evidence for clinical utility, but robustness and specificity of test methods and the overall professional acceptance may benefit from better standardization and inter-laboratory exchange.

5C-S44-03
REPORT ON THE 19TH INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION PLATELET IMMUNOLOGY WORKSHOP

L Richard[1], L Beaudin[2], L Meilleur[2], S Al Khan[3], G Clarke[4,5], A Lewin[6,7] and M St-Louis[8]

[1]Stem Cell and Reference Laboratories, Hema-Quebec, Saint-Laurent [2]Diagnostic Services, Canadian Blood Services, Winnipeg, Canada [3]Central Blood Bank, Muscat, Oman [4]Diagnostic Services, Canadian Blood Services [5]University of Alberta, Edmonton [6]Medical Affairs and Innovation, Hema-Quebec, Saint-Laurent [7]University of Sherbrooke, Sherbrooke [8]Medical Affairs and Innovation, Hema-Quebec, Quebec City, Canada

Background: The International Society of Blood Transfusion Platelet Immunology Workshop is an interesting exercise organized and performed by reference laboratories all over the world to promote and share expertise and knowledge on particular concerns in platelet immunology.

Aims: The aims of the 19th International Society of Blood Transfusion Platelet Immunology Workshop were to compare the sensitivity and specificity of the in-house and commercially available methods for the detection of human platelet antigen (HPA) antibodies currently used by participating laboratories. There was particular emphasis on the preparation of platelets for the monoclonal antibody immobilization of platelet antigen (MAIPA), monoclonal antibodies (MoABs) for the HPA-15 antibody detection and the role of anti-HLA antibodies in FNAIT. A survey was also performed to identify common practices and subjects for further discussions on the role of platelet reference laboratories in fetal and neonate alloimmune thrombocytopenia (FNAIT) management.

Methods: Twenty-nine laboratories from 17 countries participated. A set of seven serum/plasma samples for antibody identification and eight DNA samples for genotyping were sent for the case study section. In addition, three exercises, one using a commercial kit, one on platelet preparation for the detection of anti-HPA-3 antibodies and one for testing of four MoABs for anti-HPA-15 antibody detection, were provided to participants. Critical reagents and materials for the three exercises were provided including a PakLx kit and four MoABs against CD109. Finally, a survey on FNAIT case analysis and reporting by each laboratory was answered through an online survey.

Results: The participation was a great success for all the categories. Among the 29 participating laboratories, 28 submitted data. All participated in the case resolution exercise, both by serology and by genotyping. Genotyping 12 HPA systems, as proposed in the genotyping exercise, was completed by 13 participants (46%). Sixteen laboratories (57%) genotyped some of the proposed 12 HPA systems. Twenty-six of the 28 laboratories (93%) participated in the exercise on platelet preparation protocol for HPA-3 antibody detection and 27 (96%) participated in the exercise on HPA-15 detection using different anti-CD109 monoclonal antibodies. A wide variation of reactivity was observed among laboratories using MAIPA technique. Twenty of the twenty eight laboratories (71%) did participate in the antibody detection commercial

kit exercise. Less variation was observed between labs when using commercial reagents. The participation in the survey was also very good. Twenty-five participants (89%) did answer the survey on laboratory management of FNAIT cases. Details of each exercise will be depicted during the discussion.

Summary/conclusions: Detection of HPA antibodies and HPA genotyping are well performed in most participating laboratories. The workshop has identified two specific areas with room and need for improvement: the preparation of platelets for the detection of HPA-3 alloantibodies and the identification of HPA-15 antibodies. The survey findings suggest wide variation in laboratory practice with respect to antibody monitoring in FNAIT affected pregnancies and in practices related to antibody quantification. Recommendations of the Working Party on technical aspects to overcome these problems and on FNAIT laboratory management will be helpful.

5B-S44-04
GENERATION OF HPA-MATCHED PLATELET PRECURSORS FROM HUMAN IPS CELLS USING CRISPR-MEDIATED GENOME ENGINEERING

P J Newman

Blood Research Institute, BloodCenter of Wisconsin, Milwaukee, United States

Human platelet alloantigens (HPAs) reside on functionally important platelet membrane glycoproteins and are caused by single nucleotide polymorphisms in the genes that encode them. Antibodies that form against HPAs are responsible for several clinically important alloimmune bleeding disorders, including fetal and neonatal alloimmune thrombocytopenia and posttransfusion purpura. The HPA-1a/HPA-1b alloantigen system, also known as the PlA1/PlA2 polymorphism, is the most frequently implicated HPA among whites, and a single Leu33Pro amino acid polymorphism within the integrin b3 subunit is responsible for generating the HPA-1a/HPA-1b alloantigenic epitopes. HPA-1b/b platelets, like those bearing other low-frequency platelet-specific alloantigens, are relatively rare in the population and difficult to obtain for purposes of transfusion therapy and diagnostic testing. We used CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats/CRISPR associated protein 9) gene-editing technology to transform Leu33 1 induced pluripotent stem cells (iPSCs) to the Pro33 allotype. CD411 megakaryocyte progenitors derived from these cells expressed the HPA-1b (PlA2) alloantigenic epitope, as reported by diagnostic NciI restriction enzyme digestion, DNA sequencing, and western blot analysis using HPA-1b–specific human maternal alloantisera. iPS cell lines expressing other HPAs have been similarly generated Application of CRISPR/Cas9 technology to genetically edit this and other clinically-important HPAs holds great potential for production of designer platelets for diagnostic, investigative, and, ultimately, therapeutic use.

Plenary Session – Transfusion Medicine Past, Present and Future

PL5-01
TRANSFUSION MEDICINE – AN EPIC HISTORY

D Starr

Program in Science Journalism, Boston University College of Communication, Boston, United States

The history of blood is the history of a resource – one that originates in the human body, to be sure, but governed by supply and demand as well as technology. And the story of blood is one of the great sagas in the history of medicine. For centuries people have worked to understand the healing power of blood, marshal it as resource, divide it into useful components and maintain a safe and reliable supply. In this way, blood bears a strange and striking analogy to oil; although oil, to be sure, cannot transmit infections. This talk will trace the epic history of blood – from the first experiments with transfusions, to the creation of blood banks, to the management of blood supplies during the great wars. We will also discuss the tragedies of the hepatitis and AIDS as they related to the blood and plasma supplies and how public health officials learned to address them. The talk will lead to a subsequent

discussion about current efforts to ensure the safety of blood and conserve this precious resource.

ROOM TO BREATHE: GLOBAL WELLNESS IN THE 21ST CENTURY

W Dzik

Blood Transfusion Service, Massachusetts General Hospital, Boston, United States

During the 200 years that followed the pioneering work of James Blundell, scientific and technical advances have enriched the field of Transfusion Medicine and made it an essential part of healthcare worldwide. The ability of blood transfusion to sustain life through oxygen delivery is a common foundation of our profession. This lecture will examine the response to insufficient tissue oxygenation highlighting the roles of hypoxia-inducible factor and iron. The model of tumor hypoxia can be used as an analogy for current global threats to human health– threats that can be summarized as germs, guns, and steal. The single common upstream cause behind these three great challenges represents today's most pressing healthcare issue and has a solution completely within human control. A clear understanding of its importance holds the key to Global Wellness in the 21st Century.

Management and Organisation – Organisational Issues

REVIEW OF THE EXISTING LEGISLATIONS FOR BLOOD SYSTEMS OF COUNTRIES IN THE EASTERN MEDITERRANEAN REGION AND A RECOMMENDED MODEL

C Smit Sibinga[1], Y Abdella[2] and F Konings[3]

[1]IQM Consulting, ZUIDHORN, Netherlands [2]Division of Communicable Disease Control [3]Public Health Laboratories, WHO Office for the Eastern Mediterranean Region, Cairo, Egypt

Background: Essential medicines (EMs) are defined by WHO as those medicinal products that satisfy health-care needs of the majority of the population. They should therefore be available at all times, in adequate amounts and in appropriate dosage forms, with assured quality and affordability. Blood transfusion is an essential component of the health-care system and contributes to saving millions of lives every year, improves life expectancy and quality of life of patients, and supports complex medical and surgical procedures. In recognition of that blood and blood products (whole blood, red blood cells, platelets, fresh plasma, and plasma-derived medicinal products) were added to the WHO Model List of Essential Medicines, effective blood regulation is crucial for management of these products as EMs.
Aims: Requiring countries to put in place an appropriate regulatory framework (legislations, regulations, etc.) and a functioning regulatory authority. However, there are numerous situations, particularly in the less developed world, where these prerequisites have barely been implemented.
Methods: Existing legislations of Member States of WHO Eastern Mediterranean Region were collected and analysed for relevance and appropriateness for preparation and use of blood and blood products as well as use of associated substances and relevant medical devices. A literature search was done on matching combinations of regulatory system, regulatory framework, legislation, regulation, with production and use of blood and blood products, which resulted in almost exclusively references with respect to national and international legislation. WHO recommendations (Aide Mémoires) and EU Directives were used as a reference.
Results: There is a variety of formal legislations and regulatory documents issued and put in force by the Governments of these 9 countries from 1960 (Egypt) till 2017 (Pakistan – Sindh). Most are more or less detailed descriptions of the regulatory authority and the operational establishments and specific requirements. However, none of these legislations complies with WHO and EU recommended format and contents, and will not support effective regulatory oversight in order to promote and enhance quality, safety and availability of blood and blood products.

Summary / Conclusions: Ministry of Health should provide effective leadership and governance in developing a national blood system, fully integrated into the national health-care system. Essential functions of a national blood system include an appropriate regulatory framework with legislations, regulations and other non-legislative instruments administered by a regulatory body. These documents should spell out principles and boundaries, standard setting, and organization of the blood system to ensure an adequate supply of blood and blood products and safe clinical transfusion.
The structure of the national blood system will depend on organization and level of development of the health-care system. However, all critical activities within a national blood system should be coordinated nationally to promote uniform standards, economies-of-scale, consistency in staff competency, quality and safety of blood and blood products and best transfusion practices. Key is formulation of appropriate regulatory framework administered by a regulatory authority responsible for regulating the vein-to-vein chain in the preparation and use of these products.

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INSPECTION ON BLOOD ESTABLISHMENT IN TAIWAN

F Chu[1,2]

[1]Department of Clinical Pathology, Far Eastern Memorial Hospital [2]Taiwan Society of Blood Transfusion, New Taipei City, Taiwan, Republic of China

Background: Regular inspection of blood establishment has been undertaken triennially since 1992 to ensure good practice in donor recruitment, blood component processing and distribution to fulfill medical needs of patent who needs blood transfusion. The Taiwan Society of Blood Transfusion (TSBT) has been authorized to do the inspection by Department of Medical Affairs since 1992 and then by the Taiwan Food and Drug Administration (TFDA) since 2014.
Aims: To compare the performance of blood establishment after introduction of European Blood Inspection System (EuBIS) and the Pharmaceutical Inspection Convention and Co-operation Scheme (PIC/S).
Methods: A task force was called by TSBT to formulate a checklist based upon the Donor Eligibility Standard, Requirement of Blood Establishment, Taiwan and the requirement of PIC/S and EuBIS. All the blood centers and blood stations and selected mobile donation vehicle was inspected according to the checklist. The checklist covered range of service, quality management, personnel, facility, equipment, documentation, donor management, component processing, storage and distributing, audit, laboratory testing, complaints and recall, education and training, and occupational safety. All inspectors must be trained in advance by the TSBT to get consensus.
Results: From 2014 to 2017, no major (critical) unconformity events were found. Compared to 2014 inspection, the number of unconformity events was decreased from 59 to 44 events in 2017 inspection. In 2014, the most common unconformity events were in facility and/or equipment (30.5%), followed by human resource management (25.4%), and documentations (8.5%). Compared to 2014, the most common unconformity was changed into human resource management (19.1%), followed by facility and/or equipment (17.0%) and screening of blood donors (14.9%) in 2017.
Summary / Conclusions: The blood program has achieved an annual donation rate of over 75 per thousand population that fulfill transfusion needs of healthcare organizations. However, we try to introduce more and more requirement from other standards to further ensure transfusion quality and safety. With regular systemic inspection, the unconformity remained decreasing.

P-005

NATIONAL SECURITY & BLOOD BANKS: PUBLIC–PRIVATE PARTNERSHIPS ON ALTERNATIVE TECHNOLOGIES FOR CS–137 BLOOD IRRADIATION

M Taalbi

U.S. Department of Energy, National Nuclear Security Administration, Washington, DC, United States

Background: A common application of high-activity radioactive material is the irradiation of blood components to prevent transfusion associated graft vs. host disease (TA-GvHD). Historically, the most common method of preventing this disease is through the application of gamma radiation by self-shielded irradiators containing cesium-137. However, non-radioisotopic technologies, such as X-ray irradiators or ultraviolet pathogen reduction, have become increasingly available in the U.S. commercial market.

Aims: Radioactive materials play a critical role in medical, industrial, and commercial applications. Technology advances, such as in the case of blood irradiation, have led to the increased availability of non-radioisotopic alternatives, such as X-ray irradiators. As part of its mission to protect, reduce, and eliminate radioactive materials, DNN's Office of Radiological Security (ORS) within the Office of Global Material Security leads efforts to reduce the need for high-activity sources by supporting viable non-isotopic alternative technologies to replace the most common devices that use high-activity sources. The result is permanent risk reduction through the elimination of risk-significant radioactive materials.

Methods: ORS is currently engaged in efforts both domestically and internationally to exchange information on the status of technology, invest in and encourage the improvement of technologies where possible, understand and reduce obstacles preventing implementation, and promote the transition to alternative technologies where feasible. All of these programs are voluntary and aimed at finding mutually beneficial solutions that maintain or improve the intended end result, while also achieving permanent risk reduction.

Results: ORS partners with commercial licensees in the United States who choose to replace their cesium-137 irradiators with X-ray irradiators through the voluntary Cesium Irradiator Replacement Program (CIRP). Through CIRP, qualified sites receive funding toward the purchase of the new irradiator. In addition, ORS removes and disposes of the cesium-137 based irradiator through the Off-Site Source Recovery Project at no cost to the site, given the lack of commercial disposition options for these sources. ORS continues to work with many sites around the United States to replace cesium-137 irradiators through CIRP and has developed broader partnerships as a model for engagement in other regions.

Internationally, ORS is exploring partnerships on alternative technology with interested countries under existing radiological security cooperation activities. ORS has supported several bilateral and multilateral engagements on sharing experiences among operators using or considering alternative technologies for Cs-137 blood irradiation. In addition, ORS prioritizes cooperation with relevant industry stakeholders, including NGOs and international organizations, to support information-sharing and technical exchanges among operators.

Summary / Conclusions: Interest in alternative technologies for Cs-137 blood irradiation has grown around the world. This can been seen in part by multilateral endorsement of political statements and demonstrated site-level interest. Under its radiological security mission, ORS has a unique role to facilitate the integration of national security and health considerations while supporting the needs of the blood bank community.

P-006

RECONSTRUCTION OF THE SERBIAN BLOOD TRANSFUSION SERVICE

P Djordjevic

Blood Transfusion Institute NIS, NIS, Serbia

Background: The latest law on transfusiology medicine passed in April 2017. Serbia has established national blood transfusion services in line with European transfusion guidelines and recommendations.

Aims: The services are divided into authorized blood transfusion services and blood banks. Authorized blood transfusion services are independent institutions and will deal with the collection, testing and processing of blood as well as the distribution of blood to the blood banks. Blood banks will be part of the clinic or hospital centers.

Methods: Literature, law on transfusiology medicine, data from the transfusion services.

Results: The implementation of the law began gradually taking over the territory of smaller transfusion centers. It is planned that by 1 January 2019, the collection, testing and blood processing will continue to be performed by 4 authorized blood transfusion institutions instead of 46 as there have been.

So far, all blood establishments have different degrees of direct and indirect costs data management, equipment, materials, staff, support functions, and facilities. The advantage of the new organization is primarily the increased safety of blood and uniform quality and safety throughout the country. It is also expected that a better distribution of blood will eliminate blood shortages in parts of the country where it occurs, due to a weaker response from donors or seasonal character.

In economic terms, lower total cost per unit of blood is expected due to centralized procurement of equipment and tests, as well as dependent costs. The centralized model has good opportunities to optimize procurement processes and to gain low prices for consumables.

Centralization enables better management of personnel, their training in accordance with the standards and needs of the services. In addition to better economies, increased investment in research work in the field of raising quality and safety of blood is expected.

A centralized information system facilitates easier administration of donors, easier national planning and quick response if there are shortcomings of individual blood components. It also helps to alleviate and correct geographical differences in the response of the blood donor. Centralized distribution throughout the country allows the availability of blood components to all hospitals and eliminates the occurrence of local deficiencies in blood components. The risk of accumulating unnecessary amounts of blood components or their obsolescence due to fear of shortages is reduced.

Summary / Conclusions: Authorized blood transfusion services will have the obligation to improve good transfusion practices, staff training, quality improvement and monitoring, monitoring and analyzing trends and needs, as well as creating national policies

P-007

IMPROVE LINE EFFECTIVENESS OF 24 HOUR AUTOMATED POST DONATION CALL BACK LINE

C Goh, J Liew, H Wongso, H Chong and S Lam

Blood Service Group, Health Science Authority, Singapore, Singapore

Background: The Blood Services Group (BSG) in Singapore secures the national blood supply, ensuring all patients in Singapore have access to adequate and safe blood. BSG provides an automated voice-prompt 24-hour post donation call back line (call back line) as an added measure for the provision of safe blood.

The call backline is for donors who (i) feel that the donated blood should not be given to any patient, (ii) have forgotten to declare relevant information that may compromise blood safety and/or (iii) developed infective symptoms in the first two weeks following blood donation. This allows BSG to reduce the risk of transfusion transmitted infections (TTIs) which mandatory infectious disease testing may not cover or detect during time of testing.

This call back line is automated in October 2016, allowing donor to provide key information through voice prompt guidance for unsuitable use of their blood donation without the need to speak to an operator. There is a "speak to operator" option in the call back line which operates in sync with opening hours of HSA Blood Bank to answer donors' general enquiries.

Current data reveals that donors called multiple times to call back line, implying low line effectiveness. It is important to improve the line to ensure no possible cases of call back is missed.

Aims: To identify possible root cause(s) of low line effectiveness and enhance donors' experience on the call back line.

Methods: Business Process Map was used to identify possible factors that may have contributed to low line effectiveness. Statistical analysis of data recorded from May to July 2017 was performed using SigmaXL software. Phone survey was conducted to understand issues donors faced.

Results: 5 possible root causes were identified: (i) 24-hour coverage not available for all options, (ii) operator busy, (iii) call back cases going to the wrong department, (iv) non-required information asked and (v) abrupt line cut off. The first 3 causes were applicable to the "speak to operator" option, while (iv) and (v) were applicable to the "donation call back" option.

The call log data of 3 months' period revealed that 51% of the donors used call back line for general enquiry purposes, of which 59% enquired on information pertaining to donation call back. These donors were advised to call again using the "donation call back" option, resulting in low line effectiveness.

A phone survey revealed that 53% of donors tried multiple times to reach an operator. It also showed that 9% of the donors made repeat calls as they could not remember their donation date when prompted. Some donors were unsure if their details were registered thus making multiple calls. These reasons contributed to the low line effectiveness.

Summary / Conclusions: Although majority of the calls were made in regards to donation call back, the purpose of call back line can be better explained to donors with the 'Thank-you' card that is passed to them after donation. The call back line flow can also be redesigned to make it more user-friendly and accessible to meet the needs of donors.

P-008

ESTABLISHING A FECAL MICROBIOTA TRANSPLANT SERVICE WITHIN THE BLOOD- AND TISSUE TRANSPLANT SERVICE IN THE REGION OF SOUTHERN DENMARK

D Holm[1], M Skov Kragsnæs[2], A Nilsson[1], J Kjeldsen[3], T Ellingsen[2], M Agerbæk Juel[3], H Holt[4], S Thue Lillevang[1] and J Georgsen[1]

[1]Department of Clinical Immunology [2]Department of Rheumatology [3]Medical Gastroenterology [4]Department of Microbiology, Odense University hospital, Odense, Denmark

Background: Fecal microbiota transplantation (FMT) has become a well-known and highly recommended treatment for recurrent Clostridium difficile infection. In addition, FMT is currently investigated as a therapeutic option in various autoimmune diseases. Consequently, there is a rising demand for easy and rapid access to high quality FMT. Currently, no international standardized recommendations regarding the recruitment, selection and screening of feces donors are available and likewise no standardized recommendations regarding production, storage and distribution of the FMT have been established. Furthermore, no European legal framework concerning the donation of human feces exists.

Aims: The aim was to establish a stool bank at Odense University Hospital, Denmark, as a collaboration involving the Blood- and Tissue Transplant Service at the Department of Clinical Immunology, the Department of Medical Gastroenterology, the Department of Rheumatology and the Department of Clinical Microbiology. To fulfill the demands of FMT for both treatment of recurrent Clostridium difficile infections in the Region of Southern Denmark and for research of FMT as therapeutic option in various autoimmune diseases, we aim to recruit a minimum of six feces donors per year.

Methods: A quality management system of the stool bank as well as a system for traceability of the FMT was developed by using already existing quality management systems (QualiWare) and laboratory information systems (ProSang) at the Blood- and Tissue Transplant Service at the Department of Clinical Immunology. A screening strategy of potential feces donors was determined and eligible unpaid, volunteer feces donors were recruited from the present blood donor corps by advertising in the donor waiting area in the blood bank.

Results: Within less than a year a well-organized stool bank has been established. Standard operation procedures, equipment and registration of competences for the personnel involved in the stool bank are handled in the quality management system. Traceability of the FMT from donor to patient is ensured using the laboratory information system. However, a new "tissue module" developed as part of ProSang will be implemented, as we found the newer version more suitable for handling feces donations. Until now four donors have been recruited and have each donated stool 4–5 times. More donors have shown interest. Most donations have so far been used for research purposes and in addition five patients suffering from recurrent Clostridium difficile infection have been successfully treated by FMT.

Summary / Conclusions: Some of the larger difficulties when establishing stool banks are due to the lacking regulatory aspects and legislative formalities. In this aspect, establishing a centralized stool bank as a collaborative effort in an already existing non-profit Blood- and Tissue Transplant Services has several advantages. All processes from donation to transplantation are handled by personnel with experience of working with GMP standards as well as the regulation of blood- and tissue donation. Patients are treated with FMT of high quality from a well-known population of donors and full traceability during the production ensures that possible safety issues can be addressed. At the end the cost effectiveness of using systems already in place is considerable.

Information Technology

P-009

Abstract has been withdrawn

P-010

HOSPITAL TRANSFUSION DURING IT DOWNTIME – LEARNING LESSONS FROM THE MAY 2017 CYBER-ATTACK

CS Booth, J Lancut and S Allard

Haematology, ROYAL LONDON HOSPITAL, LONDON, UK, London, United Kingdom

Background: Hospital transfusion services depend on Information Technology (IT) systems for maximising transfusion safety. Automatic transfer of Group and antibody screen (G&S) results from analyser to patients' electronic records ameliorates the risk of human error in transcription. Results are checked against historical groups (providing protection against Wrong Blood in Tube) and any special requirements identified. This supports electronic crossmatch without need for serological crossmatch in the majority of patients without red cell antibodies. Electronic tracking with use of remote fridges supports ready availability of blood near to clinical areas. In May 2017 a Cyber-attack hit organisations across the world, including the UK National Health Service. At our London Trust, within 7 min of detection of the virus, the entire network was electively taken down to protect against spread, leaving four hospitals without access to various IT systems. A Major Incident was declared which in total lasted 12 days.

Aims: We aim to draw learning points for managing future IT downtime.

Methods: We reflect on debriefings following the event involving pathology managers, transfusion scientists and transfusion clinicians.

Results: In a transfusion laboratory handling over 62,000 G&S samples per year, there was a vast increase in manual workload. All patients needed two separate samples to confirm the G&S result and every unit of red cells had to be crossmatched manually. Clinicians initially sent additional samples on all patients who might need blood 'just in case'. Lab staff needed to check with clinical teams to establish urgency of requests. The resulting telephone enquiries and dealing with doctors entering the lab encroached upon the time needed to undertake additional serological testing. Meticulous paper records of components issued had to be kept to maintain traceability. Remote fridges could no longer be used and all stocks were returned to the lab. Increased numbers of experienced transfusion scientists were needed – more challenging as the attack occurred at the start of a weekend. Alternative means of ordering stocks from the national blood service had to be negotiated as the online ordering system was unavailable.

Ongoing active discussion between Hospital managers, Transfusion Consultants, senior pathology scientists, anaesthetists and surgeons led to an agreed approach towards maintaining patient safety. Elective surgery was cancelled and while major trauma was initially diverted from Accident and Emergency, this was soon reinstated. Routine outpatient transfusions were deferred wherever feasible. Clinical haematologists worked with the laboratory team to vet requests and provide advice to clinical teams. Regular meetings and teleconferences and communication via Whatsapp kept all involved updated. On restoration of the network, the electronic records for the downtime were rebuilt.

Summary / Conclusions: All hospitals should have a specific Major Incident policy for IT downtime in Transfusion which sets out roles and responsibilities, designates lead staff, defines lines of communication and identifies how expertise is distributed and additional staffing needs met. There should be agreed criteria for cancelling elective surgery and priority should be given to restoring laboratory IT systems and remote fridges. This forward planning should extend to the national blood service and be supported by national recommendations.

P-011

VALIDATION OF THE PNEUMATIC TUBE SYSTEM (PTS) FOR THE TRANSPORT OF BLOOD SAMPLES

E Krstova Krajnc, B Bizjak, K Perbil Lazič and M Šega

Center of transfusion medicine, University hospital of Maribor, Maribor, Slovenia

Background: The pneumatic tube system has been a major development in the laboratory practice. It is commonly used in hospitals to transport blood samples to

diagnostic laboratories. At our blood centre, blood samples are delivered by human courier. Recently, we considered using PTS to transport blood samples. We decided to validate our Proton 3000 PTS by comparing routine immunohematology and coagulation test results, and sample integrity between same samples transported either manually or by PTS.

Aims: Our goal was to evaluate the impact of a pneumatic tube system (PTS) compared to hand-delivered transport of samples.

Methods: Paired EDTA and citrate blood samples were collected from 46 randomly selected patients. The validation was performed within two days; on the first day at the Recovery Department and the second day at the Department of Laboratory Diagnostic. 18 samples in four different series were sent on day 1 and three immunohematology tests (ABO blood group, Indirect coombs test, cross-matching) were conducted. On day 2, 26 samples in five different series were sent and seven coagulation tests (BCS XP, Siemens) were conducted: prothrombin time (PT), international normalized ratio (INR), thrombin time (TT), activated partial thromboplastin time (aPTT), D-dimer, platelet count (PLTC) and platelet aggregation test (PAR-4, Hart Biologicals). Acceptability criteria was determined as follows:

For containers and blood samples: after being transported to another location, they must remain closed;

For the results of immunohematological tests: the results must be identical before and after transport;

For the results of haemostatic examinations: the results before and after transport can vary by 10% due to biological variability.

Results: The results for immunohematology tests following the transport were identical to the ones prior sending the samples. In addition, the transported samples had no visible signs of haemolysis. After the statistical analysis of coagulation tests was performed the highest variability rate noted in the thrombin time test was, 6. 21%.

Summary / Conclusions: The PTS that was investigated in this study is acceptable for reliable sample delivery in routine immunohematology and coagulation laboratory tests. The tubes did not show any signs of congestion, they did not overturn in the stand and there were no open tubes. There were also no visible signs of haemolysis.

P-012

NEW IRRADIATION INDICATOR FOR BLOOD COMPONENTS IMPROVES BLOOD SAFETY

M Schmidt[1], W Sireis[2] and E Seifried[3]

[1]Quality Management, German Red Cross, Frankfurt [2]Management, German Red Cross, Kassel [3]Management, German Red Cross, Frankfurt, Germany

Background: To prevent graft versus host disease (GVHD) especially in immunosuppressed patients, blood components are radioactively irradiated with a dose of 30 gray (Gy) thereby inactivating nearly all residual leucocytes. Successful irradiation is controlled by indicators. Most of them switch their color from red into black. Unfortunately, this color change already occurs at lower irradiation doses. Therefore, these indicators cannot guarantee an efficient irradiation with 30 Gy. Moreover, the adhesive strength of the indicator used and the reliability of the color change process are important, since a potential loss of the indicator or its missing legibility after irradiation would prohibit the secureness that the respective blood component is successfully irradiated.

Aims: To include an electronic data management system after irradiation of blood components.

Methods: A newly designed irradiation indicator (RAD-Control) and the previously used indicator (RAD-SURE) were tested in parallel at different irradiation doses in 10 Gy steps between 10 and 40 Gy. In a second study part, the stick strength of the new indicator was tested under routine conditions on different blood component (packed red cells and platelets).

Results: Both irradiation indicators were tested at an irradiation with 10, 20, 30 and 40 Gy in replicates of n = 50. Figure 1 shows both indicators after the statutory irradiation of 30 Gy. The success of the irradiation procedure with the new RAD-Control indicator is indicated by a scannable barcode ("ok") as well as by the notion "bestrahlt". Both become visible during the irradiation after a minimum irradiation dose of 20 Gy. In contrast, the RAD-Sure indicator changes the color from red into black which holds already clear at a dose of 10 Gy. Moreover, 500 RAD-Control indicators were tested under routine conditions applying an irradiation of 30 Gy. The barcode was reliable visible and scannable all times without any exceptions.

Summary / Conclusions: The RAD-Control indicator improves blood safety to monitor the irradiation dose of blood components. A scannable barcode appears after a minimum dose of 20 Gy thereby guaranteeing an efficient irradiation. After the irradiation process, the barcode could be scanned and the results added to the electronic data set stored of the respective blood component. This could be an additional

information concerning the blood component independently of the indicator itself. Finally, the indicator can be stored at room temperature, thus facilitating its handling. The new indicator documentation technology described is in line with the requested complete monitoring strategy of all production steps concerning blood components therefore importantly contributing to fulfill the good manufacturing practices.

P-013

PRECODED BLOOD SAMPLE TUBES IMPROVES BLOOD SAFETY

M Schmidt[1], W Sireis[2] and E Seifried[3]

[1]Quality Management, German Red Cross, Frankfurt [2]Management, German Red Cross, Kassel [3]Management, German Red Cross, Frankfurt, Germany

Background: Usual blood donor samples were labeled at the donation side before venipuncture. In case of unsuccessful venipuncture re-labeling of samples tubes might be necessary. In the blood donor service Baden-Wuerttemberg- Hesse two donors were donating blood side by side separated by a table in the middle of two beds. Mix up failures between both donation occurred approximately 2–3 times per year and will be identified in the laboratory by blood grouping.

Aims: Pre-coded sample tubes from Greiner Bio One were used in a pilot study to exclude all mix up failures at the blood donation side. Therefore an alpha-numeric code was labeled by the sample tube manufacturer on the tubes.

Methods: All tubes were scanned at the blood donation side before filling and merged together with the blood donation number on the sample bags. In the laboratory all numbers (donor number, donation number and precoded sample tube numbers) were handled by the laboratory information system. After testing all test results were transferred into the blood donation program (Inlog Edge blood).

Results: In total three first time donors with three different precoded samples tubes per donation and six multiple time donors with two different precoded samples tubes were tested in the pilot study. All sample tubes were scanned and electronical merged together with the blood donation numbers. Testing at all instruments (preanalytic decapper Sarstedt, Beckman Coulter, Hamilton pooling instruments, Roche Cobas 6800 and 8800, ABBOTT PRISM, and Beckman Coulter PK7300 instruments) was able without any out of specifications (OOS). After testing data transfer from the LIS into the blood donation programme was in addition possible without any failures.

Summary / Conclusions: The pilot study demonstrates that the introduction of pre-coded sample tubes with alphanumeric bar-codes is feasible and able to improve blood safety in order to prevent any sample mix ups at the blood donation side. The use of pre-coded sample tubes reduce the electronic devices at the blood donation sides and optimize scanning of sample tubes in the laboratory because all barcodes were labeled exactly at the same place. Finally all samples tubes were linked to the blood donation bag immediately before filling the samples tubes. Using of pre-coded samples tubes reduces the risk of manual failures and improves laboratory testing on automated screening instruments. Therefore the blood donor service Baden-Wuerttemberg – Hesse and North-East will implement pre-codes sample tubes for all donations in 2017/2018.

P-014

HOW ETHNIC DONOR INFORMATION SUPPORTS REQUESTS FOR TRANSFUSION

T Ison[1], B Villaseran[1], C Pote[1], M Sarmiento[1], G Clarke[2] and B Gill[3]

[1]Canadian Blood Services, Brampton [2]Canadian Blood Services, Edmonton [3]Canadian Blood Services, Calgary, Canada

Background: In July 2016, with the implementation of Automated Supply Chain electronic donor questionnaire, an optional question regarding donor ethnic group was added at permanent donor clinic sites. The question once answered will not appear again on the medical questionnaire. The question reads as follows:

"This is an optional question about your ethnic background that will be used to help us identify rare blood groups. Are you willing to provide this information?"

A Business Intelligence Warehouse report was developed to gather the data from the responses and is used in selecting donors for additional phenotype or genotype testing.

Aims: Donor ethnic information will support in the identification of rare blood group phenotypes to improve the frozen inventory, decrease turn around time to fill

requests for red cell units with complex antigen phenotypes and will efficiently direct testing resources for phenotyping and genotyping.

Methods: A phenotype/genotype algorithm was developed to selectively test donor samples based on ethnicity. Donors with the following ethnicities will be tested for: Arabic for AnWj antigen, Asian for Ena, Gy(a) and Jr(a), South Asian for In(b) and Latin American for Ge:-2,3. Black and Aboriginal donor samples are sent for genotyping.

Results: The response rate to the ethnic question was 96.6% in 2016 with 147,767 donors responding out of 153,032 total donors. In 2017, there was little change in the response rate which was 96.9%, with 137,252 donors responding out of a total of 141,582 new donors.

The ethnic diversity of the donors were as follows (ethnicity 2016/2017): Aboriginal 1.8%/2%, Arabic 1.3%/1.7%, Asian 6.5%/8.2%, Black 0.7%/0.9%, Latin American 1.3%/1.7%, South Asian 4.0%/5.0%, White 80.8%/74.4% and Other 3.6%/6.1%.

Two rare donors have been identified through testing using the ethnic donor report. Donor one is A positive Ror Fy(a)-Fy(b)-Jk(b)-K-S-V-VS-Jo(a)- and was identified in December 2017. Donor two is O positive R2R2 Fy(a)-Fy(b) + Jk(b)-K-S-V-VS-hrB-hrS- and was identified in November 2017.

In addition, the ethnic donor report was an important tool to fill an urgent demand request. A request for 6 red cell units, group O Rh positive C-E-Fya-Fyb- for a pregnant sickle cell patient. The ethnic donor report provided a list of Black donor samples which were phenotyped for the above antigens, and reduced the testing time required to find matched units.

Summary / Conclusions: Identifying rare donors through the ethnicity question was a successful strategy to improve the frozen rare phenotype inventory and provide red cell units with complex phenotypes in a timely manner. The ethnic donor report is an effective tool to reduce testing time required to fill a demand request for statistically difficult antigen combinations.

P-015

EFFECTIVENESS OF A NEW DECISION SUPPORT FOR RED BLOOD CELL TRANSFUSIONS AT A TERTIARY CARE CENTRE

A Damani[1], C Sanadi[2], S Solomon[1], L Bortignon[1] and N Shehata[3]

[1]Transfusion Medicine Services, MLT [2]Mount Sinai Hospital, Toronto, Canada [3]MD, MSc, Mount Sinai Hospital, Toronto, Canada

Background: Decision supports are intended to optimize clinical practice. Decision supports have been associated with variable effect on clinical practice, however. We developed a computerized decision support for red blood cell (RBC) transfusion at our tertiary care center that emphasized RBC transfusion triggers according to indication, the preemptive use of diuretics, transfusing one unit at a time and advising medical feedback for indications not listed.

Aims: This study aims to assess the effectiveness of the decision support on RBC utilization and to characterize transfusion practices according to clinical service.

Methods: We retrospectively determined the effect of the decision support on RBC use one year prior and one year after implementation a tertiary care university affiliated centre We collected the following data following implementation, the clinical service requesting the RBC transfusion, the hemoglobin concentration prior to RBC transfusion, whether a post transfusion complete blood count (CBC) was available after administration of each unit, and whether practitioners transfused according to criteria. We excluded patients who required a massive transfusion protocol and RBC exchange transfusion.

Results: The decision support was implemented in mid July 2015. We reviewed data from July 15, 2014 to July 15, 2015 and from August 1, 2015 to July 31, 2016. 4649 units were transfused in the year before the decision support was implemented, and 4174 units were transfused in the year after implementation, a reduction in the usage of RBC units by 10.2%. Of the 4174 RBC units transfused, 2401 units (58%) were transfused one unit at a time, 708 units (17%) were transfused as two units at a time and 1065 units (25%) transfused as three or more units at a time. Of the 4174 units, 31% (1282 units) were used by patients in the ICU, 27% (1145 units) were used preoperatively, 15% (617 units) by the Emergency room, 10% (422 units) by the Oncology unit, 8% (341 units) by the General Internal Medicine Service, 5% (217 units) by the Pregnancy unit, 3% (112 units) by the Cardiology and 1% (38 units) by the outpatient clinic. 37% (893 units) were transfused one at a time by the ICU, 33% (780 units) by the preoperative clinic, 11% (260 units) by the General internal Medicine service, 8% (201 units) by Emergency room, 5% (112 units) by the Oncology unit, 3% (65 units) by the Pregnancy unit, 3% (79 units) by the Cardiology unit and 11 units by the outpatient clinic. 86% of RBC units were transfused with hemoglobin (Hgb) concentrations less than 80 g/L, 12% units were transfused with Hgb over 80 g/L and 2% units were transfused with no pretransfusion Hgb values.

Summary / Conclusions: Since the implementation of the decision support, RBC usage has decreased by 10%. By characterizing RBC transfusion according to service and hemoglobin concentration, we were able to identify clinical units where interventions could be instituted to reduce RBC use. Ongoing assessment will determine whether the reduction in RBC usage can be maintained in subsequent years.

P-016

CHECK COMPLIANCE OF RFID TAGS WITH RESPECT TO THE REQUIREMENT OF PHASE JITTER MODULATIONS (PJM) RFID TAGS RECOMMENDED IN THE GUIDELINES OF VOX SANGUINIS APRIL 2010 VOLUME 98 SUPPLEMENTAL 2

G Murdoch[1] and A Ng[2]

[1]R&D, Sato Vicinity Pty Ltd, Sydney, Australia [2]Healthcare, NA, Singapore, Singapore

Background: A blood bank performed a non-PJM RFID evaluation in 2011 to evaluate an RFID tag and equipment program. The RFID tags failed to be read quickly and were unable to be tracked in bulk accurately. The tags failed to read after the centrifugation process and the encoded blood information was corrupted post radiation. The encoded information did not match the encoded information prior to radiation. Due to these failures, the test was discontinued.

Aims: A different form of RFID tag, PJM RFID Tags, were attached to blood products and subjected to various processes and read at a specified distance from the reader, including the speed of bulk reading at the capacity of the PJM RFID Tags whilst checking the accuracy and integrity of the data stored in these tags

Methods: A total of 192 blood bags (450-ml and 350-ml) were filled with tap water and affixed with a PJM RFID Tag on the uppermost position of the base labels for each of the blood bags to represent: 48 units of the following were tested: Red Blood Cells (RBC), Platelets (PLT), Fresh Frozen Plasma (FFP) and Buffy Coat (BC). Data was encoded onto each PJM RFID Tag using the ISBT 128 data structures. Blood components with PJM RFID Tags were subjected to the following standard treatment conditions with the specified duration: centrifugation, irradiation, refrigeration

Results: All PJM RFID Tags were successfully read (at the temperatures if specified) after each of the following tests: 192 blood bags were subjected to 5000G centrifugation for 30 min, 48 PLT bags and 48 FFP bags were subjected to a second round of centrifugation of 2560G for 30 min, 48 BC bags were subjected to a normal radiation exposure of 25 Gy and subsequently refrigerated at 4°C for 1 day, 48 RBC bags were subjected to a double radiation exposure of 50 Gy and subsequently refrigerated at 4°C for 5 days, 48 PLT bags were subjected to a double dose of radiation (50 Gy). Read distances of 96 irradiated PJM RFID Tags were measured with a PJM RFID Desktop Reader were within the specified range. 48 FFP bags were rapid frozen to −30°C, then frozen to −55°C for 24 h, followed by −80°C for 4 days, 4 weeks and 12 weeks.

Summary / Conclusions: The PJM RFID solution meets the requirements and objectives outlined in the Vox Sanguinis RFID guidelines. It provides high-speed bulk reading unaffected by centrifugation, irradiation or refrigeration based on these test results showing that all PJM RFID Tags could be read throughout the test.

Cost/effectiveness

P-017

IDENTIFYING THE COST OF OVER ORDERING STOCK AND IMPLEMENTING STRATEGIES TO MINIMIZE WASTAGE

F Chowdhury[1,2], C Hyam[3], D Johnson[4] and L Chapple[4]

[1]Haematology, Imperial College Healthcare NHS Trust [2]Haematology [3]Blood Stock Management Scheme, NHS Blood and Transplant [4]Blood Transfusion, Imperial College Healthcare NHS Trust, London, United Kingdom

Background: The NHS has been under huge financial pressures over recent years to provide effective clinical care with limited resources. Blood component wastage is an important financial issue for all hospitals. With the implementation of patient blood management (PBM) in 2012, there has been increasing focus in using blood components appropriately and minimizing inappropriate use. To aid cost savings in this large NHS Trust which houses specialties who are known to be high users of blood components, we looked at the causes and extent of blood wastage within the

blood transfusion laboratory to implement interventions to minimize wastage without compromising patient care and whilst following UK guidelines.

Aims: To ensure blood stock ordering and stock management is undertaken with the aim of preventing wastage without compromising clinical care.

Methods:

1). To review the ordering of blood components against regular usage via the blood stock management scheme 'VANESA' system.

2). To ensure that ordering is peer group reviewed.

3). To provide training across the Trust on how to appropriately order blood components correctly to minimize time expiry wastage.

Results: Comparing data after 10 weeks from implementing the change with data for the same months from the previous 2 years shows a total fall of RBC stock of 42.25%. This equates to a reduction of 68 units in average daily stock holding. This reduction in stock equates to a saving of £8500 as a one of saving. Revising our daily stock ordering based on information from 'VANESA' on the previous 2 years data resulted in a reduction of TIMEX units from an average of 43 units to 10 units monthly which is a potential on-going saving which equates to an excess of £4000 per month.

Summary / Conclusions: Over the first year we expect to potentially save £56500 with on-going cost savings of £48000 per year.

P-018

THE GOLDEN HOUR: SAVING POUNDS BY CHANGING THE 30 MINUTE RULE TO 60 MINUTES

D McKeown[1], F Regan[2,3], F Chowdhury[2,3], L Chapple[1], L Noble[1], S Sharma[1] and D Johnson[1]

[1]Blood Transfusion [2]Haematology, Imperial College Healthcare NHS Trust
[3]Haematology, NHS Blood and Transplant, London, United Kingdom

Background: The Joint UKBTS Professional Advisory Committee Change Notification No. 33 (June 2016) advised that blood could be returned to a fridge after being out for up to 60 min rather than 30 min, provided it had not been out more than twice previously for up to 60 min. They also advised that RBC units must be refrigerated for >6 h between outings. We established from the authors of the 60 min rule, that a RBC unit out of the fridge for 60 min could be collected for transfusion within 6 h after return to a fridge, provided the transfusion was completed within 4 h. The risk of bacterial proliferation was only increased if the RBC unit had been removed from the fridge for up to 60 min, then returned for <6 h (so not fully cooled again), before being removed again for a second time for up to 60 min and not transfused.

Aims: We wanted to assess how much blood was saved from implementing this rule and to identify the cost in monetary terms.

Methods: A flowchart for managing a blood outing was devised to ensure that units were checked on RETURN to the fridges. Units returning for a second or third time, were checked for refrigeration of >6 h between outings, to qualify for return to the fridge. Units returning to satellite fridges were quarantined remotely, using electronic blood tracking. This was implemented with full change control. We retrospectively audited how many units could have been saved between June – December 2017 to estimate the impact of the change.

Results: Reductions in cold chain wastage can safely be made by extending the 30 min rule to 60 min, with a simple system to ensure quarantine of units for 6 h before a further outing, unless for imminent transfusion. Between from June-Dec 2017, we identified 125 RBC units were prevented from being wasted; this resulted in savings of over £15,000.

Summary / Conclusions: If this rule was implemented nationally, savings to the NHS would be significant.

P-019

IMPROVEMENTS IN PERIOPERATIVE BLOOD MANAGEMENT FOR PATIENTS ELIGIBLE FOR ELECTRONIC CROSSMATCH

B Pasko, C Darrell, H Kurbaj, M Mohammed and K O'Brien
Pathology, Beth Israel Deaconess Medical Center, Boston, United States

Background: The Joint Commission on Accreditation of Healthcare requires that blood is available for all patients undergoing procedures that might require intraoperative transfusion. The majority of patients undergoing procedures are eligible for electronic crossmatch (ECM) packed red blood cell (PRBC) units. To be eligible for ECM, a patient must have two concordant samples prior to surgery. ECM units are readily available and can be sent to the operating room (OR) without delays or compromising patient care. Thus, preoperative crossmatching and storage of PRBCs for patients eligible for ECM creates unnecessary waste of blood bank and hospital resources including: technologist time, PRBC storage time, and dollars. With this in mind, in September 2016 our institution implemented a new protocol for handling preoperative requests for PRBCs in patients eligible for ECM. This protocol specified that blood was not to be crossmatched for surgeries in ECM eligible patients prior to an order requiring the units in the OR, thus blood was prepared "On-Demand".

Aims: The goal of this study was to evaluate effectiveness of the new "On-Demand" blood bank program for all ECM-eligible preoperative patients, who might require intraoperative PRBC transfusions. We defined effectiveness as reduction of total PRBC units unnecessarily crossmatched, issued, and returned to the blood bank.

Methods: A systematic retrospective review of all OR procedures requiring at least a type and screen prior to surgery was performed for January through March of 2016 and 2017, both prior to and after the implementation of the PRBC "On-Demand" program. In our analysis we reviewed the number of ECM units prepared and stored for surgeries across multiple surgical disciplines, including: Cardiothoracic, Vascular, Neurosurgery, OB/GYN, Urology, Transplant, and Orthopedic surgery. We evaluated total number of patients and PRBC units crossmatched, issued, returned, and transfused in the OR. For our analysis, we used a one-tailed t-test for crossmatched units, due to the known plan to decrease the total units crossmatched, and a two-tailed t-test for all other variables (number of patients, issued, returned, and transfused).

Results: Significantly fewer patients eligible for ECM were crossmatched following implementation of the "On-Demand" program between January and March 2017 compared to the prior year (Patients eligible for ECM that were crossmatched: 1005 vs 717, P = 0.03), while the number of total patients eligible for ECM was unchanged for the same period (2004 vs 2189, P = 0.07). There were significantly fewer PRBCs crossmatched January through March of 2017 than January through March of 2016 for ECM eligible patients (3715 units vs 2408 units, P = 0.03). While there was a decrease in the total PRBC units issued, returned, and transfused between January and March 2017 when compared to the same time period in 2016, these were not statistically significant differences (Issued: 1545 units vs 1355 units, P = 0.21; Returned: 1031 vs 908, P = 0.33; Transfused: 532 units vs 447 units, P = 0.36).

Summary / Conclusions: Implementation of the "On-Demand" ECM program resulted in significantly fewer patients requiring crossmatch. Crossmatching ECM units "On-Demand" has proven to be more efficient in managing preoperative ECM eligible samples, without compromising patient care.

P-020

THREE YEARS WASTAGE MANAGEMENT OF BLOOD AND BLOOD PRODUCTS IN THE IRANIAN BLOOD TRANSFUSION ORGANIZATION

S Sharifi, A Pourfathollah, K Shams Asanjan, A Ali Balazadeh and M Asadi
High Institute for Research and Education in Transfusion Medicine, Tehran, Islamic Republic of Iran

Background: Waste management is one of the most important priorities of each transfusion organization. The wastage reduction of blood and blood products in the blood transfusion organization can lead to huge savings and optimal use of health resources.

Aims: In this study, we aimed to evaluate the management of blood and blood products wastage during a three year period in Iranian blood transfusion organization.

Methods: This study conducted in the blood transfusion organization of IRAN during the years 2014–2016. Firstly, in order to manage the avoidable waste of blood and blood products in 2014, an instruction developed which contained the main causes of the wastage and how to control them. In a workshop, the instruction trained, by the head quarter for the wastage reduction of blood and blood products, to all deputies and blood distribution authorities in 31 provinces.

Monitoring of wastage, the rate of production of blood components, and corrective actions were monitored monthly from all provinces.

To reduce expired products, the stored inventory reduced from 5–7 day consumption to a maximum admissible volume for 4–4.9 day consumption.

Tariffs of blood and blood products developed. The costs of blood and blood products were paid by health centers to Blood Transfusion Organization.

The equipment for components production were serviced and calibrated. Blood and blood products transferred from low consumption centers to high consumption centers.

Results: The amount of waste reduced from about 20% of production in 2014 to about 10% of production in 2016 years. Therefore, the waste reduced by 50% using aforementioned methods.

The amount of waste decreased from 870,074 units in the year 2014 to 566,062 units in the year 2016. This is equal to saving of 77,749,878,880 Rials (Iranian currency).

Summary / Conclusions: According to our findings, it is essential to improve the wastage management process including monthly monitoring of wastage, surplus movement of blood and its products, continuous training of staff, and equipment monitoring.

P-021

NATIONAL MACRO ASSESSMENT OF UKRAINIAN REGIONAL BLOOD SERVICES OPERATION

A Chuhriiev

Zhytomyr Regional Blood Centre, Zhytomyr, Ukraine

Background: Timely access to a sufficient quantity of safe blood products of assured quality, effective operation of regional blood services and optimal clinical use of blood components significantly affect the reinforcement of healthcare system of each country. Annually European Directorate for the Quality of Medicines and Healthcare (EDQM) conducts the assessment of self-sufficiency of EU countries with donor blood in several sections, using relative intensity values in the form of indices: per 1000 population, specific weight in the structure, per 100 000 donors, per 100 000 blood components transfused.

Aims: The aim was to create a system for macro assessment of the state of transfusion medicine in the regions of Ukraine.

Methods: The criteria for macro assessment were determined by Delphi method and the ranking of each region was carried out by rank evaluation method.

Results: Macro assessment criteria, being final values of blood centers operation, were divided into two blocks.

The first block "Population Procurement" consisted of five criteria: number of donors, number of red blood cells units and apheresis platelets units (APUs) issued to hospitals and amount of plasma suitable for fractionation. Criteria were calculated per 1000 population.

The second block "Operation Efficiency" consisted of 6 criteria in two areas: staff productivity (donors, donations, APUs, amount of donor blood procured by 1 worker) and efficiency of equipment utilization (amount of plasma and APUs per device for apheresis)

Summing up the points for each criterion, the ranking of each region was defined in the first block "Population Procurement" and in the second block "Operation Efficiency".

On the basis of the results of two blocks, the ranking of blood services of each region was defined at the national level.

Summary / Conclusions: The macro assessment of blood services operation allows to identify problem areas in the operation, level of population procurement with blood components, usage effectiveness of main resources of regional blood centers and to ensure coordination of development and organisation of measures for achieving economic efficiency of the national blood service.

P-022

EVALUATION OF TURNAROUND TIME AS A MEASURE OF INSTRUMENT CAPABILITY TO MEET WORKLOAD NEEDS IN THE IMMUNOHEMATOLOGY LAB

T S Casina[1] and W Malomgre[2]

[1]Ortho Clinical Diagnostics, Raritan, United States [2]Ortho Clinical Diagnostics, Turnhout, Belgium

Background: The evaluation and selection of a new immunohematology testing instrument for the laboratory is often challenging because of the way the manufacturer of the product provides information about the instrument. Often the information to base a decision is centered on a stated throughput of the instrument. The throughput is often stated in terms of tests, columns or profiles per hour. Clear understanding of this information is difficult to achieve and utilize for comparison of the instruments capabilities usually because there is no commonality. The most important criteria for evaluation is turnaround time (TAT) and delivery of accurate, timely results which are critical to providing transfusion therapy.

Aims: The study was designed to evaluate IH instruments from a TAT perspective with a mix of test profiles typical of the laboratory from both speed of delivery of results and consistency of performance utilizing standard workloads in the laboratory.

Methods: Three instruments were evaluated, Bio-Rad IH-500 (IH-500), ORTHO VISION (OV) and ORTHO VISION Max (OVM) with four workload protocols (WLP) with varying volumes representative of workflow. Each protocol tested was analyzed for load pattern time, test type % and TAT. The test profiles included blood group (BG), Rh/K phenotype (RHK), antibody screen (ABS), major crossmatch (XM), antibody identification (AbID) and direct antiglobulin test (DAT). The following WLPs were evaluated: WLP1- 64 tests – 5 h- BG (42%), RHK (6%), ABS (49%), XM (3%); WLP2-69 tests-2 h- BG (46%), ABS (54%); WLP3- 45 tests–3 h–BG (35%), RHK (7%), ABS (38%), XM (13%), AbID (7%); WLP4 -71 tests-3 h-BG (53%), RHK (14%), ABS (20%), DAT (13%).

Results: For WLP1, IH500 completed 95% of all tests in ≤ 39 min with a TAT range from 15–69 min; OV 95% in ≤ 28 min. TAT range 7–29 min; OVM 95% in ≤ 26 min. TAT range 7–28 min. For WLP2, IH500 completed 95% of all tests in ≤ 61 min with a TAT range from 35–61 min; OV 95% in ≤ 47 min TAT range 12–53 min; OVM 95% in ≤ 38 min TAT range 11–38 min. For WLP3, IH500 completed 95% of all tests in ≤ 52 min with a TAT range from 14–55 min; OV 95% in ≤ 32 min TAT range 8–35 min; OVM 95% in ≤ 27 min TAT range 8–29 min. For WLP4, WLP3 IH500 completed 95% of all tests in ≤ 39 min with a TAT range from 16–45 min; OV 95% in ≤ 31 min. TAT range 7–34 min; OVM 95% in ≤ 26 min. TAT range 7–26 min.

Summary / Conclusions: Evaluating instrument performance to determine best fit to a laboratory is challenging. This study demonstrates the importance of using workload, arrival/ load and TAT to determine the capability to manage the workload of the laboratory. In this situation comparing these instruments, the ORTHO VISION platform instruments demonstrated the capability to routinely and consistently provide shorter TATs as compared to the IH-500. Additionally, it was demonstrated that OVM with workloads that are concentrated in shorter arrival times provides improved TAT.

P-023

A COMPARISON OF TWO INSTRUMENTS FOR IMMUNOHEMATOLOGY TESTING FOR WORKLOAD MANAGEMENT

TS Casina[1] and W Malomgre[2]

[1]Ortho Clinical Diagnostics, Raritan, United States [2]Ortho Clinical Diagnostics, Turnhout, Belgium

Background: When evaluating the need for new immunohematology instruments, it is necessary to consider the workload volume, the mixture of test profiles, timing of arrival within the laboratory and the frequency of urgent samples and complexity of patients tested as evaluation criteria. This permits the laboratory to identify which IH system to select and how many instruments that would be needed to manage the workload. Often this is done based on throughput numbers which does not always accurately reflect the true need.

Aims: The study was designed to evaluate which and how many IH instruments that would be necessary and would effectively succeed in routinely completing the workload of various test profiles typical of the laboratory as well meet the turnaround time expectations.

Methods: The instruments that were evaluated were 3 Grifols Erytra (GE) systems and 3 ORTHO VISION Max (VISION) systems. There were three comparison scenarios evaluating turnaround time (TAT). The instruments were first evaluated on current practice of using three instruments each one performing testing with the samples of specific classification 1) Routine 2) Urgent and 3) Surgery. Load time/scan time and result were captured for each sample on each Erytra systems. This was then paralleled on the comparison instruments. The second scenario kept the same load based on arrival, urgency requirement and then optimally spread the workload without regard for the unique sample classification on 3 OV. The third scenario ran the same workload respecting the sample arrival time on 2 OVM. Additionally, STAT sample TAT was evaluated with 1 GE, 1 OV and 3OV instruments.

Results: The following results of TAT were found for a total of 239 samples: Scenario 1 GE1 84 samples (TAT Range 11–72 min with 95% of all tests ≤ 69 min) OV1 84 samples (TAT range 12–57 min with 95% of all tests ≤ 54 min); GE2 70 samples (TAT range 12–51 min with 95% of all tests ≤ 42 min) OV2 70 samples (TAT range 8–28 min with 95% of all tests ≤ 27 min); GE3 85 samples (TAT range 11–46 min with 95% of all tests ≤ 45 min) OV3 70 samples (TAT range 8–28 min with 95% of all tests ≤ 27 min). Scenario 2: 239 samples across all 3 instruments were analyzed

with the following results: GE1, 2, 3 239 samples (TAT Range 11–72 min with 95% of tests ≤ 67 min); OV 1,2,3 239 samples (TAT range 7–57 min with 95% of tests ≤ 51 min); 3OV 239 samples (TAT range 7–34 min with 95% of tests ≤ 33 min). Scenario 3: 239 samples on 2 OV (TAT range 7–40 min with 95% of tests ≤ 39 min). STAT: GE 2 70 samples (TAT range 12–51 min with 95% of tests ≤ 42 min; OV2 70 samples (TAT range 8–27 min with 95% of tests ≤ 26 min; 3OV instruments; OV2 70 samples (TAT range 8–27 min with 95% of tests ≤ 25 min).

Summary / Conclusions: Evaluating instrument performance to determine how multiple instrument systems perform on managing workload and meeting result delivery timing can be accomplished with proper comparisons. This study demonstrates the importance of using workload, arrival/ load and TAT to determine the capability to manage the workload of the laboratory. Significant reductions and consistent, predictable TAT can be achieved as seen in this comparison of the ORTHO VISION Max system versus the Grifols Erytra.

P-024

THE MANDATORY OF ANTIBODY SCREENING TEST IN VOLUNTEER BLOOD DONORS AND COST ANALYSIS OF A REFERENCE CENTER AT MIDDLE ANATOLIA: A SELFIE PICTURE OF TURKEY

M Yay, E Unal and B Eser

Erciyes University, Erciyes University, Kayseri, Turkey

Background: In the Turkish guidelines; national preparation, use and quality assurance of blood and blood components, updated in 2016, it was reported that "donors who donated blood/blood components for the first time and donors with a history of pregnancy or transfusion history since last blood donation, should be screened for erythrocyte antibodies".

Aims: International studies have reported that the positive rate of antibody screening in blood donors is around 0.8%. In this study; as advised in the national guidelines, donors carrying these characteristics began to be screened for antibodies by June 2017 and the result, and cost analysis of these 7 months study period were examined.

Methods: Between June 2017 and January 2018 volunteer blood donors who donate for the first time or had a pregnancy or transfusion story since the last blood donation at the Erciyes University Blood Center were screened for triplet cell antibodies were scanned with the Immucor-Neo device for donors

Results: Between June 2017 and January 2018, a total of 16,373 people were donated blood and blood products. Of these donors, 6,980 (43%) were of blood donors for the first time. 1,451 (8.9%) of the donors were female, and 577 (40%) of the donors were pregnant donors.

Within the study period a total of 7,557 (6,980 first donations + 577 pregnancies) antibody screening tests were performed. 4 (0.05%) of the tests, (Chi square: 7541 P: 0.00001) showed positive antibody screening in the donor. 4 positive donors; 2 Anti-D, 2 Anti-K antibodies were detected. The total cost spent for antibody screening in donors during this period; 1.25 euro (Unit test cost) X 7.557 (total number of tests) = 9.446 euro.

In this study, a 7-months test cost was calculated only in the regional blood center for a period of time. We calculated that the annual cost of this test approximately will be 16.000 euro. This additional cost is not covered by the SGK in any way. The non-increasing charge of anywhere, erythrocyte suspensions for more than 15 years for the periodical blood center which is preparing erythrocyte suspension outside the Red Crescent, as well as increasing cost of bag and test, adds a negative impact to the final costs.

Summary / Conclusions: We speculate that in order to reduce the cost of this test, which is found at a rate of 0.05% in the volunteer donor group, the donor specimens are considered to be 4–6 donors pooled or a single pooled cell instead of 2, 3 test cells can be considered. These strategies should reduce annual cost in Turkey which is estimated as 2.3 millions unit blood donations per year in which half of these donations are first donation.

P-025

TYPE AND SCREEN (TS) WITH IMMEDIATE SPIN (IS) CROSSMATCH POLICY: ARE WE THERE YET?

HB Othman, Z Khalid and W Wan Mohd Saman

[1]*Centre for Pathology Diagnostic & Research Laboratories, Universiti Teknologi Mara, Sungai Buloh, Malaysia*

Background: The policy of releasing blood after immediate spin (IS) crossmatch or electronic crossmatch (EC) for blood recipient with negative antibody screening (AS) has been practised worldwide. This practice has saved time and cost as well as has expedited the release of blood to the patients. As there is growing in the clinical services in our new tertiary care centre, the blood requests are becoming more frequent.

Aims: To evaluate the possibility of implementing type and screen (TS) with immediate spin crossmatch policy of recipient with negative AS in our centre.

Methods: This was a cross sectional study done in the Transfusion Medicine Unit, UiTM Medical Specialist Centre from August 2017 until January 2018. A retrospective analysis was performed by retrieving all data on pretransfusion testing performed during the study period. Current practice includes a standard pretransfusion testing i.e. blood group and type, three cell panels of AS test, full crossmatching procedures (IS, at 37 C and anti human globulin-AHG phase) prior releasing of blood.

Results: Out of 589 standard crossmatches performed on 242 patients with negative AS, about 2.5% (15/589) of crossmatches were found to be incompatible at AHG phase. The most common reason for incompatibility was due to positive Direct Coombs' Test (DCT) of the blood units being crossmatched (12/15). There was no extended DCT being performed to determine the specificity of each DCT reaction. The incompatibility was also detected in one crossmatch (1/15) for blood unit that was tested negative for DCT. The most likely reason for the incompatibility was the presence of alloantibody towards low incidence antigen. However, further investigation was not performed as a compatible blood was obtained following the subsequent crossmatch with other blood unit. There were two crossmatches (2/15) with mixed field reactions which could be due to fibrin formation during sample storage. As our centre is not a blood collection centre, thus we have no direct access to the donor information and blood processing. All blood and blood products come from our local National Blood Centre (NBC), Kuala Lumpur, Malaysia. Currently, all DCT positive blood units will be returned back to the NBC for further management. As there was a significant number of crossmatch incompatibilities due to positive DCT of the blood units, the implementation of this new policy in our centre is unfavourable as we tend to miss the reactions if the AHG phase is omitted from the routine procedures.

Blood release after IS and EC are made possible for institution that has a software which is validated with safety elements especially in assigning compatible blood for negative AS and preventing release of ABO incompatible blood. Our existing basic blood bank information system does not fit the safety criteria needed for this policy as we still assign ABO compatible blood unit manually through the system.

Summary / Conclusions: The transfusion medicine unit at the healthcare facilities is responsible for the safety of the blood issued to the recipients. As there were incompatible AHG crossmatch detected among our negative AS recipients, we concluded that we are not ready for this TS with IS crossmatch policy even though it is eminently cost effective. Standard crossmatch at all phases is still relevant in our centre and we will adhere to the current practice until sufficient technical and infrastructural support available in our centre. In addition, sufficient screening cell panels relevant to our local population need to be developed so that clinically significant antibodies will be detected.

P-026

Abstract has been withdrawn

Training and Education

P-027

Abstract has been withdrawn

P-028

TRANSFUSION SAFETY OFFICER RESOURCE MANUAL

L De Biasio[1], D Berta[2], Y Davis-Read[3], A Escorcia[4], L Harrison[5], K Syer[6] and B Weaver[7]

[1]Ontario Regional Blood Coordinating Network, Sunnybrook Health Care Sciences Centre, Toronto [2]London Health Sciences Centre, London [3]St. Michael's Hospital [4]University Health Network, Toronto [5]Trillium Health Partners, Mississauga [6]Lakeridge Health, Oshawa [7]Kingston General Hospital, Kingston, Canada

Background: The report from the Royal Commission of Inquiry on the Blood System in Canada or the Krever Inquiry was released in November 26, 1997. The Transfusion Safety Officer (TSO) role was established in 1997 to enhance the safety and quality of blood transfusions in Canada, in response to the Royal Commission recommendations. The TSO's fundamental role is to improve patient safety in all aspects of transfusion practice. This position comes with several responsibilities that encompass the following areas: technical and clinical, utilization management, quality and risk, professional and educational, and research. A guide to assist a healthcare professional's transition into the role of a TSO is advantageous; however, there are limited resources to date.

Aims: The TSO resource manual was developed to provide convenient access to resources such audit tools, educational tools, algorithms, monographs, checklists, and guidelines for those facilities without a TSO in place or facilities which have opened up a new TSO position.

Methods: In 2013, the clinical project coordinator-transfusion safety nurse from a provincial blood coordinating network visited various large healthcare institutions. Information was collected through observations and discussions with the TSOs about the daily activities and responsibilities. The TSOs from each institution identified that there was minimal guidance and limited resources to assist with their transition into the role. Each acknowledged that TSOs might come from diverse backgrounds in healthcare, which could contribute to limitations in the understanding of clinical or technical terminology and gaps in communication. Experienced TSOs from six large provincial healthcare institutions were closely involved in the development of this resource.

Results: The Transfusion Safety Officer Resource Manual delivers detailed information regarding the roles and responsibilities of a TSO, and the expected time commitments for each. 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

A WordPress plug-in feature is being used to monitor the amount of user downloads, since the release of the Transfusion Safety Officer Resource Manual in March 2017 on the Ontario Regional Blood Coordinating Network (ORBCoN) website. A recent report from February 2018 displays 568 user downloads since the release of the resource manual.

Summary / Conclusions: The Transfusion Safety Officer Resource Manual was developed as a reference guide for Medical Laboratory Technologists, Registered Nurses and other healthcare professionals appointed to the TSO role. It is also intended to be utilized by hospitals that do not have a formal TSO position but which have delegated the responsibilities to other staff. The Transfusion Safety Officer Resource Manual provides helpful information to assist with education in transfusion safety, adverse event investigation and reporting, product administration guidelines or monographs, and links to information about the equipment used for infusion of blood. This resource manual will serve as a useful reference tool to assist with a healthcare professional's transition into the TSO role.

P-029

PHYSICIAN ENGAGEMENT: DISCOVERING A COMMON PURPOSE

S Cope[1], T Cameron[2], S Scheuermann[3], T Thompson[1] and A Wendt[1]

[1]Ontario Regional Blood Coordinating Network (ORBCoN), Sunnybrook Health Sciences Centre, Toronto [2]Ontario Regional Blood Coordinating Network (ORBCoN), Ottawa Hospital Research Institute, Ottawa [3]Ontario Regional Blood Coordinating Network (ORBCoN), McMaster University, Hamilton, Canada

Background: The Ontario Regional Blood Coordinating Network (ORBCoN) was created in 2006 to provide an organized and integrated approach to blood management in Ontario. One of ORBCoN's strategic goals is to develop high quality, relevant, evidence-based transfusion medicine educational resources in collaboration with transfusion medicine experts and end-users to help facilitate the adoption of best practice and improve patient safety. As a first step in increasing physician buy-in or engagement with transfusion medicine educational resources, ORBCoN evaluated the utilization, content and accessibility of each resource to ensure the educational needs of each end-user were being met. Encouraging end-users to adopt evidence based practice changes with ORBCoN's accessible and informative resources will provide the necessary pathway to reach our common purpose, ensuring patients are getting the right product, at the right time for the right purpose.

Aims: The aim of this project was to determine the needs and gaps between current educational resources to ensure future development of transfusion medicine resources address the educational needs of the end-user.

Methods: An educational needs assessment was undertaken as a qualitative analysis using a 17 question survey created using web-based software called LimeSurvey™.. The survey was distributed to all Ontario hospitals with a transfusion service (n = 150) via email to Transfusion Medicine Medical Directors and Transfusion Committee Chairpersons. There were specific clinical scenarios included as a means to determine gaps in transfusion medicine knowledge amongst the intended target audience.

Results: A total of 34 responses were received with small, community and academic hospital settings representing 13, 13, and 8 responses respectively. Staff physicians accounted for 61% of respondents and 13% were classified as 'other' which represented professionals such as Lecturer, Laboratory Director and Transfusion Safety Officer. Mandated transfusion medicine competency was enforced in only 6 hospitals (17%). The most common motivation for choosing CME was to increase knowledge (61%) followed by reassurance current practice was consistent with standard of practice (50%) and to adopt a new practice (39%). Respondents were then asked to consider targeted clinical situation scenarios regarding the routine dosing of Intravenous Immunoglobulin, Plasma, Prothrombin Complex Concentrate and Albumin.

Summary / Conclusions: Despite a low response rate, the needs assessment provided insight into gaps between what is available and what end-users require in order to remain current and maintain competency in transfusion medicine. ORBCoN will continue to collaborate with end-users of blood components and products to provide current and relevant resources. As learners, we are unable to assess what we don't know and what we need to know in any given topic or specialty therefore, in order to provide content that is both current and relevant to our service receivers, addressing needs to encourage knowledge translation into best practice ensures the patient is receiving the best care by using the right product at the right time for the right purpose.

P-030

UMBILICAL CORD BLOOD COLLECTION TRAINING FOR A NATIONWIDE RELATED PROGRAM

F Coria, I Gimenez, L Lazo, M Polop, L Scalercio, M Veloso, C Gamba and S Kuperman

Centro Regional de Hemoterapia, Hospital Garrahan, Ciudad Autonoma de Buenos Aires, Argentina

Background: Umbilical cord blood (UCB) is a source of hematopoietic progenitor cell (HPC) for transplantation. GMP regulation and standards require training of personnel who perform procurement. Since 1996, our Related Program was launch in a Pediatric hospital aimed at families that have a child with a condition in which allogeneic HPC transplantation constitutes a therapeutic alternative. UCB collection was offered to this families through our own staff. Later, the program was opened to other institutions becoming nationwide in 2003. New tools were developed for appropriate training of healthcare professional involved in collection and shipping.

Aims: Our aim is to present the different tools we developed to train healthcare professionals in the UCB collection technique for our Related Program.

Methods: Retrospective descriptive study. For descriptive purposes three periods were defined:

A. Initial stage: 1996–2002, n = 65 UCB collections.
B. Expansion stage: 2003–2014, n = 549 UCB collections.
C. Improvement stage: 2015–2017, n = 222 UCB collections.

Results: In the initial stage, the Program was open to patients of our Hospital and all the collections were made in a near maternity by UCB Bank staff following SOP (mean 9 collections/year).

Since 2003, by allowing the enrollment of patients nationwide, it became necessary to organize the collections in distant centers (expansion stage, mean 46 UCB collections/year).

Collections were done in 152 facilities covering 17 out of 24 provinces (71% of our country). New tools for training healthcare professional were implemented.

Lectures were supported with powerpoint presentations and written instructions were handed to each trainee covering collection techniques and shipping instructions.

Mainly, we performed training via phone calls. In some cases designated personnel from the maternities (obstetricians, midwifes, nurses, surgical technician, blood bank technician) come to our center to receive on-site training or we travel to centers with the same purpose.

During the improvement stage (mean 74 UCB collections/year, covering 78% of the provinces) we use our hospital's telemedicine services and a standardized form to guide the distance training allowing us to improve the fulfillment of the SOP among new cord blood bank staff. Finally, we made a training video using a birthing simulator (MamaNatalie) creating a realistic scenario.

This video shows the UCB collection technique in detail (8 min length).

Summary / Conclusions: We have achieved a nationwide network of professionals able to provide UCB for the Related Program.

The use of new tools for training at distant collection facilities increased patient access to healthcare, especially in underserved areas.

The most distant procurement was done in Santa Cruz (2587 km from our processing facility).

The use of telemedicine services has been highly motivating for trainees from remote small-medium size facilities without the chance to travel.

The video will be accessible on-line thorough our Hospital campus, where registered health care professional can request training and received a certification after a standardized assessment is completed.

Our training efforts seek continuously to improve the techniques to guarantee an adequate cell dose for its future use in transplantation.

This Program allowed 25 allogeneic HPC transplantation in children from our country.

P-031

Abstract has been withdrawn

P-032

KNOWLEDGE OF CLINICAL TRANSFUSION AMONG POSTGRADUATE RESIDENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

W Wan Alkamar Shah[1], S Othman Tan[1] and N Mohd Noor[2]

[1]Advanced Medical and Dental Institute (AMDI) Universiti Sains Malaysia, Kepala Batas [2]Transfusion Medicine Unit, Department of Haematology, Hospital Universiti Sains Malaysia, Kubang Kerian, Malaysia

Background: Blood transfusion is one of common therapy prescribed by clinicians. Despite that, injudicious and unsafe transfusion contributes to leading causes of morbidity and mortality globally, as it jeopardies quality of care and cause wastage of blood product resource. Therefore, it is vital that clinicians, mainly postgraduate residents to possess knowledge on clinical transfusion. The current level of knowledge among postgraduate residents in Hospital Universiti Sains Malaysia (HUSM) is not yet known.

Aims: To study the clinical transfusion knowledge level among postgraduate residents within the Department of Anaesthesiology and Intensive Care, Accident and Emergency, Obstetric and Gynaecology, General Surgery, and General Medicine in Hospital Universiti Sains Malaysia (HUSM) and demographic factors that are associated with it.

Methods: This was a cross-sectional study using a validated self-administered questions, which were distributed to 210 participants from five departments in HUSM. The validated assessment tool consisted of six demographics survey and 20 questions on clinical transfusion knowledge (total score of 20). Score of 0 - 9 were categorised as 'poor' knowledge level and score of 10 - 20 were categorised as 'good' knowledge level. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) program version 23.0. The first objective (demographic factors) and second objective (knowledge level) was analysed using descriptive analysis. The third objective (associated demographic factors with knowledge level) was analysed using simple logistic regressions. Variables in simple logistic regression in which p value of <0.25 was analyzed using multiple logistic regressions. A P value of <0.05 was set as statistically significant.

Results: Majority of participants (27.6%) were from Department of Accident and Emergency. Based on postgraduate year, Year 1 accounts for majority of participants (31.9%).Mean (SD) age was 32.9 (1.45) years. Number of male and female participants in both gender were nearly balanced, which were 104 (49.5%) and 106 (50.5%) respectively. Formal training was attended by 111 (52.9%) of participants. Mean (SD) working experience is 7.46 (1.07) years. Question on platelet transfusion for prophylaxis procedure were correctly answered by highest percentage of the

participants (80.5%).Highest percentage of participants (94.3%) had wrongly answered question on reporting of transfusion reactions. Mean score (SD) is 8.77 (1.77).A total of 125 (59.5%) participants obtained poor knowledge level. No significant association found between the demographic factors (department, gender, age, postgraduate year, working experience, formal training) with the knowledge level.

Summary / Conclusions: In general, majority of the participants have poor knowledge level in clinical transfusion. The results were consistent with the most of the knowledge based studies. However, no significant associations were found between demographic factors and knowledge level. Thus, the Blood Transfusion Service should focus on collaboration with the respective clinical departments to conduct continuous medical educational (CME) sessions and speciality based training for the improvement of knowledge of clinical transfusion among postgraduate residents. Factors such as awareness or attitude, that might have association with poor knowledge, can be considered to be tested, as well as pre- and post- interventional study can be done in similar group of participants to test the impact of educational methods on clinical transfusion knowledge.

Risk Models, Standards and Regulation

P-033

INTERNATIONALLY STANDARDIZED CODING AND LABELING IN BLOOD TRANSFUSION – 24 YEARS LATER

M Freire and T Knight

ICCBBA, San Bernardino, United States

Background: In the early 1990s, in the course of the First Gulf War, blood units dispatched from many countries to the combat zone lacked unique identification and common product descriptions. Duplication of donation numbers and highly variable label designs in different languages caused confusion and increased the risk of errors associated with blood transfusions. As a strategy for improving transfusion safety, an international task force—formed by members from ISBT, AABB, the American Red Cross, the Department of Defense, and the Health Industry Manufacturers Association—was asked to design an internationally standardized coding and labeling system. Consequently, in 1994, the "ISBT 128 Standard" was first published. In 2010, the World Health Assembly approved resolution WHA63.22, which affirmed the urgent need for the implementation of globally consistent coding systems for human cells, tissues, and organs.

Aims: To understand the extent of adoption of internationally standardized coding and labeling by countries in different categories of human development during the past 24 years.

Methods: The ICCBBA internal database was used to generate the list of countries and facilities registered to use ISBT 128. For the purpose of this abstract, the countries were categorized using the classification according to the Human Development Index (HDI) from the United Nations Development Programme, which is: (1) very high HDI, (2) high HDI, (3) medium HDI, and (4) low HDI.

Results: The ISBT 128 Standard has been adopted by facilities in countries across all categories of human development. At present, facilities in 53 out of 195 countries in the world have adopted the standard for blood transfusion services. A total of 4,073 facilities—blood collection centers and transfusion laboratories—around the world are registered to use ISBT 128. However, the data shows a significant disparity between the number of facilities per category: 3,478 (85.39%) from the very high HDI, 546 (13.41%) from the high HDI, 38 (0.93%) from the medium HDI, and 11 (0.27%) from the low HDI. This trend is also reflected in the data corresponding to the percentage of countries with facilities that have adopted ISBT 128 in each category: 57% in the very high HDI, 18% in the high HDI, 17% in the medium HDI, and 12% in the low HDI.

Summary / Conclusions: Twenty-four years after the first publication of the ISBT 128 Standard, the vision of internationally standardized coding and labeling in blood transfusion has become a reality, predominantly in countries assessed as having very high human development. The unequal adoption of the standard amongst the different categories of human development and the minimal adoption in some categories raise the question of whether it is necessary to develop a new strategy to make a change in this trend. In the years to come, international cooperation, re-evaluation of national and international policies, increased support by software developers and labeling manufacturers, as well as the use of emerging technologies in the fields of information technology and healthcare, may create the necessary opportunities to attain global standardization and to decisively improve safety in blood transfusion for everyone.

P-034

HYGIENE AND ENVIRONMENTAL MONITORING IN BLOOD BANKS

S Bhatti, B Hermundstad and A Llohn

Immunology and transfusion medicine, Akershus University Hospital, Lørenskog, Norway

Background: Environmental monitoring in blood banks is described in regulations and guidelines. How the environmental monitoring should be done, which areas should be included, and what are the acceptance criteria is however not clearly defined.

The actual regulations and guidelines are: The Council of Europe: "Guide to preparation, use and quality assurance of blood component", PIC/S: "Guide to good manufacturing practice for Medicinal product" and our national regulations based on the EU-Directives.

Interaction with our colleagues in Norway told us that we are practicing environmental monitoring differently and national guidelines are unclear.

Aims: The aim of this study was to see how environmental monitoring was performed and followed up in Blood banks in Norway.

Methods: The survey was sent to 28 blood banks in Norway, with the following aspects:

1. Which method was used?
2. What are the acceptance criteria?
3. How are these acceptance criteria chosen?
4. Which areas are monitored and how often?
5. How are the results followed up? 6. Rules for visitors to blood component lab.

Results: There are two methods used in Norway.

-Agar plates, which are placed on the surface to get samples. Colony forming units (CFU) are calculated after incubation at 22 $^{\circ}$ C.

-Measuring ATP from a given surface area, measured in relative light units (RLU).

Both methods give hygienic status of a surface area.

1. 9 out of 28 blood banks used Hygiena system SURE plus (ATP-based). 20 out of 28 used agar plates, mainly Hygicult TPC (Orion Diagnostica)
2. The majority using agar plates had 20 CFU per 10 cm^2 as acceptance limit, while the rest had acceptance limit from 10–100 CFU per 10 cm^2.

In case of ATP-based technique, 7 out 9 had less than 100 RLU per 100 cm^2 as acceptance criteria.

3. 20 Blood banks followed instructions from the distributer for choosing acceptance limits; the others had established their own acceptance criteria after validation.
4. All the Blood banks monitored production and donation areas. The majority monitored storage rooms and about 50% also monitored immunohematology lab. 13 monitored 4 times per year. 15 monitored from 1 to 12 times per year.
5. All the Blood banks had written standard operating procedure to follow up the results. Corrective measures were taken when results failed acceptance criteria.
6. The majority allowed visitors into the component lab, only after using shoe cover and lab coat. While 7 Blood banks had no special requirements to enter and 3 used adhesive doormat, which reduced dirt into the production room.

Summary / Conclusions:

- There are no concrete requirements for hygiene control given in available guidelines.
- Cultivation method and ATP based method are used.
- Acceptance criteria vary widely.
- Frequency of monitoring varies.
- Different rules for visitors to component lab.
- All Blood banks have written procedures with good follow-up routines.
- Our survey shows that there are a great desire to establish national recommendations and/or guidelines for environmental monitoring.

P-035

COUNSELLING FOR INFECTIOUS DONORS

A Verma, P Negi, J Singh, S singh and M Khan

Transfusion Medicine, Max Super Speciality Hospital Vaishali, Ghaziabad, India

Background: Blood donor counselling is a confidential dialogue between a blood donor and a trained counsellor about issues related to the donor's health and the donation process. It may be provided before, during and after blood donation. Worldwide, more than 92 million blood donations are collected annually. Of these, an estimated 1.6 million units are discarded due to the presence of markers for transfusion transmitted infections (TTI), including HIV, hepatitis B (HBV), hepatitis C (HCV) and syphilis. The scale of these discards and deferrals underlines the importance of public health information, donor education and counselling to enable prospective donors who may be unsuitable to donate blood to self-defer at any stage in the donation process. However, many national Blood Transfusion Services do not recognize the importance of blood donor counselling.

Aims: The main aim of this case study is to highlight the importance of blood donor counselling and the need to establish counselling systems for individuals who are not accepted as blood donors.

Methods: The study was conducted at the Department of Transfusion Medicine where we retrospectively analyzed the counselling methods over a period of 2 years from January 2016 to December 2017. In total 9,419 blood donor counsellings were done in four stages during the blood donation process. First stage was pre-donation information before an individual registers for blood donation. Second was the pre-donation counselling during the confidential interview for medical history, third stage was counselling during blood donation, last stage was post-donation counselling after blood donation.

Results: 203 out of 9419 donors had confirmed positive TTI test results. 132 (65%) turned up for counselling. These 132 donors were provided with information about the mode of infection transmission, possible implications for the donor's health, treatment opportunities for prevention of further transmissions and the need to inform contacts who might be at risk of infection so that they can be tested and treated as early as possible. Strict confidentiality of personal information about donors and their test results was ensured at all times.

Seven HIV reactive blood donors were referred to an Integrated Counselling and Testing Centre (ICTC), 19 syphilis-reactive blood donors were referred to STI clinic, 52 Hepatitis B and 54 Hepatitis C reactive donors were referred to Gastroenterology department. Donors were also informed that their donated blood has been discarded and that they are deferred from further blood donation permanently.

Summary / Conclusions: Training in blood donor counselling should be provided for all staff who interact with prospective and current blood donors. These include nurses, phlebotomists, doctors, donor recruitment staff, laboratory technicians and volunteers. The purpose of training in blood donor counselling is to provide staff with the necessary knowledge and skills to conduct counselling effectively.

There are benefits for both the Blood Transfusion Services and the wider health system in implementing blood donor counseling. It contributes to the continuum of care in the health system, plays an important role in preventing the further transmission of infections, contributes to the containment of epidemics and reduces the disease burden on the national health system.

P-036

IMPLEMENTATION OF INFECTION CONTROL STANDARDS IN EGYPTIAN NATIONAL BLOOD TRANSFUSION SERVICE

HA Fouad[1] and N Mohamed[2]

[1]Infection Control Department [2]Egyptian National Blood Transfusion Services, Cairo, Egypt

Background: Health care associated infections are a worldwide problem. They occur across all points of health care delivery. Thus, the fundamentals of infection control need to be employed regardless of constraints in resources and support. These fundamentals are essential to protect the donor, patient, clients and health care providers against exposure to infectious microorganisms and against the morbidity and mortality associated with these agents.

Aims: Implementation of infection control standards in Egyptian blood transfusion services

- to ensure prevention and control of health-care associated infections.
- to minimize occupational hazards associated with the delivery of health care.
- to promote sound infection control practices focusing on injection safety and safe blood transfusion.

Methods: The infection control team developed an action plan for implementation of the infection control program in the Egyptian national blood transfusion services. It included maintaining an appropriate infrastructure, ensuring the availability of supplies, establishing effective infection control practices, improving the occupational health management system, development of surveillance for nosocomial infection and training of health care providers. The plan is reviewed and updated annually. In 2013 the infection control team initially formulated infection control standard operating procedures and distributed them to one central and 27 regional blood transfusion centers. They referred to Egyptian national infection prevention and control guidelines and policies for health care services as well as American association of blood banks standards. The standard included infection control practices concerning hand hygiene, waste management, personal protective equipments, safe injection & prevention of needlestick and sharp injuries, environmental

cleaning, post-exposure prophylaxis, aseptic techniques, reprocessing of instruments, surveillance of nosocomial infection, facing emerging and re-emerging illness, laboratory working instructions and dentistry working instructions. The infection control team provided initial training and guidance to a total of 181 individuals including infection control officers, heads of different departments and health care providers of national and regional blood centers. Periodic assessment, supervision, monitoring and training of health care providers as well as annual evaluation of infection control program were performed.

Results: Improvement of the infrastructure as regards construction of hand washing basins and establishment of central sterile services area for reprocessing of instruments to ensure high standards of decontamination. Introduction of new supplies of infection control as disposable aprons and disposable tourniquets. Vaccination coverage of health care providers for hepatitis B is more than 96%. Training of the majority of health care providers. Statistical evaluation of the implementation of the infection control program has increased from 33.5% in 2013 to more than 82% in 2018. Increasing the compliance of the health care providers to infection control standards from 30.4% in 2013 to 80% in 2018.

Summary / Conclusions: Infection control is a necessary component of safe, high quality blood supply. The infection control program is not only committed to prevent adverse outcomes such as health care associated infections but also contributes to qualitative improvement of blood transfusion services.

P-037

THE STATUS OF STANDARDIZATION SYSTEM RELATING TO BLOOD TRANSFUSION IN CHINA: COMPARISON WITH THE GUIDE TO THE PREPARATION, USE AND QUALITY ASSURANCE OF BLOOD COMPONENTS

W Hu[1], H Zhou[1], Y Wang[2] and Z Meng[2]

[1]Blood Center of ZheJIang Province, HangZhou, China [2]Quality Management, Blood Center of ZheJIang Province, HangZhou, China

Background: The 19th Edition of the Guide to the preparation, use and quality assurance of blood components was released for publication by the Council of Europe's in November 2016. The 19th Edition of the Guide contains updated, comprehensive and systematic information related to the preparation, use and quality assurance of all blood components in the field of blood transfusion. The Blood Donation Law of the People's Republic of China took effect in 1998. Since then the Ministry of Health (MOH) of the People's Republic of China has developed a few standards related to blood transfusion in dribs and drabs, but the construction of standardization system in China is still in its infancy.

Aims: The aims of this study were to compare the differences between the Guide to the preparation, use and quality assurance of blood components published by the Council of Europe and standards in China, and to assess the status of standardization system relating to blood transfusion in China.

Methods: In March 2017, the Chinese version of copyright agreement was signed by Fresenius Kabi AG. and EDQM. In May of the same year, Fresenius Kabi AG. authorized the blood center of Zhejiang province to complete the work of translation and publication in China. The likely differences between the Guide to the preparation, use and quality assurance of blood components and standards related to blood transfusion in China were estimated.

Results: The 19th Edition of the Guide provides standards of quality and safety for the collection, testing, processing, storage, distribution and use of human blood and blood components, which has been separated into three sections. The first section, entitled Good Practice Guidelines, contains an updated version of the Good Practice Guidelines to fully reflect the most recent changes in good manufacturing practices relevant for blood establishments. The second section, entitled Principles, encompasses background information that has to be considered in forming policy decisions thus providing the "why and how". The third section, entitled Standards, states "what must be done". In China, by the end of 2017, although more than 20 standards had been issued in the field of blood transfusion, the basic standard system did not cover all processes from blood collection to use. The main differences between them are the following:(i)system standardized method;(ii) statistical process control;(iii)maneuverability and integrity;(iv)social economic evaluation;(v) uniform data processing system.

Summary / Conclusions: To develop the health standard system with Chinese characteristics, it is urgent to take several effective measures in China, including top-level design, system plan, coordination, learning from advanced experiences and adequate education.

P-038

MISSED OPPORTUNITIES FOR PATIENT BLOOD MANAGEMENT IN ONCOLOGIC LIVER SURGERY

T Ritchie[1], G Martel[1,2], D Touchie[1,2] and E Saidenberg[1,2]

[1]Ottawa Hospital Research Institute [2]The Ottawa Hospital, Ottawa, Canada

Background: Patient blood management (PBM) is a multidisciplinary approach to minimizing patient exposure to risks associated with anemia and with the transfusion of blood products. In patients undergoing liver resections, preoperative anemia has been consistently associated with an increased risk of blood transfusion, increased length of hospitalization, increased risk of major morbidity, and inferior overall survival. Additionally, there is an indication that pre-operative anemia and perioperative blood transfusion may be associated with worse oncologic outcomes in patients undergoing resection for primary or metastatic malignancies.

Aims: The objective of this work was to identify missed opportunities for the offering of preoperative blood management to patients undergoing liver resections for oncologic indications.

Methods: A retrospective review of medical charts was conducted. Patients who underwent liver resections for oncologic indications between 2010 and 2017 at one tertiary academic hospital were included.

Results: Three hundred and seventy-two patients underwent liver resections for oncologic indications between January 2010 and May 2017. The median time between surgical consent and surgery was 24 days. At the time of consent, 36.8% of patients had a recent (within 3 weeks) complete blood count (CBC), and 3.0% had a recent test of blood ferritin or vitamin B12. Only 2 patients of the 372 patients had a CBC, blood ferritin test and vitamin B12 test at the time of consent (0.5%). Pre-operative anemia was present in 32.6% of patients, and 22.3% of patients received at least one red blood cell transfusion. Pre-operative anemia was associated with an increased risk of transfusion (P < 0.01).

Summary / Conclusions: This work demonstrates that most patients undergoing oncologic liver surgery at one tertiary academic hospital did not have adequate CBC, ferritin, and vitamin B12 levels available at the time of consent. This identified lack of timely anemia screening may represent an important opportunity for improved application of patient blood management interventions in this population. These data will be used to inform and validate a pre-operative PBM strategy for patients requiring liver resection at our centre.

Blood Supply Management and Utilization

P-039

NHSBT SUPPLY OF RARE RED CELLS 2015–2017

R Anand[1], E Watkins[1] and G Howarth[2]

[1]NHS Blood and Transplant, Birmingham [2]NHS Blood and Transplant, Liverpool, United Kingdom

Background: The provision of rare phenotypes may require international collaboration. NHS Blood and Transplant (NHSBT) in the UK receives on average nine enquiries per month for the potential provision of rare red cell phenotypes. Enquiries originate from the UK and abroad. In 2014, a national improvement initiative led to the establishment of a central database for national requests and provision. We present data from the first three years.

Aims: To provide an overview of the demand and supply of rare red cell phenotypes and to identify the most common phenotypes requested.

Methods: A retrospective review was performed of all enquiries to NHSBT for rare phenotypes, logged from 1 January 2015 to 31 December 2017. Enquiries were logged by the NHSBT's National Frozen Blood Bank (NFBB), clinical staff and the International Blood Group Reference Laboratory.

Results: NHSBT received a total of 335 enquiries (113 in 2015, 141 in 2016 and 81 in 2017) and could have fulfilled 87% of them. 63 (18.8%) enquiries during the three-year period were from 24 different countries outside of the UK. Orders were generated for 149 (44.5%) of the total enquiries. Enquiries were made for over 50 different phenotypes. The commonest enquiries were for U- red cells (98 enquiries; 29.3%), Jkb- red cells (34 enquiries; 10.1%) and Fya-b- red cells (35 enquiries; 10.4%). These were followed by Kpb-, Fya-, Yta-, r'r', Jka-b-, Jsb- and Jka-. For countries outside of the UK, the commonest enquiry was still for U- red cells (17.5%). Only one or two enquiries were received for the following phenotypes: D–/D–; Cw-; Ge2; Dr(a-); Gya-; Dob-; Doa-; Anwj-; Co(a-b-); McLeod; MkMk; hrs-; and

f-. NHSBT could have provided red cells in 55% of cases. Where phenotypes could not be supplied, it was often due to the patient's specific combination of antibodies. Of the 149 orders generated, 69.8% of orders were fulfilled with thawed frozen red cells, 14% from liquid units in stock; 25% from donor call-ups and the remainder from a combination of the three. Red cells were exported from NHSBT by air in 27 separate orders from 2015 to 2017, to 10 different countries outside of the UK.

Summary / Conclusions: Requests for rare phenotypes account for a considerable proportion of red cell demand. This work provides an overview of potential and actual supply and will be used to inform future planning. NHSBT had the potential to fulfil the majority (87%) of requests for rare phenotypes and orders were generated for 44.5% of enquiries. The majority of rare blood was provided as thawed units from the NFBB, which limits the clinical options. However, 25% of orders were fulfilled with liquid units, provided by calling in specific donors. NHSBT has achieved this through developing and maintaining a loyal pool of rare blood donors, managed by well-practised, documented procedures.

P-040
O NEGATIVE RED CELL UTILIZATION – COMPARISON TO NATIONAL RECOMMENDATIONS

SN Nahirniak, H Blain and H Gerges

Laboratory Medicine and Pathology, Alberta Health Services / University of Alberta, Edmonton, Canada

Background: In Canada, approximately 7% of the general population is Group O Rh (D) negative (O neg) but requests from the national blood supplier for O Neg red cells (rbcs)have approached 12%. In March of 2017, due to concerns regarding shortages Canada's National Advisory Committee on Blood and Blood Products (NAC) posted a position paper on the Utilization and Inventory Management of Group O Rh(D) negative red cells to help narrow the supply and demand gap. The Edmonton zone transfusion service is the largest transfusion service in the country transfusing over 4500 rbcs per month so has a huge impact on the available national inventory of rbcs. Our local policies already restrict O neg as unmatched rbcs to females under the age of 45 years but it was unclear there were other areas of improvement.

Aims: Improve O negative red cell utilization by understanding where possible inappropriate use is occurring.

Methods: The number of O nega rbcs to non group O individuals were extracted from the Sunquest Laboratory information system for two time periods. One prior to the position paper - January to July 2016 and one after -September 2017 to January of 2018. The number of rbcs were broken down by appropriateness according to the NAC categories. 1) Mandatory – Intrauterine transfusion or emergency transfusion to females of childbearing potential; 2) Generally acceptable – Non O neg infants less than 1 year of age where group specific units are not available and non O neg patients requiring phenotypically matched or antigen negative units when group specific units are unavailable and 3) Likely unacceptable – O neg males /females over 45 years without anti-D requiring large volume transfusion of more than 4–6 units or non O neg patient because unit is close to expiry plus two Non-NAC categories of 4a) no confirmatory blood group (acceptable) or 4b) inventory stocking practices (likely unacceptable).

Results: In 2016, a total of 1257 O neg rbcs were transfused to non- O neg individuals. Of these, 158 were in category 1, 459 in category 2, 267 in category 3, 119 in category 4a and 254 in category 4b. This totals to 12.5% mandatory; 46% acceptable and 41% unacceptable rates. After the NAC paper, a total of 1177 O to non O rbcs were transfused with 129 category 1, 352 in category 2, 190 in category 3, 71 in category 4a and 435 in category 4b for 11% mandatory, 36% acceptable and 53% unacceptable. A 26% increase in category 4b due to remote allocation and provision of irradiated stock units is our highest proportional increase.

Summary / Conclusions: Despite being consistent in the mandatory plus generally acceptable and improving in the likely unacceptable categories, we have identified that we still have a significant proportion of inappropriate utilization that needs to be addressed. Most of this is secondary to inventory stocking practices not explicitly discussed in the NAC paper. The impact of inventory management for remote allocation for satellite blood fridges or rural hospital facilities needs further discussion and development of recommendations due to our geography to lessen this impact on this limited resource.

P-041
ESTABLISHMENT OF IVIG UTILIZATION PROGRAM AND IVIG UTILIZATION INDEX, A STEP FORWARD FROM FANTASY TO REALITY OF POTENTIAL SAVINGS IN IVIG USAGE

M Shabani-Rad[1], S Zolfaghari[1], J Hendry[2], J McCarthy[2] and L Baskin[1]

[1]DPLM, CLS/Ucalgary [2]Transfusion Medicine, Calgary Lab Services, Calgary, Canada

Background: Supplement of intravenous immune globulin (IVIG) is entering to a challenging phase considering continuous annual growth, limited plasma resources and uptrend costs driving health authorities to come up with plans to ensure vigilant and appropriate use of this product. Alberta is one of the highest IVIG users in Canada. Approach to this issue requires a robust patient data registry and information system to manage and monitor IVIG utilization effectively.

Aims: To establish a structured IVIG utilization program and comprehensive database to record patients' demographics, multiple clinical and laboratory parameters with well defined clinical categories. In addition it was essential to have a reporting system with capacity of trend recognition for all reliable parameters and indicators to enhance the efficiency of patients' medical management and product dispense in a timely manner.

Methods: Patients' clinical diagnoses registered in three categories of primary, secondary and specific diagnosis to allow for extraction of precise clinical data when it is required. Patients were also allocated to three setting of inpatient, outpatient and home-based to facilitate the approval process, product dispense and periodic clinical follow-up as mandated by local and national guidelines. IVIG utilization data used to rank multiple clinical disciplines for total IVIG usage, number of patients in each discipline and specific diagnostic entities as well as average IVIG usage/patient in different settings. We also developed an IVIG utilization index (average discipline specific annual IVIG usage for each patient/mean annual IVIG usage for all patients) to compare the IVIG utilization among specific disciplines at regional or national levels in an unbiased and reliable manner. The data was registered for all patients who had received IVIG during 2015- 2017 to demonstrate a meaningful quarterly trend for different clinical disciplines.

Results: Total of 1081 active patients were registered in IVIG database during 2017. Inpatients, outpatients and home-based patients accounted for 373 (35%), 622 (58%) and 86 (8%) respectively. Adult neurology and immune deficiency patients (PID & SID) accounted for the majority of registered patients in 2017, respectively 297 (28%) and 267 (25%). Hematology patients (non-immune deficient) ranked in third place (129; 12%). Total of 373,443 g [75% of total regional IVIG usage; neurology; 239,560 g (49%), immune deficiency; 98,160 g (20%), Hematology; 35,723 g (7%)]. ITP was the top hematology indication among inpatients. All cases were reviewed in collaboration with clinical disciplines and 85% of cases were labeled as appropriate. IVIG utilization index was calculated for each discipline (please see method section). This index was 2.04, 0.81 and 0.51 for neurology, immune deficiency and hematology groups respectively.

Summary / Conclusions: Consistent and reliable monitoring of IVIG utilization and implementation of clinical IVIG guidelines require a robust database and information system. Considering the fact that 85% of IVIG utilization in CZ was considered as appropriate, the estimated saving potential by multiple measures (IVIG calculator and restricted clinical approval process) cannot exceed 10% of the current annual IVIG utilization. IVIG utilization index could be a reliable indicator for monitoring of IVIG usage for major clinical disciplines at regional and national levels.

P-042
RETROSPECTIVE REVIEW OF PROSPECTIVE TRANSFUSION ORDER SCREENING: INITIAL VERSUS LONG TERM SUCCESS?

L Richards[1], W Rammler[2], L Lieberman[3], J Pendergrast[3], Y Lin[4], C Cserti-Gazdewich[3] and J Callum[4]

[1]Transfusion Medicine Laboratory [2]Blood Conservation, Lakeridge Health, Oshawa [3]Laboratory Medicine Program, UHN [4]Laboratory Medicine Program, Sunnybrook Health Sciences, Toronto, Canada

Background: Prospective audit with approval (PAA) has been shown to result in short-term decreases in transfusion rates, which reduces both healthcare costs and the incidence of transfusion reactions. When applied to restrictive RBC transfusion guidelines (prophylactic transfusion only for Hgb <70–80 g/L, with single unit transfusions for non-bleeding inpatients), there is a strong evidence base to support this practice. However, the long-term efficacy of PAA has been questioned.

Aims: To determine if initial success was sustained (or if physicians reverted to historic ordering practices) and need for ongoing technologist intervention. To determine the long-term effect of PAA using hospital established transfusion guidelines (TG) on RBC transfusion rates for the first 3 years of screening.

Methods: Hospital TGs for a large community 3 site institution were implemented in 2014. PAA by medical laboratory technologists (MLT) using these guidelines was implemented to identify inappropriate transfusion orders (for indication and dose). This process was phased in gradually from January to July 2014 (initially on weekdays 9-5, then 24/7 for inpatient transfusions only). Simultaneous widespread education of physicians, nurses and technologists was performed. Three years (2015–2017) of 24/7 MLT PAA was retrospectively examined for annual total RBC transfusions, annual inpatient/out-patient transfusions, and mortality rates as compared to hospital baseline (pre-screening year 2013). 2014 was not included in the comparison as screening was phased in gradually for the first 6 months. Retrospective audit was conducted (October 2017) to determine how often technologist screening altered the transfusion order, as compared to a 2014 audit. Transfusion rates for oncology outpatients, for whom PAA was not implemented, served as a control.

Results: In the first year of 24/7 screening the total RBCs transfused decreased by 1 273 units (23%) compared to baseline, with inpatient transfusions reduced by 33% and progressive reductions each subsequent year culminating in a 39% inpatient reduction from baseline in 2017. There was no change in overall hospital mortality rate throughout this period. During a 2 week pilot audit in 2014, 52 units were ordered for non-bleeding inpatients of which 56% (29 units) were deemed outside of hospital guidelines and not transfused. A follow-up one month audit in October 2017 identified 18 units deemed inappropriate from a total of 231 inpatient RBC orders demonstrating that the need for technologist intervention has significantly decreased over time.

Summary / Conclusions: The efficacy of PAA in decreasing transfusion rates is sustainable over the long-term and in fact becomes progressively less resource-intensive. Interestingly, a parallel improvement was seen in a patient population not subjected to PAA, suggesting the presence of "social contagion" in improving transfusion practices. Nonetheless, there appears to be ongoing benefit in continuing PAA, as 7.8% of inpatient RBC orders are still deemed inappropriate upon review. By adopting and maintaining this process our hospital has demonstrated sustainable, continuous improvement in RBC utilization and transfusion practices.

P-043

THE ONTARIO REGIONAL BLOOD COORDINATING NETWORK – A SUSTAINABLE MODEL FOR IMPROVING BLOOD TRANSFUSION PRACTICE

W Owens[1], D Evanovitch[2], T Thompson[3], T Cameron[1], A Collins[3], S Cope[3], L De Biasio[3], E Greening[1], H Nesrallah[1], S Scheuerman[2], L Young[2] and A Wendt[3]

[1]*Ontario Regional Blood Coordinating Network, Ottawa Hospital Research Institute, Ottawa* [2]*Ontario Regional Blood Coordinating Network, McMaster University, Hamilton* [3]*Ontario Regional Blood Coordinating Network, Sunnybrook Hospital, Toronto, Canada*

Background: In 2006, a regional network was funded by the Ministry of Health and Long-Term Care (MOHLTC) to support a provincial utilization strategy in Ontario Canada. At that time, there were 158 Ontario hospitals with a transfusion service. Ontario is a very large geographical area at over one million km^2 with a population of approximately 14.2 million.

Aims: The Ontario Regional Blood Coordinating Network (ORBCoN) was established in three regional offices to provide provincial coverage and to allow for region specific issues to be addressed. The goal was to improve communication within the province and allow for identification of issues or concerns relating to blood utilization.

Methods: Initial staffing was 9 full time equivalents (FTE), with 1.7 FTE added in 2013. Five priority goals were identified: blood utilization, education, inventory management, communication and quality improvement. Contact was first established through transfusion medicine laboratories at all 158 hospitals. Annual visits were scheduled in collaboration with the blood supplier, Canadian Blood Services. The initial focus was on improvement of blood inventory management to standardize stocking decisions and minimize wastage. Educational resources, programs and events were provided to encourage standardization of best practices for all healthcare professionals involved with blood transfusion. Audit tools were created to support audits of blood components/products and safe transfusion practice on a provincial scale. In 2016, ORBCoN facilitated the development of a provincial quality improvement plan (QIP) to improve the use of red blood cells (RBC) in Ontario.

Results: Initiatives to improve inventory management of blood at Ontario hospitals, included inventory calculators, a redistribution program and benchmarking. Ontario's annual RBC outdates were reduced by over 81% between 2006 and 2016 (from 10,509 units to 1,966 units annually). The average provincial platelet outdate rate fell from 17.7% to 11.8% over the same time period. Audits of RBC, plasma, platelets

and bedside transfusion checks improved understanding of appropriate use of these products, helped with accreditation compliance and increased the use of evidence-based practices province-wide. The widely used ORBCoN Bloody Easy series of tools (31,494 distributed in past 12 months) provide standardized guidance on transfusion practice. Early adopters of the Ontario Transfusion QIP have reported an improvement in the per cent of single unit RBC transfusions from a baseline of 42% to 72%.

Summary / Conclusions: Over an eleven year period, the establishment of ORBCoN has proven that a coordinated regional network model can be effective and sustainable within a geography as large and diverse as Ontario. The network model facilitates the connection of remote clinical and technical hospital staff with those in larger centres and promotes sharing of information and collaboration. In the coming decade, ORBCoN will continue to work with healthcare professionals to ensure that patients in Ontario receive the best and safest possible care when it comes to the transfusion of blood and blood products.

P-044

SHENZHEN STRATEGY: THE SOLUTION TO SEASONAL INSUFFICIENCY OF BLOOD SUPPLY AND SHORTAGE OF CERTAIN BLOOD TYPES IN BLOOD CENTER

L Lu and W Hong

Shenzhen Blood Center, Shenzhen, China

Background: What are common problems that blood centers in China encounter? The first is seasonal insufficiency of blood supply. In China, the on-the-street blood donation mode, which is the primary way to collect blood, can be strongly affected by weather conditions, especially with cold weather, high temperature, or continuous typhoons. Second, due to uncertainty in clinical blood use, throughout the year there could be times when the inventory of blood of certain type(s) goes lower than an ideal amount.

In Shenzhen, ever since voluntary blood donation was started in 1993, street voluntary blood donation has been the main mode for blood collection, while collective blood donation is supplementary.

Aims: How to solve the problem of seasonal insufficiency of blood supply and shortage of certain blood type(s)? We have been exploring.

Methods: Our strategy consists of the following two parts:

1) We carry out a series of blood donation activities. In winter, we organize "Red Action"; in summer, we hold "Thousand Chaoshang Blood Donation", "Blood Donation Month of Angels in White", and other related activities. Over the past five years, the Center has succeeded in avoiding the insufficiency of blood supply which often happened in winter and summer.

2) We carry out "Holiday Blood Collection Mode". How to make the best use of 113 holidays throughout the year (including statutory holidays and weekends)? The principles of the plan focus on openness as a motivating force, emphasizing key blood donation stations, orderly organization, and uninterrupted connections with volunteers and staff. Our goal is to improve blood inventory within 3 days, to remit within 1 week, and to fully recover within 2 weeks, once the blood stock goes down or shortage of certain blood type(s) occurs. Also, we strive to keep the daily inventory of red blood cells adequate for clinical use for 6 days or more throughout the year.

Results: 1) The winter event "Red Action", co-organized by Shenzhen Lions Club and our Center, takes place on the 12th of December each year and runs 2 months. Over the 7 editions of the event, the number of blood donations, with the help of the Club, has reached 33476 in total. Six elements of the success of "Red Action" are: strong organizational structure, specialized and high-level planning, first-class service awareness, attention to publicity, advanced communications, and inheritance of the good intention behind blood donation.

2) The first "Thousand Chaoshang Blood Donation", launched in the summer of 2017. In the end, 1113 people participated in blood donation through the event; which set a new record of the volume of donated blood via collective blood donation in Shenzhen.

For unbalanced inventory of blood types: 1) Case 1: In February 2017, The inventory of O type blood was effectively recovered within 1 week and reached optimal volume in 2 weeks. 2) Case 2: Three consecutive typhoons in September 2017 led to the shortage of red blood cells of all types. However, we efficiently recovered the inventory within 1 week and reached optimal inventory in 2 weeks. We achieved the goal of maintaining the daily blood inventory sufficient for clinical use for more than 6 days throughout the whole year.

Summary / Conclusions: Through events such as "Red Action" and "Thousand Chaoshang Blood Donation", it shows that the systematic social linkage of voluntary blood donation in Shenzhen has been established.

The sum of blood donated during weekends is usually bigger than the sum in week-days. This means that weekends and holidays are the critical time for enhancing the blood inventory efficiently.

P-045

IMPACT OF IMPROVED BACTERIAL DETECTION ON THE AVAILABILITY OF PLATELETS FOR THE HOSPITALS

F Bernier[1], J Courtemanche[1], C Lafond[1] and C Pigeon[2]
[1]Product Qualification [2]Customer Service Hospitals and Inventory Management, Hema-Quebec, Saint-Laurent, Canada

Background: To improve the safety of platelets (PLT), Héma-Québec (HQ) modified the process for bacterial detection. In October 2015 HQ introduced a 48 h delay after collection to sample the PLT and a 12 h delay after incubation to release the PLT. Health Canada approved a shelf life of 7 days for those PLT. Before October 2015, the delay for sampling was 24 h and the PLT had a 5 days shelf life. The 60 h delay adding to the time for the different manipulations inherent to the process (sampling, inoculation, documentation and starting the incubation) added a challenge to main-tain a good customer service.
Aims: To establish a thorough and streamlined workflow between laboratories teams in order to put the platelets into inventory without impairing the remaining shelf life (RSL) of the PLT and give time to hospital to transfuse.
Methods: PLT are collected 7 days a week at fixed and mobile sites either from apheresis or whole blood. The time for collection ranges from 7am to 9 pm. Three teams are involved in the process for bacterial detection: laboratory assistants (LA) in the production lab for sampling the PLT, laboratory technicians in the regulatory testing laboratory for inoculation and result reporting and LA at the labeling depart-ment to issue the PLT. A close monitoring of those activities was performed by the supervisors to streamline the operations. The delay between collection and readiness for issuing the PLT, the RSL of the PLT sent to hospitals and the expiry rate at the hospitals were monitored.
Results: Laboratories operations are on Monday to Saturday from 7am to 23 pm, PLT collected on Saturday to Thursday are sampled and inoculated on Monday to Saturday. PLT collected on Friday are sampled and inoculated on Monday. Depend-ing on the inoculation time the PLT will be issued the same day of inoculation or the morning after. However, PLT collected on Thursday late in the day will be issued on Monday morning.
The PLT collected on Saturday to Wednesday were ready for issuing after 68 h of the collection. For PLT collected on Thursday and Friday, the mean time was 88 h.
Before November 2015, 1% had a 4 days RSL, 17% at 3 days RSL, 40% at 2 days RSL, 35% at 1 day RSL and 7% would expire the same day. Since December 2015 the RSL is now at 4% for 4 days RSL, 20% at 3 days RSL, 43% at 2 days RSL, 29% at 1 day RSL and 4% would expire the same day.
The expiry rate at the hospitals was 18% in 2015 (no data before that period), 10% in 2016 and 13% in 2017.
Summary / Conclusions: Improving the safety of PLT by raising the sampling time to 48 h and adding a period of 12 h before issuing the PLT had a positive impact on the RSL: 24% had a RSL of 3 and 4 days compared to 18% before. Furthermore, the expiry rate was reduced at the hospitals.

P-046

DELIVERING BLOOD USING DRONES TO SAVE LIVES IN RWANDA: A BOOST TO BLOOD SUPPLY MANAGEMENT AND UTILIZATION

E Niyonshuti[1], A Tuyishime[1], G Muhorakeye[1], W Sadiki[2], S Gatare[2] and J Condo[3]
[1]Planning, Monitoring & Evaluation and Business Strategy Division [2]National Blood Transfusion Center Division [3]Director General, Rwanda Biomedical Center, Kigali, Rwanda

Background: Access to life-saving medical products is mainly hindered by the fail-ure to deliver needed medicine to remote areas due to challenging environment, lack of adequate transportation, communication, short shelf life of the products or suffi-cient supply chain infrastructure. Rwanda in partnership with Zipline International, Inc. has started delivering blood products to health facilities in remote area using drones for the last 12 months to overcome the country's challenging topography, and in bid to shorten the turnaround time between ordering and receiving blood products.

Aims: The aim of this project was to assess how drone technology can help maxi-mizing blood and blood products utilization by minimizing both blood shortage and expiries in the blood supply chain system, which in the end improves the patient health outcomes.
Methods: The drones deployed in Rwanda have a capacity to serve health facilities within 75 kilometers from drone port. The project started with one drone port set up in the Southern Province, Muhanga District, capable to serve 21 health facilities in the area. The ordering process is simple, cheaper and quicker. When one of the 12 health facilities needs blood products, a Lab Technician sends a WhatsApp message or log on to Zipline's ordering website. When a drone (here also known as Zip) is ready to go, Zipline sends a confirmation message. When a Zip is within a minute of the destination, the Lab Technician receives a text message. The drone drops off the package with a parachute, and then returns to its home base. In return, the Rwanda Ministry of Health pays Zipline a fixed service fee, a base rate plus addi-tional bonus based on performance, for each successful delivery by the end of each month.
Results: The project was launched in October 2016 and after one year of implemen-tation, 12 health facilities are currently ordering and receiving blood products through the drone system. More than 6,000 blood units were delivered to health facilities using drone system and these health facilities received the ordered products within 5 to 45 min for emergency orders and 3 h for non-emergency orders. Expi-ries of blood products estimated at 6% before the project have been reduced to less than 1%. Blood products that are not commonly used and with short shelf life such as platelets and plasma are reaching to the patient in need on time and increasingly being more used to save lives. The annual health facilities satisfaction on blood deliveries (demand versus supply) has risen from around 69% to 98% for the 12 health facilities using drone system.
Summary / Conclusions: With drones, Zipline is able to deliver blood products to health facilities within a few minutes of receiving the request and moving to on demand drone delivery helped health facilities to store less blood while having unlimited access to the supplies they need when they need them. These promising results encouraged the Government of Rwanda to extend the project and cover more health facilities.

P-047

USAGE OF O RHD NEGATIVE RED CELLS IN FINLAND

T Kivipuro and H Sareneva
Hospital relations department, Finnish Red Cross Blood Service, Helsinki, Finland

Background: The Finnish Red Cross Blood Service (FRCBS) is the nationwide blood service provider in Finland, responsible for collection, testing, processing and distri-bution of blood products to all hospitals and health care providers. In recent years demand for blood products, especially RBC's, has decreased in Finland. However at the same time the usage of O RhD negative (O neg) RBC's has slightly increased. Approximately 4 percent of the Finnish population is O neg, but current average demand of O neg RBC's is more than 8.5%. This is a challenge for blood service, how to ensure that adequate supplies are available when required.
Aims: The aim of this study was to identify and analyze of changes in the usage O neg RBC's in 2014–2017.
Methods: We analyzed hospital transfusion data in 2014–2017. Data included patient blood type, product blood type, component age at transfusion, delivery infor-mation and hospital department information. Data was analyzed by using QlikView business intelligence system.
Results: Over the past 4 years an increase in the demand for O neg RBC's compared to other blood types has been observed in FRCBC. During the study, 29,406 O neg RBC products were transfused of which approximately 62% were transfused to O D neg patients. However the proportion was 63.7% in 2014 and 60.6% in 2017, which indicates a decreasing trend. 13.5% of O neg RBC's were transfused to O positive patients.
Our data shows that most of O neg RBC's are transfused in emergency ward and intensive care units. At the same time the number of emergency transfusions has been slightly increased.
RBCX treatment for sickle cell patients was started in Finland from the beginning of 2017. Due to the RHD-genetics of people of African origin, most of the RBC's used in blood exchanges has to be O neg. However the proportion of O neg RBC's issued to patients suffering from hemoglobinopathies is not more than 1,7% of all delivered O neg RBC's.
The median age of O neg RBC's at transfusion was quite high and there is clear peak of usage between 27 and 35 days. It seems that O neg RBC's are often transfused to prevent time expiry in situations where ABO identical products would have been available. However the smaller hospitals located far from FRCBC need a sufficient

target inventory of O neg RBC's to ensure the availability of products for emergency situations.

Summary / Conclusions: Detailed information and constant follow up of the usage of O neg RBC's can be utilized by the FRCBS to ensure the supply of O neg RBC's in the future

- by drawing guidelines to prevent overuse of O neg RBC's
- by planning the phenotyping strategy of blood donors across ABO groups
- by educating hospital customers
- by communication with hospitals via customer meetings, newsletters etc. sent by the FRCBS

P-048

VARIATIONS IN RED BLOOD CELL AND FROZEN PLASMA TRANSFUSION RATES ACROSS 62 ONTARIO COMMUNITY HOSPITALS

J Qiang[1], T Thompson[2], J Callum[3,4], P Pinkerton[3,4] and Y Lin[3,4]

[1]Division of General Internal Medicine, Department of Medicine, University of Toronto [2]Ontario Regional Blood Coordinating Network [3]Department of Laboratory Medicine and Molecular Diagnostics, Sunnybrook Health Sciences Centre [4]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

Background: A restrictive transfusion strategy has been shown to be equivalent to a liberal transfusion strategy in terms of mortality and morbidity outcomes in major clinical trials. Although patient blood management programs have reduced transfusion rates and improved patient outcomes, these programs have not been universally applied. Recent province wide audits of frozen plasma (FP) and red blood cell (RBC) use in Ontario showed a high rate of inappropriate transfusions.

Aims: The primary aim was to compare transfusion rates of RBCs and FP across 62 Ontario community hospitals with more than 50 active treatment beds from 2012–2017. The secondary aims were to identify clinical and hospital factors, which may account for these differences.

Methods: This study was a retrospective review of transfusion data from Ontario community hospitals between 2012–2017. RBC and FP transfusion issue data were acquired through the Canadian Blood Services data warehouse. Acute inpatient bed days and the annual average number of active adult treatment beds were obtained through the Ministry of Health and Long Term Care of Ontario. Annual transfusion rates were reported as FP and RBC units transfused per 100 acute inpatient days (AIPD), using descriptive statistics. Trend in transfusion rates over time was determined using generalized linear regression with a log-link Poisson distribution. Rates of blood component use were correlated with size of hospital using linear regression. Finally, rates of RBC transfusion were correlated with rates of FP transfusion using linear regression.

Results: From 2012 to 2017, there were decreasing rates of RBC and FP use over time (P = 0.03 for FP, P < 0.01 for RBC), with a wide range of variation amongst hospitals. The average number of FP units transfused was 0.67, 0.62, 0.50, 0.46, and 0.42 units per 100 AIPD for 2012–2013, 2013–2014, 2014–2015, 2015–2016, and 2016–2017 respectively. The average number of RBC units transfused was 6.1, 6.0, 5.5, 5.4, and 5.1 units per 100 AIPD for 2012–2013, 2013–2014, 2014–2015, 2015–2016, and 2016–2017 respectively. Larger hospitals were associated with a significantly higher FP transfusion rate (P < 0.05 for each year). However, there was no correlation between RBC transfusion rates and size of hospital. High RBC transfusion rates were associated with high FP transfusion rates for each fiscal year (P < 0.005 for all years).

Summary / Conclusions: There may be cultural differences at different institutions contributing to the variations in transfusion rates across Ontario community hospitals. Characterization of transfusion practices and understanding of institutional culture surrounding blood component use will hopefully lead to quality improvement (QI) initiatives aimed at creating better guidelines, education, and transfusion order entry systems. These data will serve as a baseline to highlight sites and practices where QI initiatives may be most beneficial and potentially replicated in other jurisdictions.

P-049

THE RELEVANCE OF RBC RETURN RATE INTO THE BLOOD BANK INVENTORY MANAGEMENT WITH IMPACT INTO WASTAGE

I Borges, A Sousa and P Mendonça

CSTLisboa, IPST, Lisboa, Portugal

Background: The Portuguese Institute of Blood and Transplantation (IPST, IP) is responsible for ensuring and regulating transfusion medicine and transplantation activities at the national level concerning donation, collection, analysis, processing, preservation, storage and distribution of blood, components, organs, tissues and cells of human origin with high standards of quality and safety. IPST.IP collects approximately 58% of the 334022 national whole blood donations (WB), through tree blood centers, located in the north, center and south of Portugal. In 2016, Lisbon (south) Regional Blood Center (CST Lisboa) collected 56549 units of WB, nearly 18% of the national collections and issued 38% according the region's demand, and consequently, depending. CST Lisboa carries out blood collection, analytical study, processing storage, and distribution of blood components to the National Health System (public and private hospitals). The protocols that have been established between CST Lisboa and hospitals allow them to return blood components within the 5 days before the expiration of shelf life.

Aims: Identify the CST Lisbon customers with the highest Red Blood Cells Concentrates (RBC) return rate according to ABO/Rh blood group. Evaluate the negative impact on stock management and into the RBC wastage.

Methods: The CST Lisbon customers consist of 72 hospitals and clinics, public (n = 43) and private (n = 29) with a wide range dimension, from small clinics to large tertiary care hospitals. The 2016 data were obtained by the house-made informatic system (ASIS), was analyzed per type of customers (public versus private) and blood group wastage. According to the RBC return rate (0–10%; 11–20%; 21–30%; 31–40% and 40–100%) the customers were grouped into classes.

Results: Of the 92.979 RBC's issued to hospitals, 2, 6% of those were returned, some were re-issued (1,9%) and the global wastage rate by expiration of shelf life was 1,2%. In the first class, with return rates between zero and 10%, there are 82% of clients; 5 with rates ranging from 10 to 20%, 3 with returns of 21% to 30%, 2 with returns of 31% to 40%, 3 with a rate of 41% to 100%. The total RBC wastage was 0, 7%: 56% AB Rh+; 19% A Rh+; 9% AB Rh-. Only 0.07% of the RBC inventory was never issued at some point. The returned RBC from public hospitals discarded by expiration was: AB Rh+ (35%); A Rh+ (10%); AB Rh- (5%). The discarded RBC returned from private hospitals was 12% each (AB Rh+ and A Rh+) and 5% (O Rh+). The public institutions transfused 81,65% of total RBS's demanding. From those, 3 had return rates higher than 2%. The private hospitals had the highest return rates reaching 49,5%. The private who had a 100% return rate was a first time client.

Summary / Conclusions: There was a clear difference between return rates from private and public customers. The wastage of RBC's by shelf life after return is highly influenced by the return RBC's policy.

P-050

ANALYSIS OF RED BLOOD CELL USE IN ELECTIVE SURGERIES OVER 12 YEARS IN KOREA

B Kim[1], Y Park[1], Y Kim[1], M Kang[2], S Kim[3] and H Kim[3]

[1]Laboratory Medicine [2]Research Institute, National Health Insurance Service Ilsan Hospital, Goyang [3]Laboratory Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Background: Red blood cell (RBC) transfusion is a life-saving process for patients with perioperative bleeding, but transfusion can cause adverse events. Maximum surgical blood order schedule (MSBOS) has been used in RBC product preparation for elective surgeries.

Aims: We aimed to investigate the recent status of RBC usage for elective surgeries and to suggest a universally applicable guideline regarding the amount of RBC units for various surgical procedures based on representative nationwide cohort data.

Methods: We analyzed the number of RBC units used during the hospitalization of patients who underwent surgical procedures from 2002 to 2013 using National Health Insurance Service-National Sample Cohort data, which include a total of 487,238 cases for 224 selected operations.

Results: RBC units were used in 39,637 (8.14%) cases. A total of 60,815 RBC units were transfused with an average of 0.125 units per patient overall and an average of 1.53 units per case receiving RBC transfusion. In addition, 56.74% of the RBC units were transfused for females, and 60.12% of RBC units were transfused into patients aged 60 or older. RBC units were used most often in orthopedic surgeries (33.8%),

followed by general surgeries (12.0%) and vascular surgeries (11.8%). The number of operations performed in the cohort increased from 27,690 in 2002 to 49,473 in 2013, and the average RBC units used per operation also increased from 0.081 units in 2002 to 0.150 units in 2013.

Summary / Conclusions: Continuous transfusion management is needed for efficient utilization of blood. Periodic revision of the policy regarding the use of blood products through nationwide studies could suggest practical guidelines applicable to various elective surgical operations.

P-051

IMPACT OF 7-DAY PLATELETS ON INVENTORY MANAGEMENT AT A PEDIATRIC INSTITUTION

A Ryder[1,2] and D Moreau[1]

[1]Le Bonheur Children's Hospital [2]Pediatrics and Pathology, University of Tennessee Health Science Center, Memphis, United States

Background: Platelet inventory management has historically presented a challenge to hospital transfusion services due to the short shelf-life of the component. In the international community, mechanisms to achieve 7-day platelet expiration have existed for some time, but in the United States, 5-day platelets have been the norm until the FDA recently approved a bacterial detection safety measure to allow for 7-day platelet expiration. The performance of the test (Platelet PGD Test, Verax Biomedical, Inc.) has been described in numerous US hospitals, but to our knowledge, there has been no description of implementation at a pediatric institution. Pediatric platelet inventory management is complex due to the majority of transfusions being aliquots that represent a small fraction of the platelet unit.

Aims: We describe the implementation of PGD testing at Le Bonheur Children's Hospital, a 255-bed pediatric hospital and Level 1 trauma center in Memphis, Tennessee. Given our hospital's traditionally high rate of platelet expiration, this implementation has been seen as an opportunity to improve inventory management.

Methods: Pre-implementation data was gathered over a 9-month period, for platelets received from January 1, 2017 through September 30, 2017. Descriptive statistics regarding platelet transfusions and expiration were compared to the 4-month post-implementation period, which includes platelets received from October 1, 2017 through January 31, 2018. Platelet products consist entirely of single-donor apheresis units. Units are considered expired if they reach outdate prior to being transfused or accessed for aliquot preparation. Other reasons for wastage are not included among the outdate units. Units that were returned to the blood center or transferred to another hospital are not included in the analysis.

Results: During the 9-month pre-implementation period, we received 344 apheresis platelet units, of which 101 units expired prior to use (29.4%). Of the platelet units received, 73 were transfused in full (21.2%) and 345 aliquots were prepared from 164 units (47.7%). 6 units were wasted for other reasons. During the 4-month post-implementation period, we received 124 apheresis platelet units, of which 17 units expired prior to use (13.7%). During this period, 27 units were transfused in full (21.8%) and 177 aliquots were prepared from 75 units (60.5%). 5 units were wasted for other reasons. During the post-implementation period, 33 platelet units were PGD tested; 12 units tested once, and 21 units tested twice, for a total of 54 tests. We estimate having spent $1620 on testing ($30/test). Of the 33 tested units, 18 were used for transfusion, representing approximately $9000 in savings ($500/unit). Additionally, the 15 outdated PGD-tested units provided an additional 29 days of platelet stock. We estimate that this amounts to an additional $5000 in cost avoidance.

Summary / Conclusions: We describe the successful implementation of PGD testing to achieve a 7-day outdate for apheresis platelets at a pediatric hospital. Over a 4-month period, we demonstrate a 53% decrease in platelet expiration, which allowed for an additional 18 platelet units to be used for transfusion, with an estimated total savings of $12,380. While there are improvements to be made in the logistics of PGD testing to achieve greater efficiency, our experience can serve as a model for other pediatric institutions to estimate the impact of PGD testing on inventory management. In our hands, this implementation resulted in increased platelet availability, while also decreasing costs and improving patient safety.

P-052

KINETICS OF CHILDBEARING AGE SINCE 1998 IN NOVA SCOTIA, CANADA: A 19-YEAR EXPERIENCE

HM Aljedani[1,2], C Campbell[1,2], P McAuley[3] and C Cheng[1]

[1]Faculty of Medicine, Dalhousie University [2]Division of Hematopathology and Blood Transfusion Services, Queen Elizabeth II Health Sciences Center, Capital District Health Authority [3]Laboratory information system management, Laboratory Department, Izaak Walton Killam hospital, Halifax, Canada

Background: The definition of 'childbearing age' is important to guide transfusion therapy. For instance, current national and international guidelines recommend transfusion of K1-negative blood to females of childbearing potential as the standard of care. Although the age limit that defines childbearing potential is not universally defined nor is it static, menopause determines a natural physiological limit. Some of guidelines define age of younger than 45, while others define age of 50 or even 60 as a cutoff limit.

Aims: This study was conducted to evaluate the kinetics of childbearing age in a major tertiary maternal hospital (IWK) in the province of Nova Scotia, Canada and examine the dynamic patterns and trends related to childbearing age that may arise from changes in society (i.e. delayed childbearing), and to inform if childbearing age is static or dynamic.

Methods: A retrospective analysis of data on the year and age at discharge of delivered and postpartum patients from January 1, 1998 to December 31, 2017 was conducted. Data was queried from the laboratory information system (LIS) at the IWK hospital located in Halifax, Nova Scotia. No patient-identifiable variables were included in this quality assurance dataset. Data were plotted as a heat map proportional to age at delivery, tables and charts and were analyzed statistically for the mean, minimum and maximum age at discharge post-delivery, and standard deviations for each year.

Results: Total of 81,378 patients were included in the study. Over the study period, the mean age at discharge after delivery increased gradually from 28.1 years in 1998 to 30.3 years in 2017. The maximum age at discharge ranges from 42 to 55 years. The maximum age of discharge showed a pattern of being higher in the recent years. Noticeably, before 2012, the maximum age of women at delivery was 47 years or younger ranging from 43 to 47 years. However, by 2012 and beyond, the maximum age was 48 or higher, ranging from 48 to 55 years.

The total number of women aged 48 years or older at delivery was 5. By 2012, the annual rate of women at age of 48 years or older at delivery ranges from 0.0 to 0.04%, with a mean of 0.017%. The minimum age of delivery had changed over the years as well. In the earlier years, 1998 and 1999, the minimum age was 17 years compared to the recent years, 2000 and after, where the minimum age at delivery is 14 years. The standard deviation of age at discharge for each year ranges from 5.3 to 5.6, with a mean of 5.5.

Summary / Conclusions: The data revealed a recent trend of increasing age of women at time of delivery. Even though most of guidelines consider a cutoff age limit of 45 years as a childbearing age, the gradual increase of maximum age of women at delivery may indicate the need to re-evaluate this cutoff in the future.

P-053

CHALLENGES TO PROVIDING BLOOD TO ALLOIMMUNIZED AFRICAN AMERICAN PATIENTS

MA Keller[1], J Maurer[2] and S Nance[3]

[1]National Molecular Laboratory, American Red Cross [2]American Rare Donor Program, American Rare Donor Program [3]Immunohematology Reference Laboratories, American Red Cross, Philadelphia, United States

Background: The American Rare Donor Program facilitates meeting rare blood requests amongst its 88 members, 44 of which are American Red Cross centers. American Red Cross uses RBC genotyping of self-declared African American (AA) and other ethnic minority blood donors to aid in identification of donor units lacking multiple or rare blood group antigens.

Aims: We examined the requests for red cell units with rare antigen phenotypes common in individuals of African descent and determined how the frequency in the genotyped donor pool at the American Red Cross compared to that expected by ethnicity and population frequency data.

Methods: Over a 30-day period, 16 distinct requests were made to the American Rare Donor Program, each for 1 or more phenotypically rare red cell units. Of these, 14 requested phenotypes could be identified via RBC genotyping. Of these, all phenotypes were K antigen negative. Most (11/14) were C, E and K antigen negative. Of these, 8 lacked Fy[a] and Fy[b], 9 lacked Jk[b] and 9 lacked S. One or more antigen

negative phenotype included Js[a], Kp[a], Do[a] or C[W]. The phenotype frequencies predicted based on reported frequencies in Caucasians and blacks (Reid ME et al., The Blood Group Antigen FactsBook, 2012) were compared to the frequency identified by RBC genotyping of nearly 25,000 primarily AA blood donors during CY2017. RareFinder, an R-based script (Agena BioScience), was used to tally specific predicted phenotypes in the entire cohort as well as in the subset of donors lacking C, E and K. The comparison did not include ABO and RhD.

Results: All of the phenotypes were more common in blacks. In all cases, the occurrence rate of the requested phenotype was roughly double in the C- E- K- cohort compared to the full cohort of genotyped donors. The frequencies ranged from a low of 0.1% [c- E- K- Fy(b−) Jk(a−) s-] to a high of 33.3% [C- E- K- Fy(a−b−)] in blacks. Ten of the 14 rare phenotypes were predicted to be found in less than 0.1% of Caucasians; the phenotype with the highest frequency in Caucasians was C- E- K- Fy(a−) Jk(b−) S- at 1.7%. Four of the types were predicted to be found in more than 10% of blacks; all of these were C- E- K- Fy(a−) with or without Fy[b], Jk[b], S and C[W] antigens.

Summary / Conclusions: Red blood cells with rare phenotypes based on negative status for combinations of common antigens in each of 5 blood group systems (RH, K, FY, JK, MNS as described here) requested from the American Rare Donor Program often are phenotypes found in blacks. The phenotypes are exceedingly rare in Caucasians. RBC genotyping of AA donors aids in the identification of such rare donors. These data show that it is still challenging to meet the needs of the alloimmunized African American patients, even while the American Red Cross has screened more than 160,000 donors since 2011. By testing C- E- K- donors preferentially, a higher number of donors with these rare phenotypes can be identified.

P-054

DECLINING RATES OF RED BLOOD CELL, PLASMA AND PLATELET TRANSFUSIONS 2012–2016: WHERE IS THE FLOOR?

P Robillard and Y Gregoire

Hema-Quebec, Montreal, Canada

Background: Aging of population in developed countries made blood bankers predict an increase in blood utilization a decade ago. However many have experienced a decline in the demand for red blood cells (RBC). Data on other components like platelets (PLT) or plasma are lacking at a population level

Aims: To describe the recent trends in the epidemiology of blood component transfusions in the province of Quebec, Canada (population of 8.4 million).

Methods: In Quebec all blood banks are computerized with the same software and managed under the umbrella of the Quebec Health Ministry (QHM) allowing for central extraction of transfusion data. Héma-Québec (HQ) is the sole blood supplier for the province. Data on all transfusions for years 2012 to 2016 were extracted by the QHM. They were matched with HQ database on products to calculate the age of products transfused. Population denominators were extracted from census data published by Institut de la Statistique du Québec. SAS software was used to conduct descriptive analyses. Rates are presented per 1000 inhabitants.

Results: Number or RBC transfusions steadily declined from 243,019 in 2012 to 214,282 units in 2016. Rates were: 2012-30.1; 2013-28.6; 2014-27.4; 2015-26.1; 2016-25.7. Rates declined in the period both for female (28.1 in 2012 to 23.9 in 2016) and male (32.0 in 2012 to 27.5 in 2016). Rates of RBC transfusions declined significantly in all age groups except for the pediatric population: 0–17: 4.9 to 4.7; 18–49: 9.4 to 8.5; 50–69: 36.6 to 29.9; 70–79: 114.3 to 86.4; 80–89: 177.3 to 136.5 and 90+: 182.0 to 156.5. For PLT transfusions, after a continuous decline for the period 2012–2015 there was an increase for 2016 (rates: 2012 4.6; 2013 4.4; 2014 4.2; 2015 4.1; 2016 4.4). In 2016 rates were for female 3.5 and for male 5.3. This difference was present in all age groups. For plasma transfusions rates declined from 5.8 in 2012 to 4.4 in 2016. This decline was present in all age groups and both genders.

Summary / Conclusions: Despite already low RBC transfusion rates compared to international figures (in 2014 UK was at 30.3, France at 37.0 and Netherlands at 25.7), demand for RBC is continuing to decrease. There seems to be a significant change in transfusion practice and the floor transfusion rate does not appear to be reached. Demand for PLT and plasma has also declined over the years except for a blip for PLT in 2016.

P-055

DETERMINING THE APPROPRIATENESS OF PLATELET TRANSFUSIONS: AN AUDIT OF 69 HOSPITALS

T Thompson[1], A Wendt[1], W Owens[1], D Evanovitch[1], J Callum[2], Y Lin[2], P Pinkerton[2] and R Cohen[2]

[1]Ontario Regional Blood Coordinating Network [2]Sunnybrook Health Sciences Centre, Toronto, Canada

Background: A retrospective audit was conducted by the Ontario Regional Blood Coordinating Network (ORBCoN) on all platelet orders from participating Ontario hospitals from January 7, 2017 to April 7, 2017. All Ontario hospitals were invited to participate in the audit.

Aims: The primary outcome of the audit was the appropriateness of platelet transfusions at participating sites in Ontario. Secondary outcomes included the percent appropriateness by type of transfusion (prophylactic non-bleeding, prophylactic pre-procedure and therapeutic for bleeding), patient location and medical service.

Methods: Data were collected retrospectively. Training material was provided to the designated individuals collecting data at each site to ensure uniform definitions. Data collection included patient demographics (age, sex); use of anti-platelets medications or anticoagulants; pre and post platelet transfusion counts; ordering and most responsible physician specialties; location of transfusion; indication for transfusion (prophylactic non-bleeding; prophylactic prior to procedure; therapeutic with bleeding); and platelet dose ordered by the physician and dose administered. Bleeding was defined as minor (WHO grade 1 or 2 bleeding) and major bleeding (WHO grade 3 or 4). Appropriateness criteria were based on a modified version as published by "Etchells et al, Vox Sang, 2017". Adjudication was performed in duplicate and independently with either a computer algorithm AND one human adjudicator OR with two individual adjudicators if the computer algorithm could not adjudicate the transfusion. The computer algorithm was developed using Excel formulas with 1465 orders being "auto-adjudicated" using this technique. Discrepancies were reviewed and resolved by consensus. Categorical variables were summarized as frequencies and percentages; continuous variables as means with standard deviation (SD) or as medians with inter-quartile range (IQR) if data were skewed. Agreement between adjudicators was assessed using a kappa (κ) statistic.

Results: A total of 69/158 (44%) hospital sites voluntarily participated in the audit, capturing 90% of the provincial platelet transfusion activity. There were a total of 1903 orders, 1465 (77%) of the orders were auto-adjudicated using Excel formulas. Preliminary data analysis on all orders showed the primary indications for ordering platelets was 1210 orders (64%) for prophylaxis (no bleeding, no planned procedure); 543 orders (28%) for therapeutic (currently bleeding) and 150 orders (8%) for prophylaxis (before invasive procedure).

Summary / Conclusions: The use of an "automated" adjudication technique significantly reduces the amount of time needed to manually adjudicate audit orders however this technique could not be used on all orders. Manual adjudication is currently being completed on all remaining platelet orders that could not be auto-adjudicated by the Excel formulas; more detailed audit results will follow.

P-056

HOW EARTHQUAKE CAN AFFECT BLOOD DONATION; KERMANSHAH EXPERIENCE DISASTER MANAGEMENT

A Salah[1], M Jalalifar[2], A Khosravi[2], M Shirmohammadi esfeh[3] and S Negravi[4]

[1]Routin Lab, Blood Transfusion Research Center High Institute for Research and Education in Transfusion Medicine Tehran Islamic Republic of Iran, Shiraz [2]Blood Transfusion Research Center High Institute for Research and Education in Transfusion Medicine Tehran, Islamic Republic of Iran [3]Blood Transfusion Research Center High Institute for Research and Education in Transfusion Medicine Tehran Iran, Islamic Republic of Iran [4]Department of English Language Teaching. Ahvaz Branch, Islamic Azad University, Ahvaz. Islamic Republic of Iran

Background: Blood transfusion plays vital role in disasters. The blood donors management during the disasters can save the blood supply and reduce unnecessary blood donations and blood discard as well as prevent to occur blood supply shortage. The Fars Blood Transfusion Service (FBTS) has the second most common in blood donation in Iran.

Aims: Determination the effects of Kermanshah earthquake on blood donations supply and safety.

Methods: The Blood donation rate, seropositivity of transfusion transmitted infections (TTIs) and demographic characteristics of donors were compared in two similar period: period 1(12 to 28 Nov 2017) and period 2 (12 to 28 Nov 2016) in the Fars Blood Transfusion Service (FBTS). The results were analyzed using SPSS software.

Results: Overly 6696 donors were admitted to FBTS in first period included of 35.91%, 35.73% and 28.36% first time, lapsed and regular, respectively. Out of that 2445(36.5%) donors were deferred from donation. While, in the second period, 3342 donors were admitted that 960(28.7%) of them were deferred. Female donors significantly increased from 4.48% to 13.59% after earthquake. Similarly, first time donors were increased from 17.41% to 35.91%. Moreover, temporary and permanent deferral increased from 25.41% to 56% and 3.52 to 5.41, respectively. The five blood donors

(117 per 100,000) have confirmed TTIs in earthquake period in comparison with one blood donor (41 per 100,000) was positive TTIs in the previous same period.

Summary / Conclusions: Our findings showed that natural disasters have great effects on donor recruitment and provide the blood supply, but the safety of blood may threatened by admission of inappropriate donors. Strict donor selection criteria and algorithms in disasters is recommended to guarantee the blood safety as well as the educational program and donors counselling for the first time donors to become them lapsed or repeated blood donors are highly recommended.

P-057

INNOVATION OF BLOOD TRANSPORTATION SYSTEM IN LUMAJANG BLOOD CENTER

H Maksum[1], Y Siti Maryuningsih Soedarmono[2], A Mufarida[3] and D Mega Melynda[3]
[1]lumajang blood centre indonesian red cross, Indonesian Red Cross, Lumajang, East Java Province [2]National Blood Services Committee, Ministry of Health of Republic Indonesia, Jakarta [3]Lumajang Blood Center, Indonesian Red Cross, Lumajang District, Indonesia

Background: Blood transportation plays key role in blood safety and efficacy. Uncontrolled of blood temperature and handling during transportation cause damage on blood cell and impact on patients treatment. Establishment of hospital blood bank in every hospital as mandated by the Ministry of Health (MoH) Decree was not efficient when the need of blood in the hospital is very limited. Lumajang is a small district in East java Province with 1.104.759 population. Delay of blood distribution for transfusion and uncertain quality of blood when received was complained by five among six hospitals that obtain blood from Lumajang Blood Centre (BC).

Aims: To evaluate impact of innovated blood transport system on decreasing hospital complaint on blood distribution.

Methods: Retrospective observation on the data of blood services complaint from the hospitals.

Results: During 2007–2011, blood distribution from Lumajang BC to hospitals was involved patient's family. This practice caused hospitals complaint on delay of blood distribution (87%) and uncertain quality of blood when received (13%). These problems impact on delay of patient's treatment and lengthen the treatment period. In 2012, the Lumajang BC introduced blood transportation system by using motorcycle equipped with simple cool box. The hospitals complaint on delayed distribution was decreased but complaint on uncertain quality of blood when received was still remaining. In 2014, the MoH Decree insisted every hospital to set up Hospital Blood Bank (HBB) that function to store and prepare blood for transfusion. The Lumajang District Hospital has set up the HBB. However, for other five hospitals, setting up the HBB was not efficient because of limited blood needs of 2–3 units per hospital per day.

These situations forced the Lumajang BC to improve blood transportation system by setting up the "BLOOD JEK" transportation System. The system involves trained BC staff in handling and monitoring blood temperature during transportation using special designed motorcycle, equipped with standardized blood cool box and temperature monitor. By "BLOOD JEK", blood and blood component can reach the hospitals on time with good condition. The term "JEK" was inspired by "GOJEK", the motorcycle transportation method that was popular in Indonesia in the last 5 years to solve the traffic jammed problem. The hospitals complain on blood distribution and quality was significantly decreased afterwards. The "BLOOD JEK" System was winning the public service innovation contest in 2017 at the provincial level.

Summary / Conclusions: Uncontrolled blood temperature and handling during transportation impact on patient's treatment. Establishing the HBB was not efficient when blood needs is low. "BLOOD JEK", the standardized blood transportation system has decreased hospital complain on blood distribution in small district areas.

P-058

USE OF BLOOD IN THALASSEMIA PATIENT POPULATION IN TIRANA

V Shano[1], A Dukaj[1], E Hoxha[1], E Nastas[2], L Qyra[1] and I Seferi[1]
[1]NBTC [2]University Center "Mother Teresa", Tirana, Albania

Background: The frequency of thalassemia carriers in our country is about 7%. Since 2000 important steps have been taken in Albania for improving the treatment of thalassemia patients, and for educating general population for prevention. During the last years we have noticed an increase in blood demand for thalassemia patients, and matching their needs has become a challenge for our blood service. About 20% of our yearly blood supply goes for covering the needs of thalassemia patients.

Aims: To evaluate the age distribution of thalassemia patients regularly transfused in Tirana and blood demand according to age group.

Methods: We analyzed retrospectively the data of age distribution and blood use for thalassemia patients transfused at NBTC during 2016. This data were extracted from the registers of NBTC Tirana. We divided the thalassemia patients in age groups 0–10 years old (y.o); 11–20; 21–30; 31–40 in order to observe age distribution and blood demand, as well as overall life expectancy, new infants born in the last ten years.

Results: The total number of thalassemia patients regularly transfused at our NBTC for 2016 was 149. There were 69 females and 80 males. According to age groups we had 33, 59, 37 and 20 patients respectively for age groups 0–10 y.o, 11–20 y.o, 21–30 y.o, and 31–40 y.o. The lack of patients above 40 y.o and the decrease of the number of patients in the age group 21–30 and 31–40 y.o, compared to 11–20 y.o group, demonstrate the low life expectancy that thalassemia patients have had in our country. It is important to mention here that in 2000 there were only 2 patients above 20 y.o treated in our center.

We also observed that their blood needs increased significantly with age. The average of blood use/patient during 2016 according to age group has been 17, 24, 30, 36 units/patient/year respectively for age groups 0–10 y.o, 11–20 y.o, 21–30 y.o and 31–40 y.o. There is a constant increase in blood demand for thalassemia patient as they grow up. Based on this data we calculate that every ten years will be an 20% increase in blood demand for our thalassemia patient population. There is a significant decrease in new infants born in the last ten years compared to the previous decade.

Summary / Conclusions: The improvement in the treatment of thalassemia patients not only with blood components but also with chelation therapy and other services implemented since 2000, has significantly increased life expectancy for this population of patients, by constantly increasing in this way their blood demand. The decrease of new infants born in the last decade demonstrate the positive influence on prevention of awareness campaigns, but still important steps need to be taken for the complete control of new infants born. A prevention strategy based not only on awareness and education but also on screening, genetic counseling and prenatal diagnosis is urgently needed in order to control this disorder that is affecting a proportion of our population and is a strain on resources such as availability of blood, medicinal products and specialized services.

P-059

PATIENT BLOOD MANAGEMENT: ANALYZING THE UTILITY OF UTILIZATION METRICS

J Kelley and F Martinez
Laboratory Medicine, University of Texas MD Anderson Cancer Center, Houston, United States

Background: Patient blood management (PBM) programs rely on metrics that analyze transfusion practices to optimize resource utilization. Metrics, suggested by certification organizations such as the Joint Commission and AABB, are often benchmarked between institutions and are used to guide development of medical practice and financial decisions. Examples of these suggested metrics include crossmatch to transfusion ratio, response to transfusion, and patient outcome data related to length of stay and hospital acquired infections as well as commonly followed metrics such as blood usage by department and monitoring transfusion reactions.

Aims: We aim to apply suggested metrics from certification standards to data from our institution, a 661-bed comprehensive cancer center in the United States, to provide a benchmark comparator and to verify the utility of less widely followed metrics.

Methods: We extracted two years of data (2016–2017) from our laboratory information system (Cerner Millennium, Kansas, MO) and electronic health records (EPIC Systems, Verona, WI). Using SAP Business Intelligence tools and Microsoft Access/

Excel, we analyzed transfusion practices and patient outcomes to guide development of performance improvement initiatives for our PBM program. All activities are approved by our institutional quality improvement advisory board.

Results: We analyzed data from up to 209,759 transfusions of 361,424 blood products in 18,731 patients. Our perioperative crossmatch to transfusion ratio was 2.38. Hemoglobin levels in patients receiving a RBC transfusion increased on average 1.03 g/dL after 1 unit and 1.83 g/dL after 2 units; platelet levels increased on average 6.9 k/μl following 1 dose; protime (PT) decreased by 0.62 s per unit of thawed plasma transfused; and fibrinogen increased on average 6.33 mg/dL per unit of cryoprecipitate transfused. In terms of length of inpatient stay (LOS), all patients averaged 7.51 days per admission; transfused patients had an average LOS of 9.99 days; patients who did not receive any transfusion averaged 7.15 days for LOS. When comparing rate of hospital acquired infections to transfusion, we found that 86% of patients with hospital acquired (HA) infections were also transfused during their admission; however, only 2% of transfused patients developed a HA infection. Of the transfused patients with HA infections, only 11% of the cases were due to organisms that could be potentially associated with transfusion / donor exposure.

Summary / Conclusions: Many metrics suggested by accreditation organizations may be less informative measures of appropriate utilization of blood products and may not apply to specific populations such as oncology patients. For example, the high rate of transfusions in patients with HA infections may reflect that transfusion and HA infection are correlated with patient severity and exposure to the health care system rather than a causative link between the two variables. Similarly, length of stay and transfusion use both independently reflect severity rather than a relationship between the two variables. However, more widespread metrics also included in PBM standards such as transfusion usage by service line or tracking adverse events (e.g. suspected transfusion reactions) may guide performance improvement efforts. Additional work is needed to see how such suggested metrics, if reported, influence practice.

P-060

PROVINCIAL REDISTRIBUTION: CREATING ON TOOLKIT TO OUTDATE OUTDATED BLOOD COMPONENTS AND PRODUCTS

T Cameron[1], L Young[2], A Wendt[3], T Thompson[3], W Owens[1], S Crymble[4], L Harrison[5] and A Pape[6]

[1]Ontario Regional Blood Coordinating Network, Ottawa [2]Ontario Regional Blood Coordinating Network, Hamilton [3]Ontario Regional Blood Coordinating Network [4]Hemophilia Ontario, Toronto [5]Trillium Health Partners - Credit Valley Hospital, Mississauga [6]Halton Health Care - Oakville Trafalgar Memorial Hospital, Oakville, Canada

Background: In 2007, the provincial outdate rate of RBCs in Ontario was 2.3% and since then there has been a decrease of 81% from 10509 units to 1966 units in 2016. In 2011 the Ontario Regional Blood Coordinating Network (ORBCoN) introduced a redistribution toolkit for components. Hospitals had a choice of using validated shipping containers provided by either ORBCoN or Canadian Blood Services (CBS). In 2013 ORBCoN partnered with The Factor Concentrate Redistribution Program (FCRP) to create a provincial monitoring and redistribution program for factor concentrate products and other plasma protein products. In 2016 CBS announced they would be phasing out the J82 and E38 shipping containers used for shipping blood. The new shipping containers would not be available for use by hospitals. The program was in jeopardy if validated shipping containers were not readily to all hospitals.

Aims: To ensure that the provincial redistribution program continued and that validated containers were available to hospitals to ship blood when patients are transferred from one facility to another.

Methods: A provincial working group reviewed processes for shipping container evaluations, documentation used to ship components and products, performed an environmental scan of equipment available for pre-conditioning ice and gel packs, courier systems and blood supplier support for the provincial program. Shipping containers were validated by two hospital partners to ensure that the containers performed to acceptable standards.

Results: The validation results of the shipping containers set the tone for updating the processes and procedures. Eighty out of 88 (91%) hospitals that responded, reported having access to freezers that provide temperatures between −25C and −40C when surveyed to identify freezer temperature for pre-conditioning ice packs. This helped develop packing configurations for validation testing. The results of the validation of the J82 and E38 shipping containers were reviewed and the acceptable times in transit were established. The provincial redistribution toolkit was updated and included operating procedures for shipping blood components and products,

reporting of near to expiring blood products, and shipping forms. A memorandum of understanding (MOU) was implemented between Ontario hospitals that ship blood components or products and ORBCoN/FCRP to ensure commitment to the program and to the standards required for shipping blood components and products. Transfer of RBCs between hospitals has increased by 92%, from 12914 units in 2007 to 24821 in 2016. Approximately 32% of the transferred units were identified as redistributed with an average annual cost savings of $2.4 million. Between 2013 and 2016 an average of 1700 vials of plasma protein products were redistributed within the province with an average cost savings of $2.3 million per year.

Summary / Conclusions: A loss of readily available validated shipping containers to transfer between hospitals for redistribution or sending products with patients would have had significant loss in savings of product and money to the province. The revised redistribution program with a validated shipping container maintained by ORBCoN and FCRP will ensure that the program continues to provide the savings.

P-061

Abstract has been withdrawn

P-062

GRANULOCYTES APHERESIS TRANSFUSIONS: THE FRENCH BLOOD MANAGEMENT IN 2016–2017

G Woimant[1], C Barisien[2], C Wertheimer[1], J Taieb[1], S Vanlaer[3], A Fillet[4], S Gross[4] and C Boulat[5]

[1]Blood Donation, French Blood Service, Paris [2]Blood Donation, French Blood Service, Besancon [3]Blood Donation, French Blood Service, Lille [4]Medical Department [5]Blood Supply & Laboratory, French Blood Service, Paris, France

Background: Granulocytes transfusions are exceptional, less than 350 products for 40 patients per year. Only life-threatening patients are concerned for severe bacterial or fungal infection. Therapeutic efficiency is difficult to evaluate according to the severity of the hematologic disease with chemotherapy and aplasia. Because of granulocyte short life span, the appointment and the collection of the donor must be performed in a short delay after the clinician request.

Aims: Provide apheresis granulocytes concentrates (AGC) throughout French territory (national self–sufficiency) with the support of 5 blood donor centers (3 in Paris area).

Ensure the security of the process (donor safety) and comply with the timelines.

Ensure the quality of the product: volume ≤ 650 ml, granulocytes count > 2. 10^{10}

Ensure the disponibility of the product in a very short delay (12 h after the end of collection)

Methods: The French Blood service (EFS) is a public national organization providing the national's self-sufficiency. The blood donor database is national. Donors are voluntary and unrelated. EFS call donors previously informed and identified with a specific code to facilitate a convocation in emergency. Regulatory requirements are: Age: 18–50, maximum frequency over 12 months: 2 donations, interval between 2 donations: 4 weeks. Minimum weight 60 kgs, 2 adequate venous access. Managing collections and process are performed according to national procedures. Prescription, donor selection criteria, safety instructions, stimulation by corticoids, heparin use, collection process, apheresis device are harmonized.

The EFS gives an expert transfusion advice to assist prescribers (guidance for indications, quality, and risk of this specific blood product infusion...). Information concerning the donor risk is given and their informed consent is obtained.

Discussion and consensus with the physician in charge of the patient, and daily follow up patient's transfusion needs according to clinical evolution, are done.

The supply of transports logistic is of major importance. Managing transport between the various sites within each regional transfusion site (ETS) is a daily challenge.

Results: In the last two years, 465 donations were collected from 380 donors. 72 donors have given more than 1 AGC.

75 patients (18 pediatrics) have received 450 AGC (3/75 patients had 2 treatments) on clinician request from 25 hospitals. The mean units transfused was 5.74 and the median 4 (1–50). Four patients had a chronic granulomatosis disease (CGD). Others patients had severe neutropenia (absolute neutrophil count <500 cells per μl) occurred during acute leukemia (53), immune deficiency (3), idiopathic aplasia (4).

All patients had severe life-threatening infection: cellulitis (perineal 24, others 17), fungal infections (13), digestive infections (6).

AGC Quality was defined by mean PNNs 2.55 x10^{10} per product (0.3 – 9.01).

Summary / Conclusions: The administration of G-CSF to healthy donors is not authorized in France, and the use of corticoids is questioning. Despite the lack of scientific evidence of real clinical effectiveness, the request of hematologists persists. Since 2016, the EFS has launched a study in order to prepare granulocytes from whole blood (as prepared by the NHSBT). This study is still going on.

P-063

Abstract has been withdrawn

P-064

PROGRESS WITH BLOOD AVAILABILITY IN AFGHANISTAN

J Mccullough[1], A Rhamani[2] and W Riley[3]

[1]Public Health, Afghanistan Ministry [2]Public Health, AATM Afghanistan country chapter, Kabul, Afghanistan [3]Public Health, Arizona State University, Phoenix, United States

Background: Because of years of strife, the blood supply of Afghanistan was limited, lacked central coordination and had less than optimal quality.
Aims: In early 2009, the Afghanistan National Blood Safety and Transfusion Service (ANBSTS) was established which has responsibility for all blood banking and transfusion services nationwide. Previously, there was no existing infrastructure and so it was necessary to develop the entire organization and processes. The objective was to: 1) provide safe, quality, and adequate blood in an equitable and cost-effective manner for all people resident in Afghanistan and 2) have a quality national blood service compliant with international standards.
Methods: A capable director was appointed, support provided by Parliament, NATO forces, US and Canadian Embassies and relationships with external experts were established. Policies were established, infrastructure was strengthened, and capable staff was acquired and trained. Standard operating procedures were developed, testing was improved, and quality systems were established. Thirty trainings were held for blood center staff. Four formal trainings were held for 39 physicians, 36 nurses and/or midwives, and 38 laboratory technicians. A donor recruitment program was established. Seven regional centers were established, and new facilities were constructed for _____ of these. A staff was established of 130 at Kabul Central Blood Bank, 26 technical staff in seven Kabul hospital branches and 44 in other regional blood banks. There are three medical officers based in Kabul. The medical officers are pharmacists and did not have formal training in transfusion.
For the first time in the Afghanistan blood safety history, blood collection drives were held inside NATO compounds and Canadian Embassy and very good advocacy for promoting voluntary blood collection drives was created inside and outside the country for the blood safety services.
Results: The standard donor history form was created a QA program established, and the ELISA testing for infectious agents introduced. Blood safety services were promoted and exposed by conducting few blood collection drives in the Afghan President Office. In 2008, prior to establishment of the ANBST S 35,602 units of whole blood were collected. In 2010 56,137 units of whole blood collected, 2011 = 68,176; 2012 = 76,259. 2013 = 47,715, 2014 = 74,887, 2015 = 78,454, 2016 = 122,695, 2017 = 154,715
Thus, since ANBSTS formation, blood collection has increased to 154,715 in 2017 for an increase of 119,113 or 434%.
Summary / Conclusions: Despite considerable difficulty, an effective national blood system has been established in Afghanistan and is function successfully as illustrated by a huge increase in blood collection by a capable staff.

P-065

THE IMPACT OF TRANSFUSION SERVICES DECENTRALIZATION ON BLOOD SUPPLY IN BURUNDI

R Niyibizi

Gitega Regional Blood Transfusion Center, Burundi Ministry of Health, Gitega, Burundi

Background: Burundi is an East African low income country with a fast-growing population currently close to eleven million and a high density up to 379 inhabitants per square kilometer.

The availability of sufficient and of good quality blood components remains a public health issue looking upon the burden of malaria, malnutrition, gynecological and obstetrical complications within the national context.
Since its establishment in 1993 until 2011, the National Blood Transfusion Center, which is located in the Capital, Bujumbura, was the sole competent institution to collect and deliver blood products to all hospitals throughout the country causing many challenges.
In 2011, four Regional Blood Transfusion Centers were created within the framework of the decentralization of transfusion services.
Aims: The aim of this study is to assess the impact of transfusion services decentralization on blood supply in Burundi
Methods: Retrospective study was done using National and Regional Blood Transfusion Centers reports and a statistical analysis performed on the volume of blood supply from 2010 to 2017.
Results: In 2010, 35489 Blood units were collected by the National Blood Transfusion Center. Since the transfusion services were effectively decentralized, the total volume of blood units collected steadily grew from 40,709 in 2011 to 91,393 in 2017.
At the same moment, the contribution of Regional Blood Transfusion Centers in total whole blood collection raised from 28.35% in 2011 to 61.77% in 2017.
Summary / Conclusions: The establishment of four Regional Blood Transfusion Centers had a significant positive impact on blood supply in Burundi. Indeed, the number of blood units collected increased more than twofold over six years. At the other side, the decentralization of transfusion services improved the proximity of blood centers facilitating the organization of mobile blood collections and the supply of blood components to provincial and rural hospitals allowing consequently the mitigation of time and resources wastage.

P-066

DID THE ACTIVE ROLE OF HOSPITAL TRANSFUSION COMMITTEE LEAD TO RESTRICTIVE TRANSFUSION THERAPY IN GENERAL HOSPITAL CELJE?

J Pajk

Transfusion Center, General Hospital Celje, Celje, Slovenia

Background: Twenty years ago General Hospital Celje (GHC) constituted the Hospital Transfusion Committee (HTC) to help the blood transfusion service introduce: the guidelines and recommendations of rational use of blood components and drugs, autologous blood transfusion and collecting and evaluating data of untoward reactions in patients and blood donors – haemovigilance.
Aims: During this period many changes were introduced in the field of extensive haemato-oncology, preoperative orthopaedic surgery and neurology treatment. We are interested in the influence of these changes on the use of blood components and drugs from FFP during last seven years.
Methods: The use of blood components and drugs from FFP in the period from 2011 to 2017 at General Hospital Celje (GHC) with 743 beds is presented. The data has been collected from the information system Datec and analysed in Excel.
Results: In last seven years, the use of red cells concentrates (RCC) and FFP has decreased; the use of platelets (PLTS), human albumins (HA) and gammaglobulins (GGL) 2017 have increased. In 2016 the usage of RCC (5150 units), PLTS (500 units) and FFP (630 units) was the most rational. Despite all activities of HTC four times a year there were some peaks of usage RCC in 2012 (7781 units) and 2014 (7778 units); PLTS (723 units) in 2015 and FFP in 2012 (2018 units); HA (4967 g) and GGL (11965 g) in 2017. The results are presented in tables and in graphs.
Summary / Conclusions: A large number of patients were treated in GHC due to serious internal diseases (haemato-oncology from 2013) and surgery operations in the analysed seven-year-period. Through exemplary cooperation between transfusiologists and clinicians, a regular activity of HTC (every three months) and considering the guidelines and recommendations for optimal use of blood components and drugs the use of blood components has decreased. The use of RBC diminished by 21.69% and FFP by 54.81%. There was only a slight increase in the use of PLTS by 0.36%. On the other hand, the use of HA and GGL has increased; HA by 200% and GGL by 68.88%. With the active role of Hospital Transfusion Committee (HTC) in the period from 2011 to 2017 we succeeded in introducing a restrictive and safe transfusion therapy with blood components in GHC. An even more rational use of drugs from FFP is expected in the future, too.

P-067

BLOOD DONATION PROFILE IN KERMANSHAH EARTHQUAKE VALUABLE EXPERIENCE FOR LEARNING TO DONOR RECRUITMENT IN FIXED AND MOBILE COLLECTION CENTERS

M Jalali Far[1,2], A Salah[3], M Shirmohammadi esfeh[3], A Khossravi[1], M Mavali[4] and M Ehtiati[5]

[1]Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran [2]Health research institute, Research Center of Thalassemia & Hemoglobinopathy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz [3]Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Shiraz [4]Blood bank, Amir-Almoemenin Hospital, Ahvaz [5]vice-chancellor in treatment affairs, Shahid Beheshti University of medical sciences, Tehran, Islamic Republic of Iran

Background: The need to blood is perpetual and the need in disaster elevating and become more vital and life-saving. Donor recruitment in this situation need highly experience and expertise to provide adequate and safe blood supply. After any disaster the need to blood and refer to blood transfusion to blood donation increase and balancing between them is necessary to avoid reducing the blood supply or blood collection more than real need and wasting the resources.

Aims: Recognize and study the people that refer during disaster to the mobile and fixed collection centers and compare with the same periods in previous year helps us in analyzing the donor management and retention them for other than disaster situations and management blood supply for any disaster.

Methods: In this cross sectional descriptive study, we surveyed all the blood donors that referred to all fixed or mobile centers of Fars province blood transfusion service (FPBTS) in day of Kermanshah disaster in 2017(13 November 2017) and compare with the same day in last year (2016). All the demographic and other donations profile was extracted from database and analyzed by statistical software.

Results: The blood donations, refer to mobile collection centers, temporary and permanent deferrals after earthquake increased two times in comparison with the same time in previous year (4324 vs 2397; 22.02% vs 11.86%;1721 and 245 vs 734 and 121 respectively). The temporary and permanents deferral rate in mobile centers during earthquake significantly reduced in comparison last year (5.63% and 8.16% vs 16.49% and 19.01%). The participants of female blood donors in disaster increase five time more than last year (520 vs 100 donations) and they preferred to donate their blood in fixed blood centers. Whereas the number of male blood donors showed just about two-time increase (3838 vs 2314 donations). Confidentially Unite Exclusion (CUE) in earthquake was half than last year (6 vs 14 donors). The plasma and platelet apheresis showed great growth in earthquake more than 8 time than previous year (116 donors vs 33).

Summary / Conclusions: According to our result the FPBTS had good response to disaster especially female blood donors and showed good sympathy with Kermanshah people. Increase the first-time blood donors during that disaster give us good opportunity to become them as lapsed or regular donors. The safety of blood supply must not be sacrificed for quantity of blood donation and more surveillance and training in mobile collection center must be applied.

P-068

PROBLEMS AND CHALLENGES: DEVELOPMENT OF BLOOD TRANSFUSION SERVICE IN MAINLAND CHINA UNDER THE CONTEXT OF HEALTH CARE SYSTEM REFORM

J Chen[1], G Xie[1], C Bei[2] and Y Fu[2]

[1]Department of Blood Collection [2]Guangzhou Blood Center, Guangzhou, China

Background: The ultimate function of transfusion service is to support local health system, so a more rational assessment of transfusion services in a country or region should be based on the development of local health system and clinical blood needs. Talking about the development of China's health system, it is inevitable to mention the new round of health system reform launched in China in 2009, which will determine the long-term direction and overall pattern of China's health care system. Similar to systems reform carried out around the world, the new round of health system reform in China has aimed to break through the situation of over-concentrated health resources in large and medium-sized cities, especially in tertiary A-class public hospitals. From the perspective of the health medical system reform, would China's blood transfusion services match it? No publication had answered this question yet.

Aims: To evaluate the development of blood transfusion service in mainland China under the context of health care system reform, providing references for decision-making in China's health system reform and blood transfusion service.

Methods: Based on the data from national survey of blood collection and supply institutes in July 2015, the total blood collection,Whole blood donations per 1000 population and supply and demand relationship were analyzed by administrative regions level. Areas with relatively high-quality health resources and the other were compared from the dimension of total blood collection and human resources.

Results: The variation in total blood collection volume in 31 provinces of mainland China in 2014 was wide, with the highest point in Beijing which was over 600 thousand units and the lowest point located in Qinghai province which was about 1 thousand unit. 29 provincial capitals collected 69% of all blood volume nationwide, while 311 non-capital cities collected the remaining 31%. Whole blood donation rate per 1000 population among provinces in mainland China range from 1.48 to 17.09. Overall, the whole blood donation rate per 1000 population in the central and western area were lower than the eastern coast. In most provinces, donation blood volume per population were concentrated between 2~4 ml and blood volume per inpatient were 20~60 ml regardless of the development of the transfusion services. 74 PhDs. in all 97 PhDs. were recruited in 32 provincial blood establishments, While the rest 23 PhDs. scattered in other 318 central blood stations which was ten times lower than that in blood centers group.

Summary / Conclusions: Under the context of China's health reform, the imbalance development and insufficient supply of blood transfusion services among regions will restrict the achievement of its goal. Therefore, China's blood transfusion service urgently needs to be redeployed on the national level according to the extent of development. Policy priority should be given to non-developed areas, imbalance in human resources should be solved by creative measures to promote the sinking of technology and management experience and break the extremely uneven development in different areas.

P-069

ANALYZING AND CLASSIFICATION OF TURKISH RED CRESCENT DONORS DUE TO DOMAINE

D Ulger[1], S Caglak[1], L Sagdur[1], A Aksoy[1], N Hafizoglu[1] and F Yilmaz[2]

[1]National Blood Services, Turkish Red Crescent [2]Department of Biochemistry, Yildirim Beyazit University, Ankara, Turkey

Background: EU and DOMAINE classifies donors according to donations. DOMAINE has created a series of detailed definitions for both donor types and donation types. The DOMAIN definitions also indicate which parameters should be used in the datasets. The descriptions in the DOMAİN are more detailed and more extensive than the EU definitions. Returned and Lapsing Donor terms were added and Turkish Red Crescent (TRC) donor definitions are based on the DOMAINE.

TRC Blood Banking Information Management System contains information of 8.5 million active persons.

Aims: Study of analyzing and classification of TRC donors due to DOMAINE.

Methods: We had analyzed our donors who donated between 2005–2017 due to the definition of DOMAINE. Between 2005–2017, an average of 2.35 units of blood were donated per capita donor. In 2009, 848,586 blood donations were collected from 730,139 people, while in 2017 2,391,573 blood donations were collected from 1,931,805 people. It is observed that 1,161,304 people were registered in the system even they didn't donate. It was also seen that there were 3,789,908 donors who were only once donated blood. The recorded highest blood donation number by single donor is 217 units. 57% of donors are young people, aged 18–35 years. 19% of the donors are female. The rate of female donors, which was 6% in 2005, has risen to 15% in 2017

Results: TRC donors based on the definition of DOMAINE;

Newly registered donor: In 2017, 35% of blood donors were newly registered donors. When these donors are analyzed, it can be seen that on average 80% donated blood, but about 20% couldn't donate blood due to deferral and other reasons

First time donor: In 2017, the rate of first time blood donors is 29%.

Regular donor: While 23% of donations were collected from regular blood donors in 2009, this ratio was 41% in 2017. Over the years the rate of regular donor growth has exceeded 10%.

Lapsing donor: 13% of donors in the database are silent donors.

Inactive donor: Approximately 50% of donors in the database are inactive donors.

In 2018, in addition to the silent donors in the sense of blood donor recruitment, there is a plan of action and projects for inactive donors. If we can change only 5% of the inactive and silent donors to regular donors, minimum of 300,000 units additional blood can be collected per year. In these two types of donors, between the ages of 26–35, they seem to have stopped giving blood again. In the first objective, projects are being prepared to reach and regain these donors.

Returning donor: Someone who has made at least two donations. This donor has made only one donation within the last 12 months AND the interval between the

last and the before last donation is more than 24 month. In 2017, 42% of donors were returning donors

Summary / Conclusions: As a result, classification and analysis of blood donors in the system seems to be able to increase the number of blood donations collected from regular blood donors.

P-070

IMBALANCE BETWEEN SUPPLY AND DEMAND FOR GROUP A AND O RED BLOOD CELLS IN KOREA: WHAT IS THE CULPRIT

H Kim[1], Y Chung[2], Y Hong[1], K Park[1], D Kim[3] and K Han[1]

[1]Department of Laboratory Medicine, Seoul National University College of Medicine [2]Department of Laboratory Medicine, Kangdong Sacred Heart Hospital [3]Department of Laboratory Medicine, Korea University Anam Hospital, Seoul, Republic of Korea

Background: Frequent periods of blood supply shortage have occurred, especially for group A and O red blood cells (RBCs) at blood centers in Korea. However, no imbalance exists in the ABO blood group distribution of blood donation (A, 34.4%; O, 27.3%; B, 26.8%; AB, 11.5%) and the general Korean population (A, 34%; O, 28%; B, 27%; AB, 11%). In Korea, group O RBCs are not frequently used as 'universal' RBCs and the ABO blood group of the recipient is strictly adhered to when selecting all blood components for transfusion. If A and O RBCs are being actually more used for a biologic or epidemiologic factor, blood donation may need to be additionally focused on groups A and O.

Aims: This study investigated if group A and O RBCs are being more used at the end of the blood supply chain, possibly related to differences among ABO blood group distribution in highly blood using diseases in the Korean population.

Methods: The top 30 disease categories that used the most RBCs, platelets, and plasma components were identified from the national database provided by the Korean Health Insurance Review and Assessment Service from January 2011 to June 2013. Blood component utilization according to ABO blood group was analyzed for these disease categories in three major tertiary hospitals in Korea from January 2011 to December 2013.

Results: Data on 127,411 RBCs (21,766 patients), 584,273 platelets (apheresis platelets were counted as 6 random donor platelets; 8,263 patients), and 76,663 plasma components (6,844 patients) were analyzed. Group A and O RBC usage were both increased by 0.4% compared with the blood donation rate for groups A and O (P < 0.001). Group B and AB RBC usage were reduced by 0.8% and 0.1%, respectively, compared with their respective rates for blood donation. Group AB platelets and plasma component usage were increased by 4.8% and 8.3%, respectively, compared with their respective rates for blood donation (P < 0.001). The ABO distribution of the patients transfused with RBCs, platelets, and plasma components were all not statistically different from that of blood donation.

Summary / Conclusions: The difference in ABO group distribution between blood donation and RBC utilization was small and insufficient to account for the low inventory level for group A and O RBCs at Korean blood centers. There may be a possibility of stockpiling or over-ordering of group A and O RBCs at hospitals that may cause an undesirable and unnecessary inventory shift of RBCs from the blood centers to the hospital blood banks. Enhancing hospital blood inventory status monitoring capability and implementing a revised national surveillance system as planned will enable further investigation on this issue.

P-071

EFFECTIVENESS OF MULTIPLE MONITORING PROCESSES TO REDUCE BLOOD COMPONENT WASTAGE

Y Huang[1], L Hsing[1], Y Chen[1], C Tung[2] and W Su[1]

[1]Department of Clinical Laboratory [2]Information office of R&D Team, Pingtung Christian Hospital, Pingtung, Taiwan, Republic of China

Background: Wastage of blood components is an essential issue facing hospitals worldwide. Many blood banks have adopted a "30-minute" rule to be in compliance with AABB require and will not accept an RBC unit that has been outside of the blood bank for more than 30 min. The extent and causes of blood product wastage were identified, and then multiple monitoring to address the causes of wastage was implemented.

Aims: Our aim is to establish a Patient Blood Management (PBM) program based on electronic data capture in order to monitor the blood components waste at a regional health care hospital.

Methods: Multiple monitoring processes, including Single Blood Bag-Single Transfer (improved transportation via electronic information system), print and digital specified patient's message on blood bag, component identification modalities and educational outreach nursing staffs, were implemented beginning in 2017. The impact on reducing blood component wastage in 2017 after monitoring processes implementation was compared with the wastage rates and cost in 2016.

Results: We made a crucial change in the computerized physician order entry (CPOE) system. When physicians order more than two blood bags, the delivery of the system will show Single Blood Bag-Single Transfer that can avoid transporting staffs' confused error of taking more blood bags. Overall, the wastage rate of blood components as a percentage of the number decreased from 0.56% to 0.30% (P < 0.001) after the multiple monitoring processes were implemented. The cost of wastage was approximately $1130. The net cost savings of the reduced waste was estimated at $565 (50%).

Summary / Conclusions: Multiple monitoring processes and electronic data capture can have a prompt and significant impact on reducing blood wastage and result in the enhancement of quality and safety in blood transfusion services, reducing the incidence of transfusion reactions.

P-072

Abstract has been withdrawn

P-073

ALIGNING PLATELET COLLECTION STRATEGY WITH PROJECTED DEMAND IN NORTHERN IRELAND

NR Cunningham[1,2] and K Morris[2]

[1]Haematology, Belfast City Hospital, Northern Ireland [2]NIBTS - Transfusion Service, Northern Ireland Blood Transfusion Service, Belfast, United Kingdom

Background: Recent benchmarking data from the Association of Blood Operators indicates a wide variation in issues of platelet components for different populations and variation in attrition. The Northern Ireland Blood Transfusion Service has detailed data on its collection performance for apheresis component donations and whole blood derived platelet component manufacture. A detailed analysis of attrition of components is presented and the fate of every component issued to hospitals in the region is tracked for multiple dosing and ABO cross grouping.

Aims: To analyse the current platelet provision for Northern Ireland matched to demand, with the aim to implement a platelet strategy for the region.

Methods: All donations of apheresis and whole blood platelet components from NIBTS where analysed over a 6 month period. Donor details, ABO group, manufacture and attrition data was collected. This was matched to clinical need, requiring specialty and attrition of each donated unit of platelet.

Results: 2207 donated platelets analysed. 192 (9%) wasted. 17% cross grouping of donor and recipient groups. Individual specialty destinations identified with haematology highest user 66% transfusions. Multiple dosing within a 24 h period performed in 2% of transfusions with most common reason identified as vascular surgical procedures. Compliance with regional and national guidelines addressed with direct comparison between Hospital Trusts and practices.

Summary / Conclusions: Final conclusions of the report recommend improvements in inventory management, productivity and efficiency of collection and component manufacture. This improvement is necessary because of a reducing donor base, cost containment measures and the likely impact of a patient demographic with increasing haematological and cancer diagnoses and more intensive treatment protocols. This has led to development of a regional platelet strategy for Northern Ireland.

P-074

INVESTIGATION OF THE BLOOD SUPPLY FOR CLINICAL FROM GUANGZHOU BLOOD CENTER DURING 2013–2017

L Weifeng

Professional management department, Guangzhou Blood Center, Guangzhou, China

Background: Our blood donation population has been increasing and transfusion safety has been effectively protected due to Blood Donation law of The Republic Of China has been promulgated since Oct 1st 1998. But because of the speciality of

blood donation population one of job objectives of the blood center is that we need to carry out a safe and timely clinical blood supply strategy in order to ensure clinical rational and scientific use of blood.

Aims: Retrospective analysis of the clinical blood supply in Guangzhou Blood Center from 2013 to 2017 so that we can grasp the overall level of clinical use of blood in Guangzhou and promote the rational and scientific use of blood.

Methods: The data of clinical blood supply in Guangzhou Blood Center from 2013 to 2017 was collected, and the whole blood and blood components (erythrocytes, plasma, platelet and cryoprecipitate) were statistical objects.

Results: Guangzhou Blood Center supplied 4,509,900 U blood products for clinical use in past five years. The whole blood was 854 U, accounting for 0.02%. The blood components were 4,509,046 U, accounting for 99.98% including erythrocytes 203,1362 U, accounting for 45.04%, plasma 1,893,735.5 U, accounting for 41.99%; platelet 364419 U, accounting for 8.08%; cryoprecipitate 219529.5 U, accounting for 4.87%.

Summary / Conclusions: The amount of blood supply and the speed of growth rate increased during 2013–2017 year by year, The blood component transfusion has been popular in hospitals and rational and scientific use of blood can partially relieve supply pressure and ensure transfusion safety.

P-075

Abstract has been withdrawn

P-076

Abstract has been withdrawn

P-077

ENVISIONING A SUSTAINED NOVEL MODEL FOR A TRANSFUSION MEDICINE RESEARCH CAPACITY-LED SAFE AND EFFECTIVE DELIVERY OF BLOOD IN RESOURCES LIMITED SETTINGS: CASE STUDY OF RWANDA

P Karame[1], T Dusengumuremyi[2], C Musanabaganwa[3] and S Gatare[4]

[1]Rwanda Medical Research Regulatory Affairs, Rwanda Biomedical Center [2]Rwanda Biomedical Center, Rwanda National Center for Blood Transfusion [3]Rwanda Medical Research Center [4]Rwanda National Center for Blood Transfusion, Rwanda Biomedical Center, Kigali, Rwanda

Background: Medical advances have enabled access to quality services for patients especially those with critical healthcare needs. Promising research-based innovative approaches have revolutionized and improved disease prevention, diagnosis, care and treatment. Transfusion science contributing to saving lives has made tremendous progress achieving safer transfusions and aiming to zero transfusion risks. Transfusion therapy has therefore constituted a need-based life-saving intervention especially in emergencies mainly due to cutting-edge technologies, improved techniques, sound regulatory policies and technical expertise of health professionals. This remarkable progress was mainly led by developed countries, specifically emphasizing their needs and rarely immediately accommodating resources-limited settings needs, especially Africa's. It is particularly disturbing that not only Africa was left behind with technology transfer, basic knowledge and skills necessary to ensure risk-minimized transfusions, and, sadly despite being the most exposed to the burden of transmittable blood-borne diseases like HIV/AIDS and hepatitises.

Notwithstanding those barriers, African countries have been setting enabling research and clinical environment to effectively adopt transfusion medicine tailored to their respective contexts. The low or absent investment in transfusion medicine research and development and rare probability that those undertaken accommodate the African context is regrettable. Key African under researched challenges concerns transfusion safety algorithms, risk mitigation, transfusion safety monitoring, gaps or lack of blood research data for evidence-based transfusion, shortages of blood cells products, accessibility, affordability of standard infrastructure and capacity adequate for blood banking, stem cell collection, processing, preservation and transfusion, etc. Given those challenges, Rwanda has envisioned and implemented country-tailored models to achieve conducive medical research environment e.g. for clinical trials, capacity building e.g. Human Resources for Health and innovative approaches for blood cells products supply especially in remote areas using drones deliver services.

Aims: This paper emphasises the analysis of newly combined models reflected as Blood Safety – Supply – Research (BSSR) incorporating the interventions adopted since 2016 including drones for blood delivery.

Methods: C1: comprehensive analysis of the transfusion medicine and practice regulatory aspects e.g. post transfusion/transplant monitoring [Safety]

C2: Comparative model contrasting the Vehicle-based and drone empowered blood delivery services [Supply]

C3: Innovation-driven medical research analysis component [Research]

Results: C1: benefits, challenges, lesson learnt prior to and after 2016;

C2: Quality, Flexibility, Cost, Supplier Reliability, Innovation, Responsiveness, Delivery Lead Time, Product diversity and Asset management between both approaches - modelling the best fitted [best practices] for resources-limited settings

C3: Challenges, Opportunities, best practices from investment in clinical research and promoting cutting-edge technology in biomedicine including transfusion science.

Summary / Conclusions: This paper underlines the achievements, challenges and opportunities as well as best practices drawn from a boldly implemented model prioritizing Blood Safety – Supply – Research [BSSR] in the framework of achieving evidence-based transfusion medicine in Rwanda and avail a model for Resources Limited countries.

P-078

MANAGEMENT OF BLOOD DONOR AND BLOOD DONATION TO FULFIL THE INCREASE OF BLOOD AND BLOOD PRODUCT DEMAND

M Rajkarnikar[1,2]

[1]Central Blood Transfusion Service [2]Blood Transfusion Service, Nepal Red Cross society, Kathmandu, Nepal

Background: Blood Transfusion Service started from 1966 in Nepal and in the start collection per year was 157 units. Since from the establishment of blood service Nepal Red cross Society with its responsibility managing blood and blood products to the needy with 106 blood centres in 73 districts across the country. Nationwide total 236,799 units were collected and 337,321 units of blood and blood components were supplied in year 2016. There is increase in demand as more treatment technology has been available in the country. Though there is no appropriate donor follow up system in the country many schools, colleges, universities, clubs, corporates, offices donating once in a year but with the motivation, awareness and talk program instead of one time most of the organizations started donating two or three times a year. Also each and every religious group also started organizing donation camp. With the increase of new organizations it is easy to fulfil the demand. In the country now started to have storage centres in hospital with this there is less number of blood discard where it save unnecessary transportation of blood and blood products from the relatives.

Aims: Motivation and awareness program realize the blood donors the importance of blood donation and it became easy to manage blood demand throughout the country. For hospital stock management hospitals started to come and receive blood and blood products which helped to maintain quality of cold chain and timely transfer the products in the destination. To manage sufficient blood available in the blood centers few regular blood collection centers also established with the help of donor organization. With this cooperation and collaboration NRCS Blood Centers Nationwide manage to supply blood to the needy as per demand.

Methods: Maintain list of all blood donor groups. Organize regular motivation and awareness program. Records and data update of donor organizations, volunteer blood donors and blood units. Communication and regular updates from all hospitals. Collaborate with stakeholders and media for the support.

Results: Blood and blood components were well managed and supplied according to the demand. Awareness and motivation helped people to understand the use and need of blood. Individual blood donors and volunteers motivated to support with blood donation. Cooperation and coordination with different stakeholders helped for the blood management without difficulty in the Country.

Summary / Conclusions: Summary and Conclusion: If Individual blood donors and volunteers motivated to support with blood donation blood can be managed properly. Cooperation and coordination with different stakeholders should be build up for the blood management without difficulty in the Country.

Key Words: Motivation awareness, blood donors, organizations, demand

P-079

AN ATTEMPT TO TAILOR WASTAGE OF BLOOD PRODUCTS IN THE FORM OF RETURNED UNITS

SA Ali, M Ali and H Mansoori

Laboratory, Patel Hospital, Karachi, Pakistan

Background: Wastage of blood products may have an atrocious outcome on health care system. With an improvement in overall health care system there is an emerging focus on limiting the cost and avoiding the practices which may lead to wastage of blood products. It is time to call for adopting the practices which minimize the wastage of such prized blood units to almost zero.

Aims: To determine wastage rate of blood products in the form of returned blood products at a multidisciplinary institute

To identify the reasons of returning blood product after allowable time

Methods: Retrospective audit was conducted in the section of blood bank from Jan-Dec 2016 designed to determine rate of products returned to blood bank after dispatch, as a part of institutional wastage-reduction program. Reasons of return and key personnel and areas involved were identified

Results: 3999(46.5%) of blood components were wasted in study duration out of which returned packed red cells after specified time contributed 7.8% (n = 315). 3.2% (n = 15) blood products were returned within 30 min and were taken back in inventory. Majority of these products were returned from Operating room 34% (n = 159). In 93% (n = 109) cases, nurses and physicians were oblivious of the acceptable duration of keeping blood products out of controlled temperature. For total of 116 patients, ordering multiple units at a time with an anticipation of excessive bleeding during procedure (37.9%, n = 44), patient's apprehensions (24.1%, n = 28) and unavailability of proper intravenous access (19.8%, n = 23), were identified as key reasons behind delaying the transfusion

Summary / Conclusions: Wastage of blood in the form of returned products was found to be significant. A multi-faceted plan was formulated as an important step towards hemovigilance in order to reduce the wastage in the form of small group educational sessions, flyers, new blood bag tags and transport box labels with 30 min rule messages on them. A re-audit is now planned to analyze the affect and outcome of these efforts

P-080

BLOOD TYPE SPECIFIC ISSUING POLICIES TO IMPROVE INVENTORY MANAGEMENT

J van Sambeeck[1,2,3], S van Brummelen[2,3,4], M Janssen[1] and N van Dijk[2,3]

[1]*Transfusion Technology Assessment, Sanquin Research, Amsterdam* [2]*Center for Healthcare Operations Improvement & Research* [3]*Stochastic Operations Research, University of Twente, Enschede* [4]*Donor Studies, Sanquin Research, Amsterdam, Netherlands*

Background: Challenges faced by blood transfusion services are becoming more complex and change continuously due to the introduction of new technologies and increasing customer expectations. One of these expectations is the ability to select extensively type red blood cell units directly from stock. Currently, all units are issued according to the first-in-first-out principle, irrespective of their specific typing. This kind of policy might result in shortages for rare units. Such shortages can be avoided retaining rarer blood units longer in stock. As this might on the other hand lead to increased wastage a trade-off between the age and rarity of units is required.

Aims: The objective of this research is to develop a matching strategy that balances the quality of a match of red blood cells against the age of the unit issued.

Methods: Due to the specifics of matching restrictions for red blood cell units, traditional (perishable) inventory allocation models cannot be applied. Therefore, we developed an integer linear programming model to optimize the allocation of the inventory. We introduce a new performance measure that indicates the quality of a match, and base the decision on which unit to issue for a given demand by balancing the rarity and age of the blood products in stock. A simulation was performed to validate the performance of the matching strategy using historical blood type requests from Dutch hospitals.

Results: A simulation was performed in which the new issuing policy was applied in a different range of settings. These included variation in stock size, priority of age versus rarity, and the number of decision moments per day. The simulations show that by applying the new issuing policy, the number of exact matches increases, whilst retaining the same supply level.

Summary / Conclusions: With the new issuing policy, a very high percentage of requests can be fulfilled with an exactly matched RBC unit. This is combined with a

significant reduction in the percentage of outdated units, and a very low proportion of matching products that are available in stock on request. Currently, units to be issued are selected manually. When more complex demands (other than ABO, RhD) have to be met, this approach is likely to become sub-optimal as the inventory of typed RBCs is far too complex for humans to manage. This will result in additional efforts to meet requests for more complex RBC units that might have been avoided by applying more advanced issuing policies as applied in our simulation.

P-081

PROCESS IMPROVEMENT TO DECREASE BLOOD PRODUCT WASTAGE AND IMPROVE COLD CHAIN EFFICACY

RS Tabao, A Omar, D Lyons, P Chai, J Godfroy and M Wong

Laboratory Medicine, Khoo Teck Puat Hospital, Singapore, Singapore

Background: Khoo Teck Puat Hospital is an acute care 590-bedded regional hospital catering to the healthcare needs of northern Singapore. The Department of Laboratory Medicine Blood Bank issues 8000 blood products each year. Over a period of 5 years, from 2012 to 2017, 76 units of packed cells, 257 units of fresh frozen plasma, 80 units cryoprecipitate and 42 units of platelets were discarded in accordance to national policy. Twenty-five percent of these can be directly attributed to breaches in the cold chain elements of blood and blood product transport within the hospital.

In the course of our investigation into these wastages, we surreptitiously followed the issued products to the receiving locations and observed how the products were handled. It was observed that many of the receiving locations had adopted non-standard materials and practices which resulted in increased risk of product spoilage.

Aims: The aim of the project is to prevent unnecessary wastage of blood products by maintaining the cold chain during transportation of the products within the hospital.

Methods: Cooler boxes to be used in the study were first validated. Intact expired blood products were stored in the cooler boxes and the maximum time appropriate temperature can be maintained with a given ratio of blood products to ice packs while being in a typical non-air conditioned ward environment was determined. All temperature measurements were performed using a National Institute of Science and Technology (NIST)-verified thermometer.

During the trial, previously validated cooler boxes were used to transport the blood products and the cooler boxes were kept in the wards until the transfusion ended. Unused blood products remain in the provided cooler boxes until they are returned to the blood bank.

Used blood product packs were also returned to the provided cooler boxes for storage and return to the blood bank. Sterility testing was performed on these packs to verify that the conditions in the cooler boxes will maintain blood product integrity throughout the time blood products are out of the controlled environment of the blood bank.

Results: All blood products returned were within acceptable temperatures and no blood products had to be discarded due to breaches in temperature control.

Sterility testing results on a total of 51 transfused units were negative. Two units were later inoculated with known microorganisms as a positive control to rule out false negative results.

From January to October 2017, there were 59 blood product wastages, of which 18 (31%) were due to breaches in temperature control. After the implementation of the process improvement on November 2017, there were 36 blood wastages, of which only 4 (11%) were due to breaches in temperature control from November 2017 to February 2018.

Summary / Conclusions: Blood is a valuable resource and wastages should be minimised. The maintenance of a cold chain requires a collaboration involving multiple stakeholders, including laboratory staff, nurses and porters. Through inter-department cooperation, we were able to maintain cold chain during blood product transportation within the hospital campus and reduce blood wastages.

P-082

MODELLING RARE BLOOD INVENTORY IN CANADA

JT Blake[1,2] and G Clarke[3,4]

[1]*Research and Development, Canadian Blood Services* [2]*Industrial Engineering, Dalhousie University, Halifax, Nova Scotia* [3]*Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB* [4]*Medical Services, Canadian Blood Services, Edmonton, Alberta, Canada*

Background: Patients with a complex red cell antibody profile or antibodies to high prevalence antigens have limited options when a blood transfusion is required. Thus,

many countries have established rare blood programs that screen donors for rare phenotypes and a registry to record information about such donors, once identified. Blood agencies may also collect, freeze, and store rare blood units to provide for either autologous or allogeneic transfusion. Frozen blood is, however, expensive; frozen units cost 5–10 times that of a fresh unit.

Aims: Canadian Blood Services (CBS) maintains a rare blood program that services all demand for rare blood in Canada, outside of Québec. The program includes a process for screening donors, registering individuals with rare phenotypes, and storing fresh and frozen inventory. There is anecdotal evidence that frozen inventory levels are not optimally configured. The objective of this study is to evaluate, using analytical methods combined with a discrete event simulation, rare blood inventory in Canada to identify operational settings that ensure demand for rare units can be met efficiently.

Methods: A two-phase approach was employed. In the first phase, an analysis of supply and demand was undertaken to identify minimum screening rates necessary to ensure a stable supply of rare phenotypes and to estimate the minimum phenotype rareness for which a stock of frozen units is necessary. Once minimum levels were identified, a simulation model was employed to evaluate the stochastic version of the rare blood network under a variety of inventory levels.

Results: Minimum rare donor population sizes were calculated and compared to estimates of the screened donor population at CBS. For 25 of the 29 the rare phenotype combinations managed by CBS, the number of known donors was less than the minimum number of donors needed to ensure a stable flow of product. Analytical results suggest the number of identified donors must be increased by a total of 2200. By exploiting the differential retention rate of rare (10% turnover/year) and regular blood donors (50% turnover/year), it is possible to build the rare donor registry; to do so requires between 3 and 10 years, depending on the screening rate adopted for incoming donors.

The simulation was executed for each of the 29 different phenotype frequencies. Experiments measured the delay between a patient request for rare phenotype blood and filling that request. Experiments assumed either 0, 2, 4, or 6 units apiece of (O+, O-, A+, and A−) blood. Results showed that holding 2 units apiece improves patient access to rare blood at almost all phenotype frequencies. However, holding 4 or more units apiece was not associated with statistically significant decreases in patient delay. For example, considering a phenotype negative for the e and c antigens in the Rh group, which occurs in 1 in 25,000 individuals, holding no frozen inventory results in an average of 42.9+/- 4.21 days to fulfil a patient request for blood. If 2 units apiece are held, access time decreases to 2.84+/- 0.47 days; no significant decrease in delay could be detected with an increased frozen inventory.

Summary / Conclusions: While some level of frozen blood is needed to buffer fluctuations in supply and demand for rare blood, large inventories are unlikely to improve access, nor will they be easily collected for very rare phenotypes. Our model suggests that modest amounts of frozen inventory, combined with increased screening, provides the greatest chance of ensuring that patients with complex serology have access to red blood cells when needed.

P-083

RARE BLOOD GROUPS REGISTER CONFIGURATION, ACCORDING TO BLOOD GROUPS DISTRIBUTION, IN BIHOR COUNTY ROMANIA

O Burta[1,2,3], H Kiss[4] and R Burta[5]

[1]Management, Blood Transfusion Center [2]Immunology, University of Oradea [3]Blood Transfusion Society Karl Landsteiner, Oradea [4]Immunology, Babes Bolyai University Cluj Napoca, Cluj Napoca [5]Internal Medicine, University of Oradea, Oradea, Romania

Background: Transfusion therapy represents a chain of specific events, in both prehospital and hospital levels, in order to minimize the transfusion risk, including the immunologic one.

Aims: By ABO, Rh(D) and minor erythrocytes systems immunologic assays, one of the major pillar of transfusion safety is covered.

Methods: The study was done on 2000 blood donors – representing about 10% of the total pool of donors at Bihor county level. Were selected 3 areas: Oradea, Salonta and Beius, upon specific criteria (ethnic, consanguinity reasons). All data were collected from donors files being respected the confidentially rules. The cases approach has a common skeleton, for each area: blood donors number/ gender/ age/ OAB, Rh(D) systems/ Rh(D) phenotypes, minor erythrocytes groups (K).

Results: The ratio of OAB groups found was in OAB system: A (43%), O (40%), B (10%), AB (7%), in Rh(D) system: positive: O (29%), A (26%), B(9%), AB (6%); and negative: A (16%), O (11%), B (2%), AB(1%).

In Oradea area: group A: Rh(D) positive were identified 12 phenotypes, seldom DᵂCeċe; Rh(D) negative - 5 phenotypes, seldom CċeKel. In O group: Rh(D) positive – 12; Rh(D) negative 3 phenotypes. In B group: Rh(D) positive - 8 phenotypes seldom DᵂCċe; Rh(D) negative - 3 phenotypes, seldom ċeKel. In AB group: Rh(D) positive - 8 phenotypes seldom Dċe; Rh(D) negative - 2 phenotypes.

in Salonta area: in A group: Rh(D) positive - 7 phenotypes, seldom DCċe Kel; Rh(D) negative - 2 phenotypes, in B group: Rh(D) positive - 6 phenotypes, seldom: DEċ, DᵂCċe; Rh(D) negative - 3 phenotypes, seldom Cċe. In AB group: Rh(D) positive - 6 phenotypes, seldom DCċe Kel; Rh(D) negative 1 phenotype ċe.in Beiuş area. In A group: Rh(D) positive - 13 phenotypes seldom DᵂEċ; Rh(D) negative - 3 phenotypes seldom ċeKel. In O group: Rh(D) positive - 7 phenotypes, seldom DCċe Kel; Rh(D) negative - 4 phenotypes, seldom ċeKel. In B group: Rh(D) positive - 6 phenotypes, seldom: DᵂCċe; Rh(D) negative - 2 phenotypes. In AB group: Rh(D) positive - 3 phenotypes, seldom DCċe; Rh(D) negative - 2 phenotypes.

Summary / Conclusions: The importance of this study is that proves the heterogenicity in blood donors category, according to some demographic, ethnic and behavior characteristics, and blood systems sometime being challenged during transfusion compatibility.

The necessity to extend the model to cover the entire pool of blood donors, to have a National chart regarding immuno-hematologic population features, having a professional approach about the way of minimizing the immunologic transfusion risk.

Based on National data can be organized a National Register for Rare Blood Groups

P-084

RED CELL PHENOTYPES FREQUENCY IN THE SINGAPORE BLOOD DONOR POPULATION

L Mei Zhee, C Sze Sze and L Sally

Blood Services Group, Health Sciences Authority, Singapore, Singapore

Background: Singapore donor population is comprised of different ethnic groups namely Chinese, Malays, Indians and other ethnic origins. It is important to have the knowledge of the frequencies of red cell phenotypes in the donor population in order to supply antigen-negative compatible Red Blood Cells (RBCs) for patients with multiple alloantibodies and prevent the development of transfusion reactions to ensure blood safety.

Aims: To study the frequency of RBC phenotypes in the blood donor population.

Methods: Mass phenotyping was performed on regular donors who have made 4 donations in the last 2 years. Phenotyping of the Rhesus antigen (D, C, E, c, e) is done using Beckman Coulter PK7300 Blood Group Analyser that is based on haemagglutination. This is followed by the detection of RBC antigens Jka and Jkb. Donor samples tested negative for Jka and/or Jkb antigens are further tested for Fya and Fyb antigens. Subsequently, Fya and/or Fyb antigen negative samples are screened for S and s antigens. The antigen typing for Jka, Jkb, Fya, Fyb, S and s are performed on Bio-Rad IH-1000 analyser which uses the gel column technique. Retrospective RBC phenotype data from January 2015 to December 2017 was analysed and the phenotypes frequencies are expressed as percentages.

Results: 33,534 regular donors, consisting of 24,967 Chinese, 2,476 Malays, 3,135 Indians and 2,956 of other ethnic origins was studied. Out of these, 7,726, 4,158, and 2,721 donors were further selected for Kidd (Jka, Jkb), Duffy (Fya, Fyb) and MNSs (S, s) antigen typing respectively.

Blood group O has the highest prevalence and blood group AB has the lowest prevalence among all the ethnicities. RhD positive rate was 97% (32,485) and RhD negative rate was 3% (1,049). The most common phenotype in RhD positive donors was R1R1 (CDe/CDe) and is most common in all ethnic groups. rr (cde/cde) is the most common phenotype in RhD negative donors and is most prevalent in Indians (91.94%), followed by other ethnic origins, Malays and Chinese. While R2R2 (cDE/cDE) is more common in Chinese (5.16%) as compared with other ethnicities, the R2Rz (cDE/CDE) phenotype was found in 97 donors and is prevalent in 0.32% of Chinese, 0.24% of Malays, 0.03% of Indians and 0.34% of the other ethnic origins.

Fy(a + b−) and Jk(a + b+) are the commonest phenotypes in Duffy and Kidd System in all ethnicities. A rare Jk(a−b−) phenotype was found in 35 donors and there is none Fy(a−b−) phenotype found in the study population. In the MNSs system, S-s+ is the most prevalent phenotype in all ethnicities, while S+s- phenotype is more frequent in Indian donors (12%) and showed lower expression in Chinese, Malay and other ethnic origins.

Summary / Conclusions: Differences in RBC phenotype frequencies is observed in the different ethnic groups in the Singapore blood donor population. This knowledge allows us to maintain a sufficient stock of antigen-negative RBCs to allow provision of compatible RBCs for patients with multiple alloantibodies readily. The information

also allows us to work with donor recruiters to recruit blood donors from specific ethnic groups for less common red cell phenotypes.

P-085

Abstract has been withdrawn

Quality Management

P-086

IN HOUSE EVALUATION OF THE AUTOMATED IH-1000 SYSTEM FOR ABO/D GROUPING AND IRREGULAR ANTIBODY SCREENING IN BLOOD TRANSFUSION INSTITUTE OF NIS

Z Andjelkovic

Blood Donor Testing Department, Blood Transfusion Institute of Nis, Nis, Serbia

Background: Irregular antibody screening and ABO/RhD grouping of blood donors are part of mandatory tests performed routinely in our institute. Possible mistakes in the sample identification, interpretation of results as well as mistakes during performance of tests could be prevented by testing on automated immuno-hematology systems. IH-1000 (Bio-Rad Laboratories, USA), is a fully automated instrument for the ABO and Rh grouping, antibody screening and identification.
Aims: In house evaluation of the automated IH-1000 system for ABO/RhD grouping and irregular antibody screening of blood donors in Blood transfusion institute of Nis.
Methods: During the evaluation period a total of 1,160 EDTA-anticoagulated samples for ABO/RhD grouping (direct and reverse typing) and 244 samples (15 of 244 samples were with previously known antibody presence) for irregular antibody screening were tested on IH-1000. All samples were tested on semi-automated Mitis 2 System (Ortho, USA) using microplate method for the ABO/RhD grouping and tube test method for antibody screening and identification in parallel.
Results: For ABO/RhD grouping, 1,160 of 1,160 samples (100%) showed a complete concordance between the microplate results and IH-1000 results (A RhD positive: 454, B RhD positive: 115, O RhD positive: 459, AB RhD positive: 26, A RhD negative: 54, O RhD negative: 41 and B RhD negative: 11). In the two antibody screening methods, 228 samples were negative in both and 15 samples showed the same positive results. Antibody specificity of 15 positive samples was: 4 anti-D, 1 anti-C+D, 1 anti-Lua, 1 anti-E, 1 anti C, 1 anti e, 1 anti c, 1 anti s, 1 anti Fya and 3 anti-K. In one case (0.4%) false-positive result was observed in IH-1000 system due to non-specific reasons.
Summary/Conclusions: The IH-1000 system has a good correlation with our routine methods, microplate method for ABO/RhD grouping and tube method for antibody screening and identification .Use of IH-1000, fully automated system in blood donor testing will reduce chances of human errors and increase the safety of blood transfusion.

P-087

THE IMPACT OF ANALYTICAL VARIATION OF HEMOGLOBIN MEASUREMENT ON BLOOD DONORS' HEMOGLOBIN AND DEFERRAL RATE

J Castrén, M Arvas, A Valkeajärvi, P Korkalainen and M Syrjälä

Finnish Red Cross Blood Service, Helsinki, Finland

Background: Donors' hemoglobin (Hb) must be tested prior to blood donation. Low Hb is the leading reason for donor deferral. Many donor-related and external factors associated with low Hb are known, but no studies have been conducted concerning the effects of analytical variation on donor Hb measurements and deferrals.
Aims: The aim of this study was to investigate the effect of analytical variation of the cHb measurement method on blood donor Hb and deferral rates.
Methods: The effects of donors' age, the seasonal and daily distribution of donations, and batch-to-batch variation in HemoCue Hb 201 + cuvettes on donors' capillary Hb (cHb) measurements and deferrals were analyzed for over 1.7 million donor visits in 2010–2016 at a national blood establishment. Furthermore,

approximately 3.1 million cHb measurements from the years 2000–2009 were included in analyses to correlate measured cHb value and Hb deferral rate.
Results: A statistically significant correlation between the mean annual cHb measurement and Hb deferral rate was observed in both women and men. The season of the donation was the strongest explanatory factor for the monthly variation of predonation cHb (explaining 25% and 31% of the variation in women and men, respectively). Batch-to-batch variation in HemoCue cuvettes explained 6.8% of monthly variation in women and 7.4% in men. Monthly changes in donors' age distribution explained 2.5% of monthly variation in women and 2.4% in men.
Summary/Conclusions: Small and, in most clinical settings, negligible analytical variation in Hb measurement methods can have significant consequences when used for Hb screening of blood donors. This should be minimized by using methods in which analytical variation is under control and kept as low as possible.

P-088

USE OF A NOVEL BLOOD BANK MODE ON THE SYSMEX XN-20 HAEMATOLOGY ANALYSER TO COUNT RESIDUAL WHITE AND RED CELLS IN BLOOD COMPONENTS

R Blanco[1], L Willmott[1], H McKenna[1], S Garner[1], J Saker[2], J Linssen[2] and R Cardigan[1,3]

[1]*Component Development Laboratory, NHS Blood and Transplant, Cambridge, United Kingdom* [2]*Scientific Affairs, Sysmex, Kobe, Japan* [3]*Department of Haematology, University of Cambridge, Cambridge, United Kingdom*

Background: European guidelines require ongoing monitoring of residual white blood cells (rWBC) in leucodepleted (LD) blood components and residual red blood cells (rRBC). Many countries monitor rWBCs using flow cytometry and the BD LeucoCOUNT assay, since levels are too low to reliably be enumerated by standard haematology analysers. Currently there are no widely accepted methods to accurately and consistently measure the levels of rRBCs in blood components. For the XN-series of haematology analysers, Sysmex are developing a novel algorithm, designed to quantitate the levels of rWBCs and rRBCs in processed components, provisionally termed the Blood Bank mode (BB mode).
Aims: We have investigated whether the BB mode algorithm measured on a Sysmex XN-20 analyser is capable of accurately and reproducibly quantitating residual WBC and RBC.
Methods: Whole blood was used to spike WBC into leucodepleted platelet, plasma and red cell concentrates (RCC) at various dilutions ranging from 32–0.25 WBC/μl (n = 4 of each). Spiked components were tested in parallel using either the LeucoCOUNT assay or BB mode. We also measured the levels of rRBCs (approx. 30,000–250 RBC/μl), present in these same components. Units of plasma (n = 40) and platelets (n = 415) from routine production were also tested for residual cell contamination.
Results: The results of spiking WBCs into platelet, plasma and RCC showed a good correlation between levels of observed and expected rWBCs over the range of dilutions tested by either flow cytometry (r^2>0.998) or BB mode (r^2>0.981). Compared with expected values, there was generally an over estimation (mean +10%) of rWBC using the LeucoCOUNT assay whilst the BB mode tended to under estimate rWBC counts (mean −2%).
BB mode data from using a spike of 32 WBC/μl in platelet and plasma components showed very little carryover between samples and repeatability testing showed a good degree of conformance (all %CV values were <7.0%, with standard deviations <0.2) for both rWBC and rRBC analyses. As most samples from routine production contain very low levels of WBC in LD components, we also assayed by flow cytometry and BB mode, units from routine production where LD had failed (range=17.8–3,629 rWBC/μl, mean %CVs for leucoCOUNT and BB mode in 3 apheresis platelets were 2.8% and 3.6% and in 11 RCCs 10.5% and 2.3% respectively).
Data for dilution of rRBC in platelet and plasma components also showed a good correlation (r^2>0.994) between the estimated and actual values measured by the BB software. Residual red cell counts from manufactured components showed that 39/40 plasma components had low levels of rRBC (mean=18 ± 5.5 RBC/μL). However, as expected platelet components showed a larger degree of variation in rRBC contamination with low levels in apheresis platelets (mean=15 ± 30 RBC/μl, n = 243) compared to those produced from pooled buffy coats (mean=1,064 ± 1,149 RBC/μl, n = 172).
Summary/Conclusions: BB mode software has the capability to accurately and reproducibly measure the levels of residual white and red blood cells in processed blood components. In order to further evaluate this software, assessment in a routine working environment is now warranted to quantify the benefits that replacing flow cytometry may bring to blood services.

P-089

REDUCING PREOPERATIVE TYPE AND SCREEN TESTING FOR PRIMARY TOTAL KNEE ARTHROPLASTY: EVALUATING ADHERENCE TO NEW TYPE AND SCREEN ORDERING CRITERIA IN A SURGICAL PRE-ADMISSION UNIT

D Touchie[1,2] and S Gagne[3]

[1]Perioperative Blood Management Program [2]ONTraC Program [3]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, Ottawa, Canada

Background: Most patients who have a preoperative type and screen (T&S) test done prior to a primary total knee arthroplasty (TKA) at The Ottawa Hospital (TOH) do not require a blood transfusion associated with their surgery. T&S testing is expensive, costing TOH over $45,000 annually for TKA procedures alone. The 'Choosing Wisely Canada' campaign recommends eliminating T&S testing for surgical procedures not routinely requiring blood transfusion. Preoperative T&S testing was previously ordered for all TOH patients scheduled for primary TKA despite very low blood transfusion rates (1%). A T&S ordering strategy was implemented in the TOH Pre-Admission Units (PAU) to limit T&S testing to TKA patients at risk of requiring a blood transfusion and therefore reduce unnecessary testing. The strategy involves using a point of care hemoglobin testing device (POC Hgb.). A T&S test is ordered if any of the following five criteria are identified during the preoperative assessment; POC Hgb. level <120 g/l, history of coagulopathy or bleeding diathesis, known alloantibodies or increased risk for developing alloantibodies, angina, and patient weight <50 kg.

Aims: The main purpose of this study was to assess whether the T&S ordering criteria were used appropriately to order preoperative T&S testing and to determine its impact on T&S rates for TKA procedures.

Methods: The study design was a retrospective chart review of 250 patients who received a primary TKA during April-September 2017.

Results: The patient population was predominantly female (61%). The mean age for all patients was 69 years. However more than 40% were well over 70 years of age. The study sample represented a slightly obese population (m = 91 kg). Most patients were otherwise relatively healthy with a small percentage demonstrating symptomatic ischemic heart disease (5%) and bleeding risks (4%). The average POC Hgb. level was 126 g/l. Preoperative T&S tests were not ordered in total for 147 patients (59%). Whereas, 103 patients did have T&S tests ordered (41%). Fifty-eight T&S tests (56%) were deemed appropriate orders whereby 44% were considered unnecessary according to the criteria. T&S tests were not ordered for seven high risk cases (3%). None of these missed cases required blood transfusion. Otherwise only one patient requiring a T&S received a red cell transfusion. PAU staff used the POC Hgb. device and assessment criteria for only 118 cases (47%).

Summary/Conclusions: Overall preoperative T&S testing was reduced by 59%. Although a reduction in T&S testing was observed, the use of the POC Hgb. device and ordering criteria were often not used to support decision making. A lack of adherence for the ordering strategy resulted in a significant number of unnecessary T&S tests ordered, in addition to a small number of oversights. When applied appropriately, the criteria appears to be an effective assessment tool to guide T&S ordering for TKA procedures and ultimately reduce costs associated with un-necessary testing. An approximate cost savings of nearly $10,000 was attributed to reduced T&S testing in this study. Ongoing education and coaching is required to improve staff engagement and adherence to this new ordering strategy.

P-090

THE ONTARIO TRANSFUSION QUALITY IMPROVEMENT PLAN: GAINING MOMENTUM

D Evanovitch[1], Y Lin[2], A Collins[3] and T Thompson[4]

[1]Regional Manager, Ontario Regional Blood Coordinating Network-ORBCoN, Hamilton [2]Transfusion Medicine, Sunnybrook Health Science Centre [3]Clinical Project Coordinator TM Physician [4]Regional Manager, Ontario Regional Blood Coordinating Network-ORBCoN, Toronto, Canada

Background: The Ontario Transfusion Quality Improvement Plan (OTQIP) Committee was struck in 2015 to drive transfusion quality improvement initiatives forward at a provincial level. The Committee planning and work is supported by the Ontario Regional Blood Coordinating Network (ORBCoN); a program funded by the Ontario Ministry of Health and Long-Term Care (MOHLTC). ORBCoN and Canadian Blood Services (CBS) have facilitated many transfusion laboratory improvements surrounding optimized inventory levels, redistribution and reduced wastage. Therefore the committee turned its focus to transfusion ordering practices.

The Committee consists of a broad range of transfusion stakeholders from across the province: ORBCoN, the Ontario Nurse Transfusion Coordinators (ONTraC), CBS, hospital administrators, quality and risk representatives, transfusion safety officers, transfusion laboratory, nurse and medical experts and a transfusion recipient.

Aims: The OTQIP Committee's objectives are to facilitate transfusion quality improvement initiatives both at the hospital level and province wide. The Committee aims to connect with other quality and transfusion organizations to raise the profile and adoption of the OTQIP.

Methods: The Committee prioritized red blood cell (RBC) utilization as they are widely used. Additionally, ORBCoN's RBC audits and surveys have demonstrated a need for improving ordering practice. The Plan calls for screening of RBC orders by technologists according to transfusion guidelines, ensuring that the pretransfusion hemoglobin is less than 80 g/l and that orders are for one unit at a time. The QIP utilized the Health Quality Ontario (HQO) model that aligns with the current hospital model. The Committee and their working groups collaborated with Choosing Wisely Canada (CWC), Canadian Society for Transfusion Medicine (CSTM) and the Ontario Hospital Association (OHA).

A supporting toolkit was developed that contained:
- An Institution QIP Narrative Template
- An Institution QIP Template
- Clinical practice recommendations
- AN order set template for blood components
- A SOP for prospective screening by MLTs
- Additional supporting documents

An information document for physicians and nurses, an online education tool for technologist screening and an e-tracker tool with which hospitals can track their baseline data and on-going audit results were subsequently developed.

Results: An informal survey revealed that 74 of 158 Ontario hospitals (47%) were interested in implementing this improvement initiative. A subsequent survey revealed that 69% were planning on adopting the OTQIP, and 23% already had adopted portions of the Plan. The toolkit was downloaded over 3,700 times from the CWC website (including CSTM hits) and 648 times from ORBCoN's website since its launch. Initial data from the e-tracker tool has shown an improvement from 45% to 84.6% for transfusions ordered when the pretransfusion hemoglobin is less than 80 g/l and for single unit transfusions, from 16.5% to 47.4%. Only 12 hospitals are entering on the e-tracker tool so the next focus will be e-tool promotion and education.

Summary/Conclusions: Facilitating practice improvement through the development of standardized templates, instructions, education and other tools for transfusion quality improvement assists hospitals and practitioners in quality improvement initiatives. A provincial approach allows for both aggregate and hospital data comparison analyses.

P-091

QUALITY SYSTEMS: DELIVERING COST SAVINGS – A RETROSPECTIVE ANALYSIS IN A MEDIUM SIZED BLOOD CENTER

J Faber[1] and P Renaudier[2]

[1]CEO, LuxConsulTrans [2]Director, NBC/Red Cross Luxembourg, Luxembourg, Luxembourg

Background: Preparation of safe, effective blood components is a complex activity, requiring strict organized measures to ensure their quality. General principles for quality management (QM) in blood establishments (BE) have been set by the EU, Council of Europe, WHO and others. Quality management systems (QMS) are nowadays mandatory by law in many jurisdictions.

Aims: To comply with these rules and regulations, investment by BEs is necessary to implement an effective QMS (reflecting GMP and ISO). These expenses (initial investment and running costs) are mainly related to specific tools for QM and additional staff putting in place/maintaining a QMS. QM does not only cause expenses, it also generates substantial savings. In well established and maintained QMS, the net gain is substantially higher than the expense, the cost-benefit balance being almost certainly positive.

Methods: A retrospective analysis of costs and savings related to the QMS was undertaken in the National Blood Center/Luxembourg Red Cross. Expenses for each major activity in the BE were easily quantifiable through accounting systems. On the other hand, costs for QM itself are often not compartmented, as some of the quality activities are shared or connected to other activities. Similarly, savings are not always delineated, not directly attributed to QM. In these cases, well founded and rational estimates were used to come to an order of magnitude for the savings.

Results: The initial cost to start organized and structured QM was rather moderate with some 50,000 EUR: the most expensive positions were the acquisition of an

electronic documentation system (including applications for document control and staff training), software for managing equipment and instruments (including calibration), analytic scale and precision thermometer. The running costs were somewhat under 100,000 EUR/year and included: additional, dedicated staff (1 pharmacist, 2 lab technicians), reagents and consumables used for QC. On the other hand the savings were substantial and out weighted the costs by far: after full implementation of the QMS and certification of it according to ISO9001, substantial savings were achieved adding up to more than 20% of the total NBC budget of the reference year (when proper QM was started stepwise). The biggest savings were made in relation with outdating of blood components (mainly, packed red blood cells RBC: from 16% pre-QM to 8% with fully established QMS) and product non-conformances (of different products, of various origins: from 8% to 2.5%). The most efficient QM interventions were training and CAPA, as they came with a low cost and a significant added value.

Summary/Conclusions: Although the data presented here are not recent, the lessons and conclusions from the NBC in Luxembourg are still valid. Confronting costs and savings for QM, it is concluded that quality is paying – and so does QM, especially in BE as demonstrated in the present case, when more than 1/5 of the annual budget was verifiably saved through QM interventions.

P-092

TRANSPORT TEMPERATURE OF WHOLE BLOOD FROM COLLECTION SITES TO PROCESSING CENTER CASE STUDY: KAMPALA UGANDA DEMONSTRATE NEED FOR FURTHER IMPROVEMENT

E Musisi[1], D Kyeyune Byabazaire[2], S Amar El Dusouqui[3] and R Schwabe[3]
[1]Processing Department [2]Uganda Blood Transfusion Service, Kampala, Uganda
[3]Blood Transfusion Service, Blutspende SRK Schweiz, Bern, Switzerland

Background: Whole Blood (WB) from donor collection sessions need to be transported under appropriate settings in order to minimize transport related degradation of cellular viability and plasma quality, and prevent related adverse effects on recipients. Many guidelines agree that transport temperature of whole blood can be held above 17.9 °C after collection and before processing for 24 h. UK guidelines do not indicate maximum levels for transport before processing, while other guidelines define 24°C as a maximum level; WHO recommends 24°C but for a maximum duration of 6 h.

To date, periodical monitoring of temperature of whole blood transported from collection sites to the blood processing center has not been performed in Uganda Blood Transfusion Service (UBTS).

Aims: To perform an inspection of transport temperature of whole blood from two collection sites and provide data and insight for optimal quality assurance at UBTS and to provide guidelines for improvement of standard operational procedures (SOP) and proper handling at the operational level in order to maintain integrity of labile blood products.

Methods: Using an infrared thermometer superficial temperatures of 25 units of WB were taken at two separate collection sessions, before transport and at arrival. The bags were cooled prior to transport from the collection venues according to standard procedure used in both cases. Transportation was direct from collection site 1 to the processing center. In the other case the bags from collection site 2 were transferred to a close blood center and stored in a refrigerator overnight at temperatures between 2°C and 6°C. The following day the bags were put into cool boxes and transported to the processing center in Kampala.

Results: Transport from Site 1 directly to the processing center in Nakasero, Kampala showed following T° measures: at departure 25.4°C (mean) ± 0.7 (SD) and 20.1°C (mean) ± 0.8°C (SD) at arrival. Transport from Site 2 to the intermediate storage blood centre showed following T° measures: 19.4 °C (mean) ± 1.75°C (SD) at departure and 15.02 °C (mean) ± 3.3°C (SD) on arrival; and transport the following day to the processing center showed 4.1 °C (mean) ± 1.1°C (SD) at departure and 7°C (mean) ± 0.7 °C (SD) on arrival.

Summary/Conclusions: Results show that pre-processing temperature from Site 1 could be used for production of PRP, provided the minimum temperature does not drop below 18°C. More effort should be employed to cool transported blood from collection sites intended for PRP processing since maximal storage temperature of platelets is 24°C.

Pre-processing temperature drops to acceptable levels for whole blood or red blood cell concentrate processing but not for PRP processing when adequate overnight storage takes place, but more effort should be employed to cool transported blood from collection sites to maximum 10°C and minimum 2°C.

Strict control of temperature and monitoring through institutional quality management systems of UBTS is necessary in order to maintain the integrity of the product.

P-093

BLOOD GROUP BY AUTOMATION – A NEAR MISS EVENT

S Basu, D Basu and M Reddy
Transfusion Medicine, Tata Medical Center, Kolkata, India

Background: Automation in immunohematology has several advantages like decreasing human error in sample identification, preventing transcription errors, improving - objectivity, reproducibility and data retrieval; and reducing turnaround-time. However discrepant results must be cautiously reviewed and interpreted to ensure patient safety. We report here a near miss event during blood grouping of a patient using automation.

Aims: To report a near-miss event so as to emphasize the need to follow SOPs and manufacturer instructions.

Methods: The automated immunohematology platform Ortho Vision has been recently installed with us and is used for blood grouping and antibody screening of both donors and patients. For blood grouping, threshold values for the forward reaction (3 +) and reverse reaction (2 +) have been set, below which the machine gives an alarm, alerting the user that there is a discrepant result which requires review. In all such cases, the blood group is repeated by tube. Alarms are also given by the machine whenever there is an abnormality in the blood sample, reagents or cards – too many cells, too few cells, calibration index, meniscus problem. The FIB alarm is given when the machine finds fibrin entangled in the micro-column. In case of an alert; our protocol is to review the image, refer to the SOP and repeat the test manually.

Results: The forward ABO group of this patient performed on the Ortho Vision showed group B, with fibrin alarm (FIB) in the anti D column. Several times earlier, we had noted FIB alarm with antibody screening tests and when these were repeated in the Biovue, antibody screening was negative. Hence the operator presumed that this FIB alarm with anti D, was due to fibrin strands (false positive due to fibrin) and interpreted the test as Rh D negative. The manufacturer's instructions state that in case of FIB alarm, the test is to be repeated using saline washed red cells and advise using packed red cells from the button avoiding buffy coat and plasma layers. Our standard operating procedure (SOP) also mentions the same and in addition requires the test to be repeated by tube method. In this case the operator assumed that the positive band in the anti D column was due to fibrin, and so the group was interpreted as B negative. No weak D test was performed. Next morning, when the image was reviewed it was noted that there was an agglutination band along with some irregularity. The blood group was then repeated by tube technique after washing the red cells with saline. The blood group was B positive and not B negative.

Summary/Conclusions: Hence it is suggested that in case of machine alarms, the internal SOP must be followed and result image carefully reviewed. In addition it is also emphasized that manufacturer's instructions must be adhered to, to ensure error free results.

P-094

TYPING NON–CONFORMING SAMPLES DUE TO MISLABELING ERRORS FOR IMPROVED DETECTION OF WRONG BLOOD IN TUBE (WBIT)

A Wilson, G Desnoyers, B Whittemore and P Pelletier
Hematology, Mcgill University Health Centre, Montréal, Canada

Background: Between 2005 and 2010, blood bank sample acceptance criteria at three sites indicated that differing policies were impacting the rate of sample rejection. All 3 sites required patient's full name and unique number on sample and paper form with sample initialed and form signed by the person collecting the sample. One adult site, having no additional requirements, rejected 1.2% with WBIT rate of 1 in 1,000. The other adult site, accepting only hand-labelled samples to encourage more attentive bedside labeling, rejected more samples (2.8%), due to transcription errors in name or number, but had less WBIT (1 in 2,200). The pediatric site, requiring a witness to sign that patient's ID-band was checked and matched sample and form, had the lowest rejection rate (0.7%) and lowest WBIT rate (1 in >24,000 samples), thought to be due, in part, to the pediatric setting and parent witnesses.

Aims: When merging the 3 sites onto one policy, it was recognized that the extra requirements at the two more stringent sites provided more indicators for the laboratory to recognize when protocol was not followed, reducing risk of accepting WBIT samples. Mandatory witness attestation for blood bank samples was implemented across sites by fall 2011 with only matching, complete and initialed samples accepted. Aims of this analysis were to determine impact on (i) WBIT detection and (ii) WBIT rate in non-conforming samples.

Methods: WBIT rate was the primary quality indicator. As samples indicating non-compliance to protocol could be 40 times more likely to be WBIT (Dzik, Vox

Sanguinis, 2001), typing of non-conforming samples was implemented to detect all possible WBIT events and obtain a more accurate rate of WBIT. The blood bank computer system was configured so blood types on "rejected" samples could be entered without impacting patients' records, but remain accessible for comparison to historical and new patient records.

Results: After implementation, 10 WBIT were found in 2012: 5 found in accepted samples, a dramatic reduction (1 in 8,258) compared to 25 in 2010 (1 in 1,600); and another 5 found in rejected samples, providing a truer rate of 1 in 4,129 (all samples). From 2012 to 2017, 91 of the total 157 WBIT (58%) were found in 5,941 "high risk" rejected samples (patient ID/signature mismatches on tube versus form; missing or incomplete name or number; missing initials/signature on sample/witness attestation), averaging 1 in 65 "high risk" samples. Rejected samples carried >56 times higher risk of being WBIT.

Summary/Conclusions: Maximizing WBIT detection by typing high-risk samples has high yield. The results support strict enforcement of sample acceptance policies. Supervisors and phlebotomists take proven WBIT events more seriously than reports of rejected samples, fostering a culture of safety. The Blood Bank has the unique ability to serve as watch guard for these serious errors, alerting other labs about samples drawn at the same time and allowing training and preventive action to be appropriately implemented. Patient safety will require high surveillance to detect all possible WBIT, until electronic patient identification systems become standard practice.

P-095

FEEDBACK OF AN EXTERNAL PROFICIENCY TESTING SCHEME BY INTERLABORATORY COMPARISON FOR QUALITY CONTROL OF BLOOD PRODUCTS AT THE EFS

S Bégué[1], A Chartois[2], S Tremblay[3], B Olivier[4], A Errami[5], S Boivin[6], N Marpaux[7], B Belcour[8], S Acquart[9], M Colombat[10], S Requiem[11], F Salah[12] and F Donnadieu[13]

[1]Direction Médicale, Etablissement Français du Sang (EFS), La Plaine-Saint-Denis [2]Quality Control, Etablissement Français du Sang (EFS), Nantes [3]Quality Control, Etablissement Français du Sang (EFS), Bois Guillaume [4]Quality Control, Etablissement Français du Sang (EFS), Toulouse [5]Quality Control, Etablissement Français du Sang (EFS), Paris [6]Quality Control, Etablissement Français du Sang (EFS), Lille [7]Quality Control, Etablissement Français du Sang (EFS), Besançon [8]Quality Control, Etablissement Français du Sang (EFS), Nancy [9]Quality Control, Etablissement Français du Sang (EFS), St Etienne [10]Quality Control, Etablissement Français du Sang (EFS), Bordeaux [11]Quality Control, Etablissement Français du Sang (EFS), Rennes [12]Quality Control, Etablissement Français du Sang (EFS), Tours [13]Quality Control, Etablissement Français du Sang (EFS), Marseille, France

Background: The Etablissement Francais du Sang (EFS) is the unique blood transfusion operator in France and French over-seas departments. Each of the 13 regional establishments is in charge of collection, preparation, quality control, distribution and issuing of blood products. To each production facility is associated a quality control laboratory (n = 18) whose responsibility is to ensure conformity of blood products to national guidelines. Currently, there are no commercially available Proficiency Testing Scheme (PTS) for QC of blood components. In 2008, we initiated a PTS by interlaboratory comparison within the 18 EFS QC laboratories in order to guaranty standardization of product quality supervision and conformity status nationally.

Aims: The primary objective was to determine the production process, storage, shipping, organization, data collection and statistical analysis of specific PTS Samples with biological characteristics matching blood components specifications. Thereafter, these schemes would become a main driver and indicator for analytical standardization between the sites.

Methods: All QC laboratories contribute to the program. Following an annual agenda, specific QC sites are designated to prepare the samples used for the scheme. The samples are issued from blood components for which the desired parameter is set to an adjusted value and validated for its reproducibility and stability. The organizing laboratory then sends the samples to each participant and collect the data. Instructions are given to proceed for the analysis in a given timeline. Data analysis follows the ISO 13528:2015 standard. The inspected parameters are hemoglobin, hematocrit, hemolysis, residual leukocytes in RCCs and PCs, platelet count in PCs, total protein in plasma, Factor VIII and fibrinogen in plasma and residual protein content for washed blood components. The organizing laboratory is in charge of the final report, following a standardized template. For each parameter the "real value" is a consensus value from the participants results. Values with Z-scores > 3 and > bias are considered as non-conforming and the laboratory must implement actions.

Results: Since the implementation of the measure, the numbers of PTS for each parameter are:ILCV stands for Interlaboratory CV (%)- Hemoglobin: 14 PTS since 2010 with ILCV < 5%; bias < 2%- Hematocrit: 14 PTS since 2010 with ILCV < 5%; bias < 7%- Hemolysis: 8 PTS since 2012 with ILCV < 20%; bias < 20%- Residual leucocytes in RCC and PC: 14 PTS since 2009 with ILCV <20%; bias < 15%- Platelet count: 16 PTS since 2008 with ILCV < 10%; bias < 10%- Total protein: 14 PTS since 2008 with ILCV < 5%; bias < 9%- Residual protein in washed RCC and PC: 14 PTS since 2013 with ILCV < 15%; bias < 15%- Factor VIII: 8 PTS since 2013 with ILCV < 10%; bias < 20%- Fibrinogen: 9 PTS since 2010 with ILCV < 10%; bias < 20%

Summary/Conclusions: Proficiency testing by interlaboratory comparison has demonstrated its usefulness for standardization of analytical methods and ensures that QC laboratory results are accurate, reliable and comparable wherever they are produced at the EFS.

P-096

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P-098

VALIDATION OF FULLY AUTOMATED MICROPLATE PLATFORM FOR BLOOD DONORS IMMUNOHEMATOLOGY TESTS

MI Puppo, S Oknaian, V Abatemarco and S Kuperman

Centro Regional de Hemoterapia, Hospital Nacional De Pediatria "Prof Dr Juan P Garrahan", Caba, Argentina

Background: The quality system of our blood bank provides a guidance in implementing procedures that assures compliance with current good manufacturing practices and sets down that the incorporation of any new technology should be validated. We want to automate the blood donor's immunohematology laboratory to decrease the human error risks linked to each step of the tests performed and to guarantee a reliable traceability of all the elements having contributed to the test process. We planned a validation protocol to evaluate the NEO Galileo, a fully automated workstation for immunohaematology determinations.

Aims: The validation purpose is to verify the device correct performance and produce documented evidence that provides with a high level of assurance, that all parts related to the autoanalyzer use, work correctly and provide reliable results. Also it is necessary to ensure compliance to the accuracy and safety standards and know regarding Neo Galileo preventive maintenance and calibration.

Methods: During the autoanalyzer setting up, three technicians received training about instrument basic operation, maintenance and calibration. The validation was carried out to evaluate the concordance between the results in blood donor samples for ABO-D group, Rh-Kell phenotype, extended phenotype, irregular antibody screen and identification, performed with automated microplate technique and the gel card system in use. A total of 500 samples were tested for ABO/D group and antibody screen, 100 for Rh-K phenotype, 50 for extended phenotype and 14 frozen donor plasma samples with known irregular antibody were tested for antibody identification. All the tests were processed, according to this protocol, in parallel with Neo Galileo microplates and with our routine method, the gel card system.

Results: The user staff received training to carry out the work routine with the instrument. The validation showed the Neo Galileo good performance in the samples processing in terms of quality of results, processing time, traceability, safety and reduction of human error. We found 100% concordance between the results for ABO/D group, antibodies screen, Rh-K and extended phenotypes in all samples with both methods. Eight of 14 (57%) samples with irregular antibodies, processed for antibody identification, were concordant. Two antibodies with clinical significance were detected by microplate technique in three samples. The gel technique identify only one antibody in the same samples. The results with microplate technique in two samples were undetermined, but with the gel technique indentify anti M in one and anti Lea in other. In one sample with anti Lea y anti Lub detected with enzymes, the result with microplates techniques was no conclusive and with gel was negative.

Summary/Conclusions: The technical users were trained in the use, preventive maintenance and equipment calibration. This validation process allowed us to verify that

Neo Galileo is a device designed to automate the error-free processing of blood samples. There was 100% concordance in the ABO-D group, Rh-K phenotype and irregular antibody detection tests. Regarding the identification of irregular antibodies, it was observed that NEO provides greater potency and sensitivity in the reactions and that the discrepant results were associated with antibodies with no clinical significance.

P-099

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P-100

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P-101

NON–INVASIVE ASSESSMENT OF RED CELL CONCENTRATES IN BLOOD BAGS USING THE PHOTOACOUSTIC TECHNIQUE: CAPTURING OXYGEN SATURATION AND INFERRING CHANGES IN THE RBC MORPHOLOGY DISTRIBUTION

E Hysi[1,2], R Pinto[1,2], K Bagga[1,2], J Sebastian[1,2], A Douplik[1,2], J Acker[3,4] and M Kolios[1,2]

[1]Physics, Ryerson University [2]Institute for Biomedical Engineering, Science and Technology, Toronto [3]Centre for Innovation, Canadian Blood Services [4]Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

Background: Annually, over 110 million red cell concentrate (RCC) units are used to meet transfusion demands. RCC units are produced through separation of (including leukoreduction) RBCs from donated whole blood and suspension in preservative fluid. The bags are stored in refrigerated environments (1–6°C), to be used up until six weeks post-donation. Biochemical and biomechanical changes, commonly referred to as "RBC storage lesions", have been known to occur during the storage of RCC units. These changes lower the efficacy of RBCs' primary function of oxygen transport and delivery post-transfusion. Furthermore, the deleterious effects increase proportionally with storage duration and have been correlated with an increase in post-transfusion morbidities.

RBC storage lesions cause: (1) a deregulation of the affinity of hemoglobin for oxygen, resulting in an increase in oxygen saturation (SO_2) and (2) more RBCs to undergo irreversible degradation, resulting in cells that are termed "spheroechinocytes" to highlight the characteristic spherical and spicule-laden morphology. Storage lesion progression as a function of storage have been well documented, however, all techniques used to study the adverse events must irreversibly destroy the sterility of RCC units to gain sample access, rendering them unfit for transfusions.

Aims: We present a novel, non-invasive technique of acquiring the SO_2 of RCC units using photoacoustic (PA) technology. The PA effect is an optical phenomenon well suited for SO_2 acquisition, as it achieves a deeper penetration depth than most other optical techniques. Furthermore, current PA technology incorporates 2-wavelength oximetry to produce SO_2 maps with their imaging platforms.

Methods: Using the Vevo LAZR® PA system, we developed a setup to acquire the SO_2 of RCC units non-invasively, and compared our measurements with the conventional, invasive technique of blood gas analysis (BGA). Seven LR, SAGM (Top/Bottom) RCC units were measured by both techniques throughout their storage lifetime. Alongside PA and BGA measurements, we measured the relative spheroechinocyte population percentage (RSPP) using an image flow cytometry (IFC) technique.

Results: The correlations between the SO_2 measured by PA and BGA were no less than $r^2 = 0.95$. The rise in SO_2 was also compared against the rise in spheroechinocyte population using the IFC technique. The temporal changes between SO_2 and RSPP for all units yielded a correlation of $0.79 \leq r^2 \leq 0.97$ with the exception of an outlier, whose uncharacteristic high initial SO_2 (84%) resulted in a plateau that correlated poorly with the RSPP.

Summary/Conclusions: Experimental evidence suggests that a consistent small discrepancy in SO_2 measurement between the PA and BGA methods is attributed to a brief exposure to external environments during sample extraction for the BGA measurement. The results show strong evidence for the accuracy and precision of our PA approach in acquiring SO_2 non-invasively. SO_2-RSPP correlations suggest that

temporal changes in SO_2 could be used to infer the approximate changes in morphology. The PA technique presented in this study could potentially provide clinicians with storage lesion assessment prior to using the RCC units for transfusions.

P-102

A COMPREHENSIVE ASSESSMENT FRAMEWORK FOR INSPECTING HOSPITALS' BLOOD MANAGEMENT

J Thilakavathi

Blood Services Group, Health Sciences Authority, Singapore, Singapore

Background: As the national supplier of blood and blood products to all hospitals in Singapore, the Blood Services Group (BSG) of the Health Sciences Authority of Singapore had to ensure that a good quality system backed by established international standards were adopted by these facilities.

There was a lack of a formal assessment structure and documentation of corrective/preventive actions taken. Hence, a comprehensive assessment framework was developed to inspect these facilities.

Aims: The aims were as follows:

- to ensure that a good quality system was in place at hospitals.
- to educate hospital staff on the requirements and standards of blood banking and transfusion services.
- to ensure the necessary corrective and preventive actions were taken.
- to provide hospitals with an official audit report of the investigations.
- to apprise the hospital transfusion committee of the findings and actions taken.
- to provide a trend analysis of the hospitals' performance.

Methods: An audit checklist based on international standards was adopted. A set of audit documents for guiding the auditors, and for conducting and reporting the audits were developed. An audit report and corrective and preventive actions templates were also crafted. A team of senior BSG staff were trained on conducting hospital assessments.

Biennially, a schedule was developed for inspection of the various hospitals. The team of BSG auditors educated the hospital staff on the standards requirements concurrently while performing the audits. A summary of the audit findings was shared with the facility at the end of the inspection.

An audit report was sent to each hospital for corrective/preventive actions. The hospitals were given a month to respond. Thereafter, the actions taken were verified and endorsed by the hospital supervisor, lead auditor, quality manager and the group director of BSG. Where further actions were required, the lead auditor would follow through with the hospital. If the corrective actions were satisfactory, the report would be endorsed, and a copy sent to the hospital.

Results: The audit report provided the hospital staff and management an insight into the lapses and the necessary corrective/preventive actions required to establish a good quality system.

The structured reporting system also prevented any disputes between both parties as the audit team provided an audit summary at the end of the inspection and ensured the hospital staff accepted the nonconformances identified.

The framework assisted BSG with an analysis of the various nonconformances and observations of the fourteen hospitals inspected and allowed both parties to work in synergy to establish a good quality system.

A trend analysis based on this framework showed that 87% of hospitals had a reduction in the number of nonconformance's recorded over 3 inspections, suggesting that the assessment framework and the corrective measures put into place had been effective.

Summary/Conclusions: BSG's comprehensive assessment framework provided a structured inspection of hospitals. It provided valuable information to improve blood banking and transfusion services. With a robust assessment framework in place, a good quality system was established assuring both BSG and the hospitals that only blood and blood products of quality were extended to our patients.

P-103

STREAMLINED PROCESS FOR INVENTORY MANAGEMENT

C Neo[1], C Phang[2], V Voon[2], M Soh[2], M S/O Karnagaran[2], S Binte Masnor[2] and M Chan[2]

[1]Blood Services Group, Patient Services [2]Health Sciences Authority, Singapore, Singapore

Background: Laboratory supplies i.e. test kits and reagents, had been managed manually by laboratory staff. This involved the staff verbally informing the manager

whenever supplies were running low or nearing expiry. Ordering and delivery of new supplies were managed solely through emails by the manager. Hence, communication was limited to the people involved, leading to information not being disseminated effectively. New supplies were required to be labelled and quarantined before quality control (QC) was done. These were tracked using 4 documents with multiple duplicated data. The documents were sometimes difficult to locate as they were sent for review by different staff. Coupled with the delay in release of supplies from quarantine after QC, frequent incomplete documentation resulted in occasional repeats of QC and time wastage. An electronic database was thus developed and utilised for supplies inventory management.

Aims: Manage the laboratory supplies more efficiently and effectively by reducing time and manpower required through digitisation.

Methods: Root-cause analysis and value stream map (VSM) were used to identify the hotspots and areas for improvement in the current process. The time taken for paper documentation were measured based on current practice and compared to the new digitised process. One-way ANOVA test was used to determine if the overall time saved was statistically significant.

Results: The overall time spent on documentation for the management of lab supplies inventory had a significant reduction of 34% per reagent (P = 0.0214).

Summary/Conclusions: The digital database was incorporated into the laboratory's Standard Operating Procedures (SOP) as of 1st January 2018. Different types of documents can be generated with a one-time entry of information for various needs, e.g. list of expiring reagents, expected delivery dates and QC forms. With less resources required for inventory management, more can be focused on routine samples and new test validations. The information in the database can be accessed by all staff. This empowers a more transparent system and also facilitates an efficient and effective dissemination of information within the laboratory staff. Staff would also have more ownership of the inventory and also inculcates a stronger sense of responsibility.

The introduction of this new system was challenging as the entire database had to build up from scratch. Staffs were trained on the use of the new system before the actual implementation of the SOP. The new inventory management system is flexible and has the potential to be customized for other laboratories in the future.

P-104

REGULATION OF BLOOD TRANSFUSION SERVICES IN THE STATE OF AZAD JAMMU & KASHMIR, PAKISTAN

N Ahmed[1], U Waheed[2], W Hussain[1] and H Zaheer[2]

[1]Department of Health, AJK Blood Transfusion Authority, AJK, Muzaffarabad
[2]Islamabad Blood Transfusion Authority, Ministry of National Health Services, Islamabad, Pakistan

Background: The state of Azad Jammu and Kashmir (AJK) having a population of 4.25 million, lies in the North East of Pakistan. The state is administratively divided into three divisions and ten districts. The healthcare coverage in the State remains inadequate. The blood transfusion services are an integral component of the health policy of AJK. The services are provided by public sector hospitals and an ever increasing number of NGO sector blood banks, many of them catering to the needs of the thalassaemia patients. One of the key issues in the blood transfusion services of AJK is weak regulation and governance of the system. The Government of AJK passed an Act in 2003 to regulate the blood system but only recently has the implementation of this Act started in earnest.

Aims: To implement the AJK Transfusion of Safe Blood Act XVI of 2003.

Methods: The AJK Blood Transfusion Authority (BTA) made an announcement in the newspapers for registration of blood banks. However, a very poor response was received for registration. In October 2014, the AJK Authority approached the Islamabad Blood Transfusion Authority for assistance and support in the regulation of blood transfusion services in the State. The IBTA coordinated with AJK BTA and shared its developed and tested technical tools and coordinated in planning and conduction of blood banks inspections in three phases. The Phase I included districts Mirpur, Bhimber, Kotli, and Sudhanoti. The inspections were conducted in November 2014. A detailed report was prepared and shared with the DOH. In November 2017, the AJK BTA conducted inspections in the remaining six districts in two phases.

- Phase II: Districts Muzaffarabad, Jhelum Valley and Neelum Valley (November 2017)
- Phase III: Districts Bagh, Poonch and Haveli (December 2017)

The blood banks were identified through an informal, unplanned mapping conducted with the assistance of local contacts. In addition, snowball sampling exercise was also applied for this purpose.

Results: During the inspection visits, 63 blood banks were inspected. The number of blood banks found was much higher than the anticipated figure highlighting the non-existence of any regulatory control. On the whole, the standard of service delivery was found to be extremely poor and unsafe. Except for five blood banks, none of the blood banks were manned by qualified pathologists/blood transfusion officers. The private sector blood banks are mostly run by unqualified technicians who are not even remotely familiar with the basic concepts of blood safety. Out of the 63 blood banks visited, only six blood banks fulfilled the minimum criteria and were granted licenses for one year. Five centres from the mapped blood banks were not operational and will seek BTA assistance before starting a blood bank. One blood bank was closed down on BTA recommendations. The remaining 50 blood banks were placed on probation for re-inspections and informed about their deficiencies and remedial actions. They will be re-inspected soon.

Summary/Conclusions: An inspection report has been prepared and submitted to the Department of Health including recommendations which if adopted in earnest will significantly improve the blood safety standards and generate public confidence in the health care system in AJK.

P-105

Abstract has been withdrawn

Blood donation – Blood donor recruitment

P-106

TREATMENT WITH MEDICAL DEVICES CONTAINING MATERIALS DERIVED FROM ANIMAL SOURCES: SHOULD WE REJECT THE DONORS?

N Diaz Padilla[1], G Nuboer[1], M El Bardiji[2], A Hopstaken[3] and A Bokhorst[4]

[1]Donor and Medical Affairs, Sanquin, Utrecht [2]Donor and Medical Affairs, Sanquin, Leiden [3]Donor and Medical Affairs, Sanquin, Eindhoven [4]TRIP Nationaal Bureau Voor Hemo- En Biovigilantie, Leiden, Netherlands

Background: In The Netherlands there is an increase in the number of blood donors who are treated with a medical device containing materials derived from animal sources (biomaterial). According to current internal guidelines these donors are permanently deferred.

Aims: The aim of this study was to assess the potential risk of these biomaterials in our blood bank (Sanquin) practices based on literature.

Methods: A literature review was conducted to generate an overview of how these biomaterials are regulated internationally and how other organizations regulated donors with such implanted biomaterials. Next, a survey was conducted among the blood donors who were rejected for biomaterials between 2009–2013. A PubMed search was performed on keywords linked with medical device containing materials derived from animal sources. An overview of the European and Dutch legal frameworks was made, including data on the current policy of other European and not European blood banking organizations.

Results: We retrieved 482 articles of which 27 were relevant for the question. None of these articles reported transmission of viruses and/or prions. According to the European legislation, the safety of biomaterials has to be proven conform a Class III regime and the prion risk is strictly monitored according to European Guideline 722/2012. European countries have different policies regarding donors and biomaterials, ranging from full acceptance to life-long deferral. Some countries only accept blood donors who have been treated with a specific brand of biomaterials.

Summary/Conclusions: Based on safety regulations and the absence of any reported transmission, donors who are treated with biomaterials in Europe can be accepted as blood donor and thus increase the pool of potential donors. The policies regarding biomaterials differ substantially among blood banks in the world.

P-107

ZINC PROTOPORPHYRIN AS AN EARLY INDICATOR OF DEPLETING IRON STORES IN BLOOD DONORS

S Zalpuri[1], J van Rosmalen[2], F Prinsze[1], K van den Hurk[1], W de Kort[1] and P van Noord[1]

[1]Donor Studies, Sanquin, Amsterdam [2]Biostatistics, ErasmusMC, Rotterdam, Netherlands

Background: Repeated blood donations lead to a lowering of haemoglobin (Hb) levels over time, but the trajectories of Hb values are subject to selection effects, for example due to donors becoming demotivated after a rejection. It becomes important to monitor the precise course by which repeated blood donation brings the probability of having a Hb level below the cut-off for donation. To this end, data on iron store indicators, such as zinc protoporphyrin, ZPP, could prove essential.
Aims: The primary aim of the study was to determine whether predictions of future Hb levels using current Hb levels can be improved by taking ZPP levels into account; and whether ZPP can be used effectively for early detection of donors who are prone to rejection due to low Hb values.
Methods: We used data from ZPP and Iron in the Netherlands Cohort study (Oct 2009- Oct 2015) consisting of approximately 9000 whole blood donors (both, new and repeat donors). With identified current ZPP levels as the primary predictor and used previous Hb levels, age, previous ZPP levels, day and time of donations, previous donation history, BMI, blood volume and blood counts as secondary predictors. Since the donors had repeated measurements, we used linear mixed models with to investigate the association between future Hb levels and ZPP (including other predictors). Since the range of ZPP shows a large variation in the population, the variable ZPP was log-transformed to reflect any marginal changes in this predictor variable.
Results: There were a total of 4,841 female donors with a mean age of 37.9 years, mean ZPP of 66.49 μmol/mol, a mean Hb of 8.7 and a mean of 2.3 donations over the study period. There were 2,817 male donors in the study with a mean age of 41.9 years, mean ZPP of 58.27 μmol/mol, a mean Hb of 9.01 and a mean of 2.9 donations. ZPP did show a statistically significant association ($P < 0.001$) with subsequent Hb levels in females, but the size of the association was quite small (regression coefficient −0.17, 95% confidence interval −0.22 to −0.11). The same was true for males and both the significance (P −0.008) and the size (−0.09) of the association were even smaller. Blood volume and age for women were significant secondary predictor variables; blood volume, age and donation interval for men. Stratifying women in to pre-and post-menopausal groups- premenopausal women showed a highly significant association with ZPP ($P < 0.001$) compared to postmenopausal women (P −0.008) but in both the cases, the size of the effect estimates was rather small again (−0.20 and −0.11 respectively).
Summary/Conclusions: Although ZPP over the donation history does seem to predict the subsequent Hb levels in both men and women donors, the size of this prediction estimate is very small. ZPP may not be a an effective iron deficiency marker in daily blood bank setting to predict subsequent Hb levels of blood donors.

P-108

EFFECTS OF BLOOD DONATION ON BLOOD DONOR CARDIORESPIRATORY FITNESS LEVEL

J Mail[1], R Mohamad[2] and A Munir[3]

[1]Transfusion Medicine, Hospital Queen Elizabeth, Kota Kinabalu, Sabah [2]Regenerative Medicine, Advanced Medicine and Dental Institute, USM [3]Lifestyle Cluster, Advance Medicine and Dental Institute, USM, Penang, Malaysia

Background: Blood donation is vital to meet patients' needs for blood and blood products. However, reduction of haemoglobin, haematocrit and blood volume following blood donation might affect the cardiorespiratory fitness level.
Aims: To determine the effect of blood donation on the level of cardiorespiratory fitness as measured by predicted maximum oxygen uptake (VO_2 max).
Methods: A total of 42 male blood donors were involved in this cross sectional study with 14 participants each for poor, average and excellent fitness groups. The 20 m Multistage Shuttle Run fitness test protocol was used to measure cardiorespiratory fitness level. The test was performed 24 h before and after a 450 ml whole blood donation. Simultaneously, haemoglobin and haematocrit were assessed 24 h before, immediately after and 24 h after the donation.
Results: The median baseline pre-donation predicted VO_2 max were 33.30 (30.73, 35.50), 38.85 (36.80, 42.65) and 50.80 (50.20, 52.60) ml/kg/min for poor, average and excellent fitness groups, respectively. The cardiorespiratory fitness level were slightly reduced at 24 h after blood donation by 0.61%, 1.29% and 3.43% in the for

poor, average and excellent fitness groups, respectively. However, the reduction was only statistically significant in the excellent fitness group (P = 0.017). The haemoglobin and haematocrit significantly reduced for all groups at 24 h after donation. The haemoglobin was reduced by 7.63% (P < 0.001), 7.82% (P < 0.001) and 5.46% (P < 0.001) for poor, average and excellent fitness groups, respectively. The haematocrit was reduced by 8.40% (P < 0.001), 9.08% (P < 0.001) and 7.21% (P = 0.002) for for poor, average and excellent fitness groups, respectively. The Spearman correlation analysis revealed no significant relationship between haemoglobin changes and predicted VO_2 max changes in all groups, poor fitness level group ($r_s = 0.001$), average fitness level ($r_s = 0.639$) and excellent fitness level group ($r_s = 0.532$).
Summary/Conclusions: The cardiorespiratory fitness level was slightly reduced at 24 h following a 450 ml whole blood donation, which was concomitant with significant haemoglobin and haematocrit reduction. However, there was no significant relationship between the changes in haemoglobin and cardiorespiratory fitness after blood donation.

P-109

PREDICTING BLOOD DONATION INTENTION: THE IMPORTANCE OF FEAR

P Gilchrist[1], B Masser[2], C Fedoruk[3], K Horsley[3] and B Ditto[3]

[1]Public Health & Primary Care, University of Cambridge, Cambridge, United Kingdom [2]Psychology, University of Queensland, Brisbane, Australia [3]Psychology, McGill University, Montreal, Canada

Background: Blood donor recruitment remains an important worldwide challenge due to changes in population demographics and shifts in the demand for blood. Various cognitive models help predict donation intention, though the importance of affective deterrents have become increasingly clear.
Aims: This study aimed to identify the specific fears that affect blood donation intention, explore their relative importance, and to determine if self-efficacy and attitude mediate this relation.
Methods: 347 non-donors (n = 269) and donors (n = 78) living in Québec responded to questionnaires assessing medical fears, psychosocial factors related to donation intention including Theory of Planned Behaviour (TPB) constructs, anticipated regret, and facilitating factors. To examine the relative importance of these factors in the context of blood donation, the same questions were also asked about other medical activities that also involve salient needle and blood stimuli, including flu vaccinations and dental examinations.
Results: There was a significant effect of medical fears on self-efficacy (β=−0.071, t (221)= −2.46, P = 0.0002) and attitudes (β=−0.030, t(219)= −2.86, P = 0.004), as well as decrease in donation intention (β=-0.029, t(220)= −2.02, P = 0.044). The proposed mediators, self-efficacy and attitudes, were both positively associated with intention, β=0.26, t(218)=5.35, P < 0.0001, and β=0.40, t(218)=5.40, P < 0.0001, respectively. Because these paths were significant, bootstrapping analyses were conducted, confirming significant indirect effects of MFS-SF mediated by both self-efficacy (β= −0.0186 (CI= −0.0328 to 0.0082) and attitudes (β= −0.0120 (CI= −0.0253 to 0.0037). Those with higher fears have lower intentions to donate as a result of reduced self-efficacy and attitudes to donate. Finally, the direct-effects of medical fears on intention became non-significant when controlling for self-efficacy and attitudes, suggesting full mediation, β=0.013, t(220)=1.09, P = 0.27. 45.9% of the variance in donation intention is accounted by both the proposed mediators. Other predictors of donation intention included anticipated regret (standardized β=0.51, P < 0.0001), past experience (standardized β=0.25, P = 0.006), and 'facilitating factors' (standardized β=0.25, P = 0.005). Underlining the importance of medical fears in the blood donation context, medical fears were not associated with attitudes and intentions for dental examinations or flu vaccinations.
Summary/Conclusions: Medical fears, especially blood-related fears, play a key role in predicting donation attitudes and intentions. Mediational pathways shed light on novel ways to intervene especially through addressing donor self-efficacy.

P-110

ASSESSMENT OF WHOLE BLOOD DONORS' HAEMOGLOBIN ACCORDING TO THE INTERVAL BETWEEN DONATIONS – 10 YEARS' EXPERIENCE OF A REGIONAL BLOOD ESTABLISHMENT

M Muon, C Caeiro, J Gomes and I Lobo

Centro de Sangue e da Transplantação de Coimbra, Coimbra, Portugal

Background: In Portugal, the low haemoglobin is the most common cause for deferral among all the whole blood donors, <12.5 g/dl in women and <13.5 g/dl in men. Frequent donors often have iron deficiency anemia and one of the way to prevent it is prolonging the interval between donations. The determination of the optimal interval between donations in our blood donors is essential to prevent the donors' low haemoglobin. Our national guidelines recommend the interval between donations of 3 months for men and 4 months for woman. However, 2 months interval between donations is permitted.

Aims: To determinate the optimal interval between donations in our whole blood donors in order to recommend the whole blood donation interval policy to the reviewing committee.

Methods: The Regional Blood Establishment maintains in a database all the records that keep track to all donors including the results of the donors' haemoglobin determinations on each presentation.

Haemoglobin is measured using point-of-care instruments that lyse the red cells, convert the haemoglobin to azidemethaemoglobin and quantify the amount present using spectrophotometry.

Data from 2007 through 2016 concerning 10 years of whole blood donors' haemoglobin determinations were analysed according to gender and interval between donations conducted in R Software (R Development Core Team. 2013).

Results: The Regional Blood Establishment database shows 948,481 donors presentations along ten years of activity and low haemoglobin determinations were present in 36,250 (3.82%) events. 739,576 donations from 160,844 donors were analysed.

Female (n = 341,465) haemoglobin and percentage of exclusion due to low hemoglobin were analysed according interval between donations: <3 Months n = 2,809 mean Hb=13.44 g/dl SD=±0.78 Exclusion=40.4%; 3–4 months n = 10,248 mean Hb=13.44 g/dl SD=±0.92 Exclusion=13.0%; 4–5 months n = 31,003 mean Hb= 13.74 g/dl SD=±0.89 Exclusion=9.9%; 5–6 months n = 70,632 mean Hb=13.76 g/dl SD=±0.90 Exclusion=8.9%; >6 months n = 149,974 mean Hb=13.85 g/dl SD=±0.92 Exclusion=7.4%.

Male (n = 361,919) haemoglobin determinations and percentage of exclusion due to low hemoglobin were analysed according interval between donations: <3 months n = 8,089 mean Hb=15.34 g/dl SD=±1.09 Exclusion=4.4%; 3–4 months n = 27,651 mean Hb=15.43 g/dl SD=±1.08 Exclusion=1.8%; 4–5 Months n = 34,150 mean Hb=15.39 g/dl SD=±1.07 Exclusion=1.6%; 5–6 months n = 67,458 mean Hb= 15.36 g/dl SD=±1.07 Exclusion=1.5%; >6 Months n = 149,561 mean Hb=15.47 g/dl SD=±1.09 Exclusion=1.3%.

Summary/Conclusions: The findings show that in our Blood Establishment there is a higher percentage of exclusions due to low haemoglobin in female donors than in male donors with the same interval between donations.

A higher percentage of exclusions due to low haemoglobin is found in donors with the interval between donations less than 3 months. In the female donors it is much more relevant reaching 40.4%

The recommendation is the need of a major focus on preventing female invitations for donations with interval between donations less than 3 months to avoid low hemoglobin exclusion.

P-111

BLOOD DONOR POPULATION: THE IMPACT OF INCREASING THE UPPER AGE LIMIT IN A PORTUGUESE BLOOD BANK

IS Machado, B Delgado, F Bischoff, S Teixeira, M Ramalho, C Monteiro, C Neves, C Vaz and C Koch

Transfusion Medicine and Blood Bank, Centro Hospitalar São João, Porto, Portugal

Background: The eligibility criteria for blood donors is dynamic over time. The upper age limit differs among countries, mainly related to maintain a balance between the evidence of safety of donation in the elderly and the contribution to the blood supply. Being so, according to the legislation, our center removed the upper age limit for donation, and the changes obtained from that moment on are to be studied.

Aims: To evaluate the blood donation by repeat older donors and its impact in the blood supply using the experience acquired in our center during 5 years' time.

Methods: A retrospective study was performed including all repeat blood donations between January 1st 2013 and December 31st 2017 in our center. Patients were divided in groups according to age (18–59 years, >59 years). Were considered adverse reactions: vasovagal syncope, convulsions, lipothymia and nausea or vomits. Data regarding venipuncture difficulty and prolonged donation time were also accounted for. All P-values are 2-sided and statistical significance was set for P < 0.05.

Results: In a population demographically comparable to the literature, were included 22,879 donors, 805 of them being 60 years or older (3.5%), with a mean age of 41 ± 12 years (in subgroups 18–59 years and 60–75 years the mean age was 40 ± 11 years and 63 ± 2 years, respectively). In a total of 91,161 donations, 5,419 donations came from donors older than 60 years, corresponding to 5.9% of all donations in the studied period. No association between age groups and venipuncture difficulty or prolonged donation time was found (P = 0.929 and P = 0.603, respectively). Regarding adverse reactions, there was a statistically significant association (P = 0.011) favoring safety in the group over 59 years old. Out of the 119 adverse reactions reported, only one occurred in this group.

Summary/Conclusions: According to our center experience, blood donation by older repeat blood donors had a positive impact in the contribution to the blood supply and may also be safely continued. Nonetheless, more data is necessary to sustain the results and optimize the decision in the extreme upper age limits.

P-112

REAL TIME MEDICAL SCREENING OF DONOR ELIGIBILITY BY BLOOD CENTER PHYSICIAN PREVENTS DONOR LOSS AND RESULTS IN HIGHER DONATION NUMBERS COMPARED TO STANDARD MEDICAL SCREENING

T Petraszko[1,2], B Eurich[3], F Flahr[3], E Alport[3], M Bigham[2], D Young[4] and S Matsumoto[4]

[1]*University of British Columbia* [2]*Canadian Blood Services, Vancouver* [3]*Canadian Blood Services, Regina* [4]*Canadian Blood Services, Calgary, Canada*

Background: The medical enquiry (ME) process enables blood center physicians to assess eligibility for donors with medical conditions not covered in the donor screening manual. Donors are temporarily deferred during this process. Previous work demonstrates an immediate loss of 14.5% of acceptable donors who are subjected to this deferral. A further 52% of accepted donors fail to return donate. Enquiries that do not require information from the donor physician may be completed immediately by telephone but historical evidence suggests that this only occurs in 5%. Obtaining real time donor acceptance by a CBS physician by telephone while the donor remains in clinic would avoid the temporary deferral of acceptable donors and allow for immediate blood donation.

Aims: A pilot study was undertaken to determine feasibility of real time verbal ME (VME) process in a single province in Canada. The first objective was to document an exclusive use of the VME process in all whole blood donor clinics for a 12 week period. The secondary objective was to document the absolute number of acceptable donors retained by the VME process compared to historical data and to model the number of donors and donations that could be saved by national implementation of this process.

Methods: Using existing work instructions, clinic staff was directed to exclusively use the verbal process for all MEs during the study period. Clinic nurses used a centralized telephone number to contact the physician who responded within 10 min while the donor remained in clinic. Information was provided to the physician who determined whether the donor was acceptable, deferred or if more information was required from the donor's physician. Documentation for all MEs, including deferrals, was sent per standard practice to the Medical Office for blood center physician signature and data collection. The alternate ME process was followed if physician calls were not returned within 10 min.

Results: A total of 36,953 donors attended whole blood clinics in Alberta during the study period. Medical enquiries were required for 167 (0.45%) lower than the national rate of 1.2%. Seventy-one were completed verbally (42.5%), 11 required input from donor physicians and were temporarily deferred. Protocol violations occurred in 96 of which 33 did not require donor physician input and could have been done verbally. Input from donor physicians was required in 44% overall, lower than historical rate of 70%. Acceptance rate for all donors was over 85%. Exclusive use of the VME process would have resulted in 21 additional immediate donations and possibly 40 additional donations annually.

Summary/Conclusions: This pilot study demonstrates feasibility of adopting a VME process in a single province. Increasing the VME rate to 100% nationally could result in the immediate retention of up to 903 annual whole blood donations. The overall rate of medical enquiries in the study was much lower than suggested by historical data, reducing the potential benefit of the intervention.

P-113

BLOOD DONATION DETERMINANTS AMONG NON-DONORS IN BRAZIL: STRUCTURAL APPROACH

ML Zucoloto[1], T Goncalez[2], W McFarland[3], B Custer[4] and E Martinez[5]

[1]Social Medicine, University of São Paulo, Ribeirão Preto, Brazil [2]Blood Systems Research Institute, San Francisco [3]University of California San Francisco [4]Blood Systems Research Institute, San Francisco, California, United States of America [5]University of São Paulo, Ribeirão Preto, Brazil

Background: Blood donation determinants vary across the countries due to the difference in traditions, cultures, religion, and level of education. In Brazil, the prevalence of blood donors is below adequate. However, few studies have evaluated which are the blood donation determinants and associated factors among individuals who have never donated blood.

Aims: To investigate the psychosocial and sociodemographic role in the attitude of non-blood donors in a large and representative sample of users of healthcare services in a Brazilian municipality.

Methods: We conducted a cross-sectional survey using a stratified random sample of primary healthcare users in Ribeirão Preto-SP. We grouped 41 primary healthcare facilities into 12 strata according to geographical area and the São Paulo Social Vulnerability Index (IPVS). We drew the sample of 1,054 interviews from each of the 12 strata based on regional population size and number of total patient visits by facility per month. Participants answered questions on lifetime donation profile (frequency of donation, never donated, unable to donate), attitudes regarding blood donation among non-donors (intention to donate in the future, never thought of donating), self-perception of health (good, regular, poor), knowledge regarding blood donation, religious beliefs, fear, and blood donation of peer groups (households and close friends). The knowledge regarding blood donation was estimated using the Blood Donation Knowledge Questionnaire (BDKQ-Brazil). Religious beliefs were investigated through Duke University Religious Index (DUREL) that measures three dimensions (Organizational religiosity, non-organizational religiosity, and intrinsic religiosity). To assess fear of blood, injections, and vasovagal reactions the Blood or Injections Fear Scale (BIFS) was applied. All instruments used were previously validated to the study sample. The sociodemographic variables considered were sex, age, socioeconomic status and educational level. The data were included in a structural equation model and the attitude regarding blood donation was considered the dependent variable (central construct). The structural model was evaluated using polychoric correlation matrix through Weighed Least Squares Mean and Variance Adjusted method. The fit of the model was analyzed considering the goodness of fit indices and the significance of causal paths (β), assessed using z tests, considering a significance level of 5%.

Results: Of the 1,055 primary healthcare users who agreed to participate, 669 never donated blood and were included in this study (85.5% females; mean age=36.6 [SD=13.5] years). The fit of the structural model was adequate. The variance explained of the model was 35%. The variables that showed significant influence on attitude regarding blood donation were age, socioeconomic status, knowledge, and fear (P < 0.01). Older individuals, with lower socio economic level, lower knowledge about the donation process, those who reported fear of blood, fear of injection and, fear of vasovagal reactions were more likely to have negative attitude towards blood donation.

Summary/Conclusions: The results of the present study may be useful to understand the multifactorial determinants for blood donation among non-donors. Our findings provide guidance for future recruitment campaigns focused on individuals who have never donated blood and, may expand the knowledge regarding determinants of blood donation in other populations.

P-114

PREVALENCE OF CARDIO-VASCULAR RISK FACTORS AMONG BLOOD DONORS IN FRANCE

B Danic[1], C Vidal[2], D Benomar[3], A Fillet[4], A Pugin[2], F Charpentier[5], F Gueyffier[6], L Malard[4], M Pagadoy[2], R Djoudi[7], D Binda[2] and S Gross[4]

[1]Direction ETS Bretagne, EFS, Rennes [2]Centre Investigation Clinique, CHU, Besançon [3]Direction de la Collecte ETS Ile-de-France, EFS, Ivry sur Seine [4]Medical Department, EFS, La Plaine Saint-Denis [5]Blood Products Collection Department, EFS, La Plaine Saint-Denis [6]UMR CNRS 5558, Université Claude Bernard Lyon I, Villeurbanne [7]Responsible Person for Blood Components, EFS, La Plaine Saint-Denis, France

Background: Cardiovascular disease risk in the population of blood donors is lower than in European general population. However, acute coronary syndromes have been occasionally reported in blood donors. Decompensation of cardiovascular disease is prevented by permanent deferral. Criteria to select blood donors are defined by French health authorities in agreement with European directives. Cardiovascular risk factors are not included in selection's criteria.

Aims: We aimed to estimate the prevalence of cardiovascular risk factors among blood donors and to assess the impact on blood supply of various risk factors combinations of donor's deferral.

Methods: A nationwide, epidemiological cross-sectional non-interventional study was performed in all mobile blood drives and blood centers, between March 25 and April 6, 2013. The survey period lasted two days randomly selected for whole blood donation and two weeks for apheresis. The characteristics of donors (sex, age, blood pressure, body mass index (BMI), regular exercise, tobacco use, alcohol drinking, diabetes, ongoing therapy, medical history, family cardiovascular history) and of donations (number and type in the previous year) were collected. All donor candidates could be included, except those who did not consent to participate. The higher rate of men than women in this study, different from that usually observed, is related to two facts. On one hand, because of the high participation rate and the scarcity of apheresis donors, those were firstly recruited. On the other hand, plasma apheresis was done almost exclusively for therapeutic use and subsequently collected only from men in order to prevent TRALI.

Results: Among 18,871 candidates, 1,251 were deferred and 17,268 donations were done (352 missing data) and distributed as follows: 10,298 whole-blood; 3,066 plasma and 3,839 platelets apheresis (65 missing data). Among 15,511 blood donors whose gender was reported, 61.8% were men and 38.2% women. 37% of men were older than 50 yo and 7.7% of women older than 60 yo. 2.5% of donors had a BMI>35, 22.5% were smokers, 22.9% had hypertension, 1.2% had diabetes, 6.7% had family cardiovascular background. Around half of donors younger than 50yo had at least one risk factor. The association of two risk factors was rare, smoking and diabetes (0.2%), hypertension and diabetes (0.6%). The association of three risk factors was very rare: smoking and hypertension and diabetes (C1, <0.1%), hypertension and diabetes and family history (C2, <0.1%), smoking and diabetes and family history (C3, <0.1%), smoking and hypertension and family history (C4, 0.3%). In combination with sex and age, some donors had 4 risk factors: 22 men older than 50 yo (10 C1, 4 C2, 1 C3 and 7 C4) and 2 women older than 60 yo (0 C1 and C2, 1 C3, 1 C4). The impact on donor's deferral of various risk factors combinations is currently being assessed.

Summary/Conclusions: Blood donors with at least one cardiovascular risk factor were frequent representing about half of donors younger than 50. Donors with very high cardiovascular risk were very rare. This raises the question of their deferral to avoid a potential cardiovascular adverse effect after donation.

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THE JOURNEY TOWARD PLASMA SELF-SUFFICIENCY – AN OPPORTUNITY YET A CHALLENGE

S Daigneault[1] and B Bernier[2]

[1]Marketing and International Affairs, Héma-Québec, Montréal [2]Donor Recruitment, Héma-Québec, Québec, Canada

Background: The demand for plasma-based therapies has increased sharply around the globe. The result has been an increased focus in recruiting source plasma donors. Thousands of Quebecers need these products to treat immune deficiencies or other diseases, such as hemophilia. Collecting plasma to manufacture these medications is thus a key issue. As part of its strategic plans, since 2012, Hema-Quebec is working to increase its self-sufficiency in immunoglobulin (IVIg) from human plasma. In 2013–2014, the volume of plasma collected locally and sent for fractionation was able to meet only 14.5% of the need for IVIg in Québec

Aims: Héma-Quebec wants to gradually increase the proportion of immunoglobulins derived from Québec plasma. To do this, the organization aims to increase the collection of plasma for fractionation in order to achieve a target of 150,000 l by 2020. The purpose of this presentation is to share our journey to get there and learn about the different strategies, tactics and approaches that we had develop in order to reinvent our model and ourselves

Methods: To accomplish this goal of self-sufficiency, two obstacles will have to be overcome with regard to plasma collection: the very high cost of collecting it and the ability to recruit a large number of voluntary non-remunerated donors, and that without affecting the overall availability of the blood supply. In order to deal with the challenges of recruiting donors and achieve a competitive cost for the collection of plasma, Héma-Quebec has created the first collection center intended exclusively for the collection of plasma for fractionation. This first PLASMAVIE Plasma Donor Lounge was opened in Trois-Riviéres in November 2013. This first pilot set the

ground for the development of a network of plasma centers which now include four of them. The new model needed for us to revisit every aspect of what we do. From the branding and the spirit of the center, it's layout and the donation process and flow to the staff hiring profiles, from the donor recruitment, management and retention strategies to each volunteer and employees roles.

Results: From 2013 to 2017, we went from 52,416 to 95,881 l collected, from an immunoglobulin self-sufficiency rate of 14.5% to 21%. The average donations, per donor, per year, has reached 6.5% with 28% of the donor giving more than 8 times.

Summary/Conclusions: It became clear, very early on, that the journey to self-sufficiency would keep challenging us and that the key to our success would rely on our human capital, our ability to engage the community; our capacity to collaborate as a team, innovate and try new ideas, measure, evaluate and implement them on an ongoing basis.

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KNOWLEDGE, AWARENESS AND ATTITUDES ON BLOOD DONATION AMONG POTENTIAL FUTURE BLOOD DONORS IN COLOMBO, SRI LANKA

M Krishnapillai[1] and S Jayasekara[2]
[1]National Blood Centre [2]National Blood Transfusion Service, National Blood Centre, Colombo, Sri Lanka

Background: Sri Lanka received the award for the best transfusion service among the developing countries in 2012 at the 32nd International ISBT Congress. Voluntary non remunerated donors play the key role in such efficient transfusion practice in the curative health care service. In order to maintain the donor pool and supply with the increasing demand from the patients, it's our duty to create awareness and encourage the younger generation who will be the potential blood donors in the future.

Aims: Aim was to assess the knowledge, awareness and attitudes of potential future blood donors in Colombo, Sri Lanka

Methods: A cross sectional descriptive study was conducted among 960 Tamil speaking high schoolers who have never donated before, from three different schools in Colombo, Sri Lanka. Data was collected from self-administered structured questionnaire and statistically analysed with the SPSS software and Microsoft Excel.

Results: Among the students, 482 (50.21) were female and 478 (49.79%) were male. Mean age was 17.2 years. Most of them (81.97%; 787) did not know their blood group. 86.25% (828) of them were interested to become blood donors in the future.

The common motivating factors identified were helping others (716; 86.47%), and having a family member/friend who was a donor (494; 59.66%). 76 (9.17%) of them would like to have their blood tested through donation.

While analysing their knowledge on basic criteria for blood donation, 68.02% (653) of them were either wrong or not aware of the minimal age requirement, haemoglobin level (92.91%; 892) or minimum body weight requirement (93.54%; 898). Most of them were aware that people with chronic illnesses (90.31%; 867) or commercial sexual workers (93.02%; 893) cannot donate but 824 (85.83%) of them considered menstruation as deferral criteria.

The commonest misconceptions were gaining body weight (83.95%; 806), acquiring infections (76.97%; 739), and other diseases (52.91%; 508). 87.91% (844) of them were interested to learn more about blood donation, and they preferred educating through mass media (77.39%; 743), newspapers (680; 70.83%) and leaflets (642; 66.87%). 574 (59.7%) of them preferred including a chapter on blood donation in their routine curriculum.

Summary/Conclusions: Majority of the study population showed an interest to donate blood in the future, while most of them were unaware of their blood group. The basic knowledge on blood donation was found to be poor but the students were aware of certain absolute deferral criteria. Since the majority showed an interest to learn more about blood donation, and most of them had false beliefs and misconceptions, educating through the preferred medium and inclusion of a chapter in their curriculum could be helpful in eliminating the common misconceptions from the younger generation. This would increase the number of donors and further improve the quality of transfusion service in Sri Lanka.

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KNOWLEDGE, ATTITUDES, AWARENESS AND MOTIVATION DETERMINANTS TO DONATE BLOOD AMONG BLOOD DONORS IN COLOMBO DISTRICT, SRI LANKA

CG Kohombange[1], A Dissanayake[2], S Jayasekara[2], K Kuruppu[1] and N de Silva[2]
[1]Quality Management [2]National Blood Center, Colombo, Sri Lanka

Background: National Blood Transfusion Service of Sri Lanka is a centrally coordinate system with 99 Blood Banks. Blood requirement is fulfilled by voluntary non remunerated blood donors.

According to global data, there is a gradual decline in voluntary non remunerated blood donations throughout past decade. It has become a challenge for transfusion services to recruit low risk donors. Increase in the life expectancy, rates of accidents and specialized surgeries have increased the rate of blood usage. It has become a global need to study on blood donation to promote blood donation among individuals.

According to prevailing researches, act of blood donation can be influenced by factors including altruism, social behavior, social pressure, level of knowledge on blood donation etc. Identification of these characteristics is essential to develop strategies to motivate, recruit and retain blood donors.

Aims:
1. To determine the factors which motivated first time donors to donate blood.
2. To determine the factors which motivate regular donors in continuing blood donation.
3. To assess knowledge, awareness and attitudes on blood donation among blood donors.

Methods: Descriptive cross sectional study was carried out using a sample of 427 donors who visit to blood donation campaigns in Colombo district for blood donations. Data collected using a self administered questionnaire, which was pretested and validated in a different setting.

Results: From 427 blood donors 94 (22%) were first time donors. 67(72%) of first time donors noted blood donation as a social responsibility, 223(67%) regular blood donors admitted the same. Further 52 (55%) of first time donors and 212 (63%) of regular donors consider blood donation as a religious act. Peer pressure was a motivation factor for 58(61%) of first time doors, in contrast to regular donors it was 27 (8%). Out of the 427 blood donors, 335(78%) were aware about the acceptable gap between blood donations, 85(19%) were not aware about the same. 327(76.5%) donors were aware about the minimum requirement of body weight for donating blood. 97(22.7%) were not aware of the correct body weight for donating blood. 312 (73%) donors were aware about the age limits for donating blood. 52(12.2%) of donors were responded incorrectly. 43(10.1%) has not responded for the question. 402(94%) donors wish to receive a certificate for blood donation. 127(29.7%) favored a token of appreciation and 367(85.9%) favored a free health check. 112 (26.2%) mentioned to have priority in government clinics for blood donors. 9(2.1%) of donors deny obtaining any gifts or notes of appreciation. None of the participants admit to obtain a payment for blood donation.

Summary/Conclusions: Donating blood is considered as a social responsibility by majority of both regular and first time donors. Considerable amount of donors in both categories considered blood donation as a religious act. In first time donors, peer pressure was a significant motivating factor in contrary to the regular donors, in which the majority accepts donating blood as a social responsibility and a religious duty. Thus it is required to motivate the new donors by adopting behavioral and motivational strategies. It would be effective to offer a certificate or a token of appreciation in recruitment and retention of donors.

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CONSULTATION OF BLOOD DONORS WITH HIGH LEVELS OF HEMOGLOBIN. IS THERE ANY BENEFIT?

M Papadogiannaki, P Kanellou, E Lydaki, I Stagakis, J Liapis, I Nikoloudi, I Bolonaki and K Fountouli
Transfusion Medicine, University Hospital of Heraklion, Heraklion, Greece

Background: According to the latest 2016 revised World Health Organization (WHO) guidelines, lower levels of hemoglobin (Hb) are required for the diagnosis of polycythemia vera (PV), an incurable disease in which early diagnosis leads to effective management of related symptoms and better thrombosis-free survival. Therefore, lowering the upper limit in the current Hb reference intervals could increase the number of patients being assessed for PV, however this possibly can lead to the exclusion of a significant number of blood donors.

Aims: The purpose of this study was to screen and assess volunteer blood donors with levels of Hb over the upper limit at the Blood Donation Department of the University Hospital of Heraklion during a 12-month period.

Methods: During the 12-month period 84 volunteer blood donors were examined (1.43% of the total number of donors). Criteria for assessment was hemoglobin >16.5 g/dl in men and >16 g/dl in women, or hematocrit >49% in men and >48% in women. Assessment included: (i) recording of risk factors for erythremia such as, smoking, living at high altitude, snoring, family history and symptoms like dizziness, headache, tinnitus, hypertension, facial erythema etc, (ii) blood examination of liver and kidney function, vitamin B12, ferritin and erythropoietin (EPO) levels, (iii) JAK2 mutation if EPO levels were low. Based on the results the blood donors were either: (i) excluded permanently and referred to haematologist (low EPO) (ii) excluded temporarily (e.g. reference to sleep specialist if there is snoring etc), (iii) free to donate blood.

Results: Of the total 84 volunteers who were examined 41 (48.8%) had 1 risk factor for erythremia, 12 (14.3%) had 2 risk factors, the 6 (7.1%) had ≥3 risk factors, while 25 (32.1%) had unremarkable medical history. Seven donors had erythremia symptoms, laboratory evaluation was remarkable in 12, whereas 22 (26.2%) had low levels of EPO. Of the 18 blood donors who were examined for the JAK2 mutation one was found positive. The remaining 16 blood donors were referred for further examination of other functionally similar mutations (e.g., JAK2 exon 12 mutation) and possible bone marrow biopsy and were excluded from the blood donation permanently. In 46/84 (54.8%) blood donors the high levels of hemoglobin were considered to be secondary (e.g. smoking) and were able to continue to donate blood, while the remaining 16 were excluded temporarily and were referred to a pneumologist or to an internist for further evaluation. It is important to note that 14 blood donors didn't care about the results of their laboratory tests and they didn't cooperate for further investigations.

Summary/Conclusions: According to our study we found that the 26.2% of the blood donors with high hemoglobin had low levels of EPO and need further investigation in order to determine the presence of a myeloproliferative disease. The detection JAK2 mutation in one of the donors establishes the significant benefit of this consultation in the blood donation departments, not only for the early diagnosis of a myeloproliferative disease but also for the recruitment of an important number of blood donors with benign secondary erythremia for blood donation.

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AUSTRALIAN BLOOD DONORS' AND NON–DONORS' VIEWS ON NON–CASH INCENTIVES FOR BLOOD DONATION

N Van Dyke[1], K Chell[1], B Masser[2], S Kruse[1], T Davison[1], C Gemelli[1] and K Jensen[1]
[1]Clinical Services & Research, Australian Red Cross Blood Service, Melbourne
[2]School of Psychology, University of Queensland, St Lucia, Australia

Background: Increasing the volume of plasma collected is a key priority at the Australian Red Cross Blood Service (Blood Service) in order to address the growing demand for immunoglobulin. Non-cash incentives are one possible approach to address this problem while remaining committed to a voluntary non-remunerative system. Our recent literature review on incentives and blood donation (Chell, et al., Transfusion, 2018), however, concludes that the degree to which incentives succeed in attracting and facilitating repeat or high frequency donation is unclear. Moreover, it is not known how the introduction of non-cash incentives to encourage donation would be viewed in the Australian context.

Aims: The aim of this study was to explore Australian donors' and non-donors' perceptions about using non-cash incentives to promote donor recruitment and retention.

Methods: A survey of 1,028 donors and 1,201 non-donors was conducted online and via telephone by a research company. The central focus was on the perceived effectiveness of 13 non-cash incentives along with the impact of their introduction on views of the Blood Service. Other items assessed knowledge regarding domestic sourcing of plasma, intention to donate whole blood or plasma in the future, and several psychological scales relevant to incentives and blood donation.

Results: Attitudes to non-cash incentives for blood donation were mainly positive for both donors and non-donors, with donors slightly more positive than non-donors. Both groups rated 'time off work' as the incentive that would most encourage donation and 'health checks' as the incentive that would most positively affect their view of the Blood Service. Milestone plaques or certificates, the only incentive currently offered by the Blood Service assessed in the study, is more positively viewed by donors than non-donors.

Although attitudes to incentives and intention were generally positively associated for both donors and non-donors, the magnitude of the associations was typically very small (−0.04 (P > 0.05) to 0.18 (P < 0.01)).

Perhaps unexpectedly, a higher percentage of non-donors (16%) than donors (10%) correctly believe that Australia's demand for plasma is higher than our current supply. However, for both donors and non-donors, knowledge regarding plasma supply was not significantly associated with intention to donate plasma.

Summary/Conclusions: Perhaps contrary to expectations, Australian blood donors hold mostly favourable attitudes towards a wide range of non-cash incentives, and in most cases hold more positive views than do non-donors. This result may reflect changing norms in society about the offering of incentives for behaviour. Many more behaviours are now incentivized than have been previously. As a result, accepting incentives even for behaviours borne out of altruism or benevolence, such as blood or blood product donation, is now socially acceptable. The results of this study provide provisional support for the introduction of non-cash incentives for blood donation in voluntary non-remunered settings, to facilitate the recruitment of new donors and retention of existing donors. However, rigorous trials, including an examination of actual return behaviour, are required to determine whether this approach is effective prior to implementation.

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KNOWLEDGE, AWARENESS, AND ATTITUDES ON PLATELET APHERESIS AMONG VOLUNTARY NON REMUNERATED WHOLE BLOOD DONORS IN COLOMBO, SRI LANKA

M Krishnapillai[1], S Jayasekara[2], N Fonseka[1], M Gunarathne[1] and G Jayasinghe[1]
[1]National Blood Centre [2]National Blood Transfusion Service, National Blood Centre, Colombo, Sri Lanka

Background : Platelet apheresis was introduced in Sri Lanka in late nineties. Since then, a platelet apheresis donor registry is maintained by the National Blood Transfusion Service which now has the records of around 550 donors. With the increasing demand for HLA matched platelets, concern towards reducing the donor exposure to the paediatric patients through pooled platelets and other indications for apheresis platelets, it is important to create awareness and increase the number of platelet apheresis donors from the population of whole blood donors.

Aims: Aim was to assess the knowledge, awareness and attitudes of voluntary non remunerated whole blood donors towards platelet apheresis donation.

Methods: A cross sectional descriptive study was conducted among 780 whole blood donors in mobile donation campaigns from Colombo, Sri Lanka. Data was collected from self-administered structured questionnaire and statistically analysed with the SPSS software and Microsoft Excel.

Results: Among the 780 donors, 596 (76.41%) were males while 184 (23.59%) were females. Mean age was 33.8 years. Among the regular donors (476; 61.03%), only 190 (39.92%) were aware of the apheresis donation and from the first time donors (304; 38.97%), 21(6.91%) were aware of it. From the donors who previously knew of apheresis (211; 27.05%), 130 (61.61%) would like to donate apheresis platelets, and among the ones who were not aware of it (569; 72.94%), 323 (56.76%) would like to do so. Willingness to help others (379; 83.7%) and religious factors (311; 68.7%) were the most common reasons for this interest seen among the donors. Learning about the patients who require apheresis platelets (459; 58.8%), availability of a donation centre close by (421; 54.0%) and expectation of receiving special felicitation (251; 32.2%) from the transfusion service were found to be the common motivation factors. But 516 (66.2%) of them had the misconception of losing weight following apheresis donation and other side effects feared were weight gain (243; 31.2%), and acquiring infections (133; 17.1%) or other diseases (179; 22.9%). 712 (91.3%) showed an interest towards learning more about platelet apheresis and most of them (468; 65.73%) preferred to be educated by the medical staff.

Summary/Conclusions: Male predominance was noticed among the study population. Most of the population were not aware of platelet apheresis but fair number of regular donors had the knowledge when compared to the first time donors. The commonest misconception was losing the weight and most of them believed that to learn about the patients in need of such platelets would motivate them to become apheresis donors. Since the majority was interested in learning, it would be beneficial for the transfusion service to encourage the medical staff to educate whole blood donors on platelet apheresis donation.

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Abstract has been withdrawn

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PARADIGM SHIFT OF HIGH-RISK SEXUAL BEHAVIOUR AMONG INDIAN BLOOD DONORS – A THREAT TO BLOOD RECIPIENTS

S Mangwana

Blood Transfusion Services, Sri Balaji Action Medical Institute, New Delhi, India

Background: In spite of all precautions and improved methods of detection of transfusion transmitted infections (TTIs) like nucleic acid testing for blood donation, though small residual risk; transfusion recipients are susceptible from receiving contaminated blood if blood donation is made within "window period". Proper screening and selection of blood donors are crucial factor for reducing the risk of transmission of viral diseases and upgrading the overall safety of donated blood inventory. Careful selection of donors is an important and pragmatic risk management strategy to ensure blood safety.

Aims: Most non-compliance studies focused on MSM and IDU are from western countries, no Indian study, to the best of our knowledge, is reported on sexual behaviour among blood donors and blood safety. To fill the knowledge gap, observational study was undertaken to determine prevalence and trends of high-risk behaviour, to explore the possibilities for improving donors screening procedures, importance of education of general population and implementing blood donor self-deferral to reduce the risk of TTIs.

Methods: This study was undertaken in two parts. In first part, retrospective data of donors attending blood transfusion services of tertiary care centre between 2014 and 2016 was collated and analyzed. All donors were routinely given bilingual educational material along with donor forms and advised to read before filling the forms to understand risk behaviours. Statistical analysis was done using student's t- test. In second part, an online survey was conducted to assess the prevalence and awareness among donors. Survey data was compiled and analyzed.

Results: A total of 32,773 donors reported for blood donation, of which 8,974 (27.38%) potential donors were deferred. Deferrals incidence due to high-risk behaviours increased in 3 years from 2.84% through 3.36% to 9.85% (P value < 0.001) with majority of donors (99.60%) being males. 52% of donors were repeat donors. Incidence of high-risk deferrals was highest no. in less than 25 years of age (55%) with nearly 95% deferrals in less than 35 years age in 2015 and 2016. In the survey, 90% of centers question donors about high-risk behaviours, 58% of centers specifically question about sex history. 50% of seroreactive donors in first part of study and 63% of respondents found that donors give positive history of high-risk behaviour during post-donation counseling.

Summary/Conclusions: Because of almost non-existent sex education in India and lack of knowledge of its direct implication in blood safety, general population is not completely honest during blood donor screening. A new insight this study offers is that conventional, indirect questionnaires do not identify potentially infectious donors and direct questions, though leads to increased rate of deferrals, are more effective. To optimize the cost of health care services and maintaining highest level of transfusion safety, new solutions need to devise in dealing with potentially risky sexual behaviours, reviewing frequently deferral criteria for high-risk sexual behaviours with changes in disease epidemiology. Deferral policy would never be effective without donors' compliance. Efforts are also needed to educate the general population to understand potential risks of high-risk behaviours in transfusion safety and to promote the self- deferral or confidential unit exclusion.

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Abstract has been withdrawn

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CHARACTERISTICS AND RETENTION OF BLOOD DONORS WITH THALASSEMIA TRAIT

K Kittisares[1], D Palasuwan[2], A Palasuwan[2] and R Kanprakob[1]

[1]*Department of Transfusion Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University* [2]*Department of Clinical Microscopy, Faculty of Allied Health Science, Chulalongkorn University, Bangkok, Thailand*

Background: Thalassemia and hemoglobinopathy are the most common inherited red blood cell abnormalities, causing public health and socioeconomic problems in Thailand. The prevalence rate of thalassemia carriers in Thais ranges between 28.625% and 53.23%, which varies from region to region. Thalassemia trait individuals are asymptomatic and can become blood donors. Significance of thalassemia trait condition in blood donors and impact on blood donation and transfusion outcome have been concerned.

Aims: This study aims to determine prevalence, characteristics and retention of blood donors with thalassemia trait.

Methods: Prospective blood donors were randomly recruited at Department of Transfusion Medicine, Siriraj Hospital, Mahidol University, Bangkok from August to December 2016. A total of 399 blood donors were informed and consented for thalassemia diagnosis. The whole blood collections were processed using a standard procedure. Donor reactions were routinely vigilance. The hematological parameters and thalassemia diagnostics were performed on the K3EDTA-anticoagulated blood. Diagnosis of thalassemia was determined after analysis using HPLC (Variant Hemoglobin Testing System, Bio-Rad, Hercules, CA) for hemoglobin typing and multiplex Gap-PCR. Blood donors' characteristic data, including sex, age, blood group, number of previous donations and domicile, was retrieved from a blood donor information system. The return rate of blood donors was defined as the second attempt to donate within 12 months. The deferral rate due to low hemoglobin in subsequent donations was defined as any attempt to donate within 12 months which was deferred due to hemoglobin less than 12.5 g/dl.

Results: The prevalence rate of thalassemia trait in blood donor was 21.1% (84/399), of which 64.3% (54/84) was hemoglobin E related disorders and 29.8% (25/84) was alpha thalassemia trait. A significantly higher proportion of male gender was found in thalassemia trait blood donors (60.7% vs 47.9%, P < 0.05). There was no significant difference in age, proportion of first-time donors, number of previous donations, blood group and domicile regions between donor with thalassemia trait and normal blood donor. Three vasovagal reactions were recorded, one in thalassemia trait donor and two in normal donors. After 12 months follow up, the return rate of donors with thalassemia trait was not significantly different from the return rate of normal donors (63.1% VS 61.9%, P = 0.84) and the deferral rate due to low hemoglobin in subsequent donations was also not significantly different between the two groups (17.0% VS 19.0%, P = 0.74).

Summary/Conclusions: There was a high prevalence rate of thalassemia trait in Thai blood donors. Except for a higher proportion of male gender in thalassemia trait group, there was no significantly difference in characteristics between the two groups. Moreover, the return rate and the deferral rate due to low hemoglobin in subsequent donations were not significantly different between blood donors with thalassemia trait and normal blood donors.

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WELL COMMUNICATION, A KEY FACTOR LEADING TO SUCCESS ON VOLUNTARY BLOOD DONATION CAMPAIGN

M Nhat Le Pham, D Thi Nhu, B Van Tran, O Hoang Le and S Truong Nguyen

Cho Ray Blood Transfusion Centre, Cho Ray Hospital, Ho Chi Minh City, Viet Nam

Background: Cho Ray Blood Transfusion Center (Cho Ray BTC) is one of five standard blood transfusion centers in Vietnam. Cho Ray BTC has an important role in collecting and distributing safe blood components for provincial hospitals in South East Vietnam. To increase the quality of blood and blood component production as well as to use blood products effectively in the clinic, in 2008, we implemented a plan to reduce the paid and the family donations. The strategy was to educate and encourage voluntary blood donors to donate 350 ml blood instead of the standard 250 ml. The collected 350 ml blood was fractionated into at least 4 different blood components in a closed system which could subsequently be distributed to 4 different patients. In the first period after implementing this strategy we experienced some challenges, however, it has been successfully applied for 10 years now. Communication is considered an important key leading to success on voluntary blood donation campaign. They include numerous of activities to propagandize and campaign for voluntary blood donation such as commitment of government; presentations on the

meanings and benefits of blood donation; consultancy and connection with blood donor for pre and post blood donation....

Aims: The aim of the study was to evaluate the impact of the strategy to change blood donation resources and to educate as well as encourage blood donors for 350 ml volume of blood donation at Cho Ray Blood Transfusion Center.

Methods: The study was conducted in the Cho Ray BTC of Cho Ray Hospital in Ho Chi Minh City, Vietnam from 2008 to 2017. Firstly, our proposal to the provincial voluntary blood donation campaign board was approved. Secondly, we organized numerous activities and presentations on the meanings and benefits of donating 350 ml blood for potential voluntary blood donors prior the day of collection. Thirdly, we offered consultation for voluntary blood donors at fixed and mobile sites at prior and after collection. Fourthly, we established a good relationship with blood donors.

Results: In 2008, 350 ml blood donation was 39% of the total blood collection. This ratio was continuously increasing (72% in 2009, 86% in 2010, 92.60% in 2011, 96.70% in 2012, 97.20% in 2013, 97.80% in 2014, 98.70% in 2015, 99.50% in 2016 and 2017). Additionally, the ratio of regular donors and amount of collected blood also increased during 10 years. In 2017, we collected 105,995 units of blood with 61.60% retain donation. Importantly, we reduced the paid and family donors. In 2008, we still had 9% paid donation and 6% family donation. However, in 2017, the ratio of paid donation was 0.01% and 0.09% of family donation. Therefore, we can ensure the quality of blood donation source and contribute to the safety of blood transfusion.

Summary/Conclusions: With the data showed in the results, we can conclude that communication is the key an important factor leading to success on voluntary blood donation campaign.

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KNOWLEDGE, ATTITUDES AND CONCERNS ON BLOOD DONATION AMONG NON REMUNERATED MOBILE BLOOD DONATION CAMPAIGN ORGANIZERS IN COLOMBO, SRI LANKA

M Krishnapillai[1], S Jayasekara[2], N Fonseka[1], M Gunarathne[1] and G Jayasinghe[1]
[1]National Blood Centre [2]National Blood Transfusion Service, National Blood Centre, Colombo, Sri Lanka

Background: Adequate, stable supply of blood from the voluntary non remunerated blood donors supports the National blood transfusion service of Sri Lanka to fulfil the demand from the increasing number of patients who rely on blood transfusion. Blood donation campaign organisers provide an enormous support in this noble service. A timely analysis on their knowledge and concerns towards blood donation would ensure the transfusion service to address them and make necessary changes to obtain their contribution.

Aims: Aim was to assess the knowledge, attitudes and concerns of mobile blood donation campaign organisers towards blood donation.

Methods: A cross sectional descriptive study was conducted among mobile blood donation campaign organisers in Colombo, Sri Lanka. Data was collected from self-administered structured questionnaire and statistically analysed with the SPSS software and Microsoft Excel.

Results: Among the 59 participants, 42 (71.2%) were male and 17 (28.8%) were female. In the research population, 57.6% (34) had organised less than five mobiles, 30.5% (18) from 5–10 and 11.9% (7) had organised more than 10 mobiles.

Among the motivational factors, 84.7% (50) would like to help the community, 67.8% (40) had religious reasons while 20.3% (12) in the memory of beloved person or to celebrate life events. When analysing the awareness towards basic criteria to donate blood, 89.8% (53) were aware of the minimal age requirement, 88.1% (52) and 61.0% (36) knew about the minimum weight and haemoglobin level respectively.

On analysing the knowledge on the donor selection criteria in Sri Lanka, 52.5% (31) scored more than 50% while 13.6% (8) of them scored less than 10%. Many of them were wrong about menstruating females 57.6% (34) and deferral period for history of travelling abroad 47.5% (28). Concerns expressed by them were, inadequate number of staff and equipment allocated for each mobile campaign (28.8%), general public's knowledge on blood donation was poor (10.2%), organisers themselves had inadequate knowledge (5.1%). But 52.5% of them had no concerns or complaints. All 59 (100%) of them were interested to learn more and to get educated, 62.7% and preferred to attend talks/ discussions conducted by transfusion service, 35.6% of them through handouts and 42.3% of them preferred mass media.

Summary/Conclusions: Around half of the study population had good knowledge on basic criteria and donor selection criteria for blood donation. But there were still

a number of them who need their knowledge to be updated. While around half of the research population had no concerns or complaints, the most common concern was inadequate number of staff and equipment. Most of them showed an interest to learn further about blood donation. Organising such educational programmes as they preferred, by the transfusion service would improve the quality and output of mobile blood donation campaigns.

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BLOOD DONATION PRACTICE AND ITS ASSOCIATED FACTORS AMONG HEALTH PROFESSIONALS OF ADDIS ABABA GOVERNMENTAL HOSPITALS, ADDIS ABABA, ETHIOPIA

YG Tsegay[1] and L Alagaw[2]
[1]Research and Development Center, Defence University College of Health Science
[2]Quality and Safety, National Blood Bank Service of Ethiopia, Addis Ababa, Ethiopia

Background: Though World Health Organization recommends 100% voluntary none remunerated blood donation, the percentage of blood collected from voluntary blood donors and the average annual blood collection rate are low in Ethiopia around 0. 18% from the total population of Ethiopia Health workers are expected to practice blood donation so as to create a good image to the public and is crucial to meet the demand of safe blood. A study on blood donation practice may improve successful implementation of the blood donation programs in Ethiopia.

Aims: The objective of this study is to asses the practice of blood donation among Health professionals in Addis Ababa government Hospitals, Ethiopia

Methods: An institution based cross-sectional study was deployed from February to July 2017. An aggregate of 427 health workers were included in the study by using simple random sampling technique from 13 governmental Hospitals. Data were collected by using pre tested and structured questionnaire via self-administrated method. Descriptive and summary statistics were employed. Bivariate and multiple logistic regressions were computed. Odds ratios and their 95% confidence intervals were calculated to determine the level of significance.

Results: A total of 427 participants were included in the final analysis (response rate = 100%). Among these participants, 33.2% of them practice blood donation. Age above 25 years [AOR = 1.8 (95% CI 1.1, 3.0)], health professionals' knowledge of blood donation [AOR = 1.9 (95% CI 1.1, 3.1)], health professionals' attitude towards blood donation [AOR = 3.0, 95% CI 1. 8, 4.9)], and the presence of family members or relatives who received blood [AOR = 5.4, 95% CI 3.7, 8.7)] were significantly and independently associated with blood donation behavior of health professionals.

Summary/Conclusions: Blood donation practice of health professionals in this study was found to be low as compared to other studies conducted in developing countries. Health professionals' knowledge, attitude, age and the presence of family members or relatives who received blood before were independently associated with blood donation practice. Thus, awareness has to be created for health professionals to improve blood donation practices

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HAEMATOLOGICAL PARAMETERS OF REGULAR AND FIRST TIME MALE BLOOD DONORS IN A MEDIUM SIZED HOSPITAL IN NORTH CENTRAL NIGERIA

HO Olawumi[1], I Durotoye[1], A Shittu[1], M Ogunfemi[2] and A Ogunmodede[3]
[1]Haematology and Blood Transfusion, University of Ilorin [2]Haematology and Blood Transfusion, University of Ilorin Teaching Hospital [3]Medicine, University of Ilorin, Ilorin, Ilorin, Nigeria

Background: Haemoglobin concentration is the only haematological parameter that is routinely done in order to determine donor fitness. It is therefore possible for a donor with non symptomatic derangement in any of the other haematological parameters to be recruited for blood donation. Repeated blood donation may lead to depletion of iron store which may be reflected in the red cell indices even when the haemoglobin concentration is still normal

Aims: To determine the haematological parameters of male blood donors and the effect of regular blood donation on these parameters by comparing the parameters of regular and first time donors.

Methods: This was a hospital based cross sectional study involving 200 male donors between the ages of 18–59 years conducted at the blood bank of University of Ilorin Teaching Hospital, Ilorin. Purposive sampling method was employed to select 100

each of age matched regular and first time male blood donors. Only consenting donors who had been found fit to donate with haemoglobin concentration of ≥12.5 g/dl and who had been screened negative for HBsAg, HCV and HIV antibodies were recruited for this study. The full blood count (FBC) was determined by Sysmex KX21 (Sysmex, Japan) according to manufacturer's instructions.

Results: The mean age of the regular and first time donors was 29.63 ± 6.9 years and 29.06 ± 8.7 years respectively (P = 0.607). Only one donor (0.5%) had polycythaemia (Hb conc. 17.8 g/dl). Forty four (22%) had neutropaenia (absolute neutrophil count <1.5 × 10^9/l) and one donor (0.5%) had neutrophilia. Four (2%) had thrombocytopaenia (platelet count <90 × 10^9/l) and 7(3.5%) has thrombocytosis(platelet count >300 × 10^9/l). Twenty four (12%) had low MCV while five (2.5%) had high MCV. Eighty two (41%) had low MCH and 83 (41.5%) had low MCHC. The proportion of donors with low MCH was significantly higher among regular donors than first time donors (50% versus 32%; P value= 0.032). There were no significant differences between regular and first time donors in the number with low MCV (13% versus 11%; P value = 0.830) and low MCHC(47% versus 36%; P value = 0.114).

The mean values of haemoglobin concentration, MCH and MCHC were significantly higher among first time than regular donors (14.43 ± 1.26 versus 13.92 ± 1.10; P = 0.003, 27.997 ± 2.64 versus 27.004 ± 2.98; P = 0.013 and 33.448 ± 2.72 versus 32.361 ± 3.08; P = 0.009 respectively). There were no significant differences between regular and first time donors in the mean values of the other parameters.

Summary/Conclusions: Low red cell indices and neutropaenia were the most common haematological abnormalities obtained among the male blood donors in this study. Regular donors had a lower mean value of haemoglobin concentration, MCH and MCHC and a significantly higher proportion of them had low MCH when compared to first time donors.

We recommend that a full blood count should be conducted routinely for all first time donors and annually for regular blood donors. This should be followed by serum ferritin in order to determine the iron status and prescribe possible interventions in those with low red cell indices.

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Abstract has been withdrawn

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WIDESPREAD ASSOCIATION STUDIES BETWEEN DIFFERENT DEMOGRAPHIC PARAMETERS, BLOOD GROUP AND TRANSFUSION TRANSMISSIBLE INFECTIONS (TTIS) IN NEPALESE BLOOD DONORS

A Ghimire[1], N Gurung[1] and R Shrestha[2]

[1]Tribhuvan University Teaching Hospital, Maharajgunj [2]Center for Health and Disease Studies, Shankhamul, Kathmandu, Nepal

Background: A way to compensate the extensive blood loss is blood transfusion. Blood donated by a healthy individual is used for this purpose, therefore active public participation is essential. Blood bank liaises with the society and motivates the public for blood donation. Besides confirming that the blood is safe for transfusion, blood bank keeps record of the donors so that demand can be met timely.

Aims: Developing countries like Nepal struggle to meet demand of blood due to several reasons, such as lack of awareness, gender biasness, ethnic issues, unfit donors etc. As these parameters may change in times of major demographic alterations, there is a requirement of the wide correlative view of the blood donors in terms of gender, ethnic variation, blood typing and incidences of TTIs in donors.

Methods: In this retrospective study, data from 7,745 volunteer blood donors visiting blood bank of Tribhuvan University Teaching Hospital, Kathmandu were collected. Using the collected data, we projected: (i) number and age distribution of donors, (ii) blood typing variations (iii) ethnic variation, (iv) correlative study between the ethnic and blood typing variations and (v) evidence of TTIs and its correlation with ethnicity and blood typing. SPSS was used for data input and analysis.

Results: The data showed that male donors were more than females with the proportion of 70% and 30% respectively. In both male and female populations, about 50% of donors were within the age group of 21–30 years. Brahmins, Chhetris and Newars were the major contributors in blood donation, with the proportion of 36.6%, 16.5% and 24.4% respectively. Muslims (0.4%), Thakali (0.2%) and Yadav (0.4%) were among the least contributors for blood donation. "A" Positive was the

most common blood type in Newar and Chhetri ethnicities, with the proportion of 38.3% and 33.0% respectively. "O" Positive was the most common one in Brahmins. Only 0.1% of donors were "AB" Negative, indicating it as the least common blood type among the donors studied. Among the TTIs, HCV was more common in Gurung and Lama (2.2% and 1.8% respectively), followed by in 1% of Newar. Despite of lower number of population, Gurung and Lama ethnicities have higher incidence for HCV. In contrast, although Chhetri and Brahmin hold the major population of donors, incidence of TTIs in donors of these ethnicity was low, only about 0.3% in each ethnicity. Hence, this data warns further analysis on etiology for higher incidence of HCV in Gurung and Lama. HCV was the most common TTI observed in about 0.6% of donors with "O" Positive blood group. In this blood group, incidences of other TTIs were less than 0.3%. No obvious correlation was observed between other TTIs and ethnicity of blood type.

Summary/Conclusions: This analysis shows that Population of age group 21–30 is more motivated for blood donation. There is a strong association of ethnicity with blood group, blood donation and incidence of TTI.

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EVALUATION OF THE EFFECT OF "APHERESIS PLATELET DONATION AND DOUBLE HAPPINESS" ACTIVITY

Q Zhou

Blood Collection, Beijing Red Cross Blood Center, Beijing, China

Background: China will officially cancel family member's donation from Feb 2018. In order to improve the efficiency of apheresis platelet donor recruitment, increase the double-dose rate of platelet donation, cope with the off-season of collecting platelets, and better motivate donors to devote their love, there is a need for more effective, innovative and engaging thank-you activity.

Aims: To understand the positive effects of "Double Happiness" activity on coping with the off-season of apheresis platelet collection, to understand the demographic characteristics of Apheresis platelet donors and their preferred channels of knowing this activity.

Methods: The "Apheresis Platelet Donation and Double Happiness" activity refers to two donations of apheresis platelet for an extra gift rewarded during the activity. By collecting and organizing 283 active questionnaires filled out by apheresis platelet donors for this activity, we analyzed their demographic factors and their feedback on this activity. All the information of valid questionnaires was summarize for horizontal analysis and evaluation.

Results: The dose of apheresis platelet collected increased significantly by 15.5% over the same period of last year during the activity in 2017 with 20.1% growth of double-dose donation. The two times apheresis platelet donations increased by 28% during the activity. There was a significant increase of apheresis platelet donors giving continuous apheresis platelet donations. The amount of apheresis platelet dose collection increased significantly, reaching the expected goal, of which the amount of double dose donation increased significantly.

Summary/Conclusions: The "Apheresis Platelet Donation and Double Happiness" activity has a significant positive effect on coping with the declining apheresis platelet supply in the off-season of apheresis platelet collection. It has the obvious effect of increasing the donated apheresis platelet volume and stimulating the apheresis platelet donors. In terms of mobilizing apheresis platelet donors, more active publicity strategies should be taken according to their demographic characteristics, including SMS notifications and phone calls for recruitments.

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A NEXUS BETWEEN VOLUNTEERISM AND BLOOD DONATION: A CASE STUDY OF PMAS-ARID AGRICULTURE UNIVERSITY RAWALPINDI AND QUAID-E-AZAM UNIVERSITY ISLAMABAD PAKISTAN STUDENTS

M Noor-Ul-Amin[1,2], M Ramzan[3], U Waheed[4] and M Arshad[5]

[1]University Institute of Biochemistry & Biotechnology, PMAS, ARID Agriculture University [2]Department of Pathology & Blood Bank, Rawalpindi Institute of Cardiology [3]Department of Social Sciences, PMAS, ARID Agriculture University, Rawalpindi [4]Safe Blood Transfusion Program, Pakistan [5]Department of Biotechnology, Islamic International University, Islamabad, Pakistan

Background: Volunteering behavior is socially based and happens at different rates in various geographical areas. Various barriers may continue to exist in community

like concerns of family members or friends, religious or ethnic believes that influence the potential of voluntary non-remunerated donors but increase education about health and safety concerns may prove effective.

Aims:
- To understand motivation factors behind blood donation activities and response of family to blood donation act.
- To find out the links between blood donation behaviour and other volunteer activities of the university students.

Methods: This study was conducted in two most famous universities of Pakistan i.e. Quid-e-Azam University, Islamabad and PMAS Arid Agriculture University, Rawalpindi. From both universities total 200 students (also the members of blood donor's societies) were randomly selected and face to face interviews were conducted for the collection of data. All the collected quantitative data were analyzed by SPSS 19.0.

Results: The major age group of our studied population was 23–27 years (n = 152). Respondent belongs to all provinces of Pakistan but the majority was of Punjab province (n = 136). Results generated against questionnaire about the motivational factors and response of their families shows that; 57% of respondent's mothers were illiterate, 77% became voluntary donors due to convincing by their friends, 68% students did not tell their parents about their voluntary activity, When further question was asked by the interviewer that why they did not told their parents about this volunteer act than 52% replied that due to the fear of restriction, 69% participate were also involve in other routine and emergency volunteer activities, in our studied population on 17% participants donated blood as a replacement donation, 34% participants donated blood >4–5 times, 100 percent respondents replied that there is no religious restriction regarding donation of blood voluntarily, 92% replied that the patient can receive blood of donor having different religion, they further stated that for blood transfusion the relationship is only of humanity.

Summary/Conclusions: The study suggests that perceptions toward voluntary blood donation could be influenced to a large extent by socio-demographic variable. Socio-cultural barriers to voluntary blood donation exist in predominantly illiterate rural communities of the country but the young generation of Pakistan is the altruistic in nature. There is requirement of education, stimulation and motivate at national level especially to illiterate people of society to increase the number of voluntary blood donation. There is also need to make the Blood transfusion system more transparent in Pakistan.

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THE ANALYSIS OF REASONS TO RESIGN FROM DONATING BLOOD

M Sokolowski, L Gulinski and K Olbromski
Blood Center in Poznan, Poznan, Poland

Background: Blood service in Poland is based on voluntary and non-remunerated donations. Regional Blood Donor Centre in Poznan as well as other regional centres are the only entities authorized to collect, process, store and distribute blood and its components to hospitals in the region of their activity but they are also responsible to provide sufficient amounts of blood and its components. Hence, it is critical to introduce suitable measures to increase the number of donors.

Aims: The aim of the survey was to analyse the most common reasons to resign from donating blood and subsequently modify the current marketing strategy of the Regional Blood Centre in Poland.

Methods: A survey was carried out in September 2017 in group of 100 donors and 100 people that have never donated blood. They were asked questions regarding the factors influencing the decision to resign from donating.

Results: Reasons to resign from donating blood: medical reasons (84%), lack of time (50%), lack of opportunities (36%). Factors of no influence on the decision to donate blood: lack of remuneration (84%), common beliefs that donating blood is harmful (82%), that blood is wasted (80%), and that blood is traded with (70%) and finally fear of infection or side effects (56%)

Summary/Conclusions: As the donors mentioned 'medical reasons' as the key reason to resign from donating blood it is vital to ensure for constant availability of well designed, concise educational materials regarding the criteria that donors must meet to donate blood (hard copies on the premises, articles, infographics, downloadables etc. on the website, user friendly interface, ability to contact and receive support from the staff) especially as the survey regarded donors' perception and not their actual medical condition.

As 'lack of time' was second most important factor influencing the decision not to donate blood the process of blood collection must be optimised to assure for the shortest time necessary to be spent by the donor when giving blood. At the same time, effective communication regarding numerous opportunities to donate blood is

essential (www, social media etc.) to create the image of the full accessibility and donor-oriented policy.

Finally, the survey showed that often occurring false beliefs regarding blood centers wasting blood or trading with it, potential harmful effects of donating blood etc. had no influence on the donors, hence it is vital to keep the current policy regarding the transparency of the functioning of the Blood donor Centre as well as continue and develop various educational activities regarding donating blood, donor's and blood safety, qualifying criteria etc.

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PROBABILITY TO BE A BLOOD DONOR IN OSLO DEPENDING ON GEOGRAPHICAL FACTORS

L Nissen-Meyer and H Heier
Immunology and Transfusion Medicine, University Hospital of Oslo, Oslo, Norway

Background: Compared to other western countries, Norway has relatively few blood donors. Norway is self-sufficient with cellular blood components (erythrocytes and thrombocyte concentrates), but experiences increasing deficit in plasma products and correspondingly increased import of plasma products from paid donors in continental Europe. We need more information about the blood donors to reverse the imbalance between production and use of blood products.

Aims: Previous studies have indicated that voluntary, non-remunerated blood donors are recruited more often from social classes 1–3 than from classes 4–5. In Oslo, average income levels are considerably higher in the Western than in the Eastern parts of the city. A pilot study suggested, however, a higher frequency of blood donors among people in Eastern than in Western parts. We wanted to test this in a larger cohort, and also ask for other reasons to become a voluntary, non-remunerated blood donor.

Methods: The Blood Bank of Oslo has ca 18 000 active blood donors, and ca 3,000 units of whole blood per month are collected in 3 sites. We used a paper-based anonymous survey to collect information of gender, age, donation site, current address, recent migration and number of donations. During a 5 week period, 1,715 answers were obtained, of which 1,386 were from inhabitants of the city of Oslo. City regions were compared using partial regression analysis.

Results: We present demographic data for the blood donors and donation sites. As reported by other blood banks, young men are under-represented compared to young women. The frequency of blood donors in Oslo can be estimated to 2.12 per 1,000 inhabitants, slightly higher than the national average. In Eastern parts, 1.99 per 1,000 are blood donors, significantly less compared to 2.26 in Western areas (P = 0.02). In city areas neighbouring the donation sites, average donor frequency is 2.59 per 1,000. In more distant areas, only 1.71 per 1,000 are donors (P < 0.001).

Summary/Conclusions: Our hypothesis about more blood donors in the low income Eastern areas was not supported by this study. Instead, we found significant effects on blood donor frequency when we compared areas near donation sites to more distant areas. We conclude that easy access to the donation site is a main determinator for blood donor recruitment. This is in line with our previous finding that practical obstacles (e.g., parking, opening hours) are often more important for donor return probability than motivation to donate (A. Misje et al, Vox Sang, 2010). To increase donation frequency in Oslo, it seems reasonable to consider opening another donation site in the areas distant from today's centers.

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#YOUTHTUBE – A CASE STUDY ON A BLOOD DONATION SHORT FILM COMPETITION – A 2-YEAR REVIEW

I Van Schalkwyk and M Gevers
Promotions and Public Relations, Western Province Blood Transfusion Service (WPBTS), Cape Town, South Africa

Background: Research has shown that an online video outperforms other online advertisement formats in building brand awareness and driving purchase decisions. In recognising that the youth holds the future of a safe and sustainable blood supply in their hands, the Western Province Blood Transfusion Service (WPBTS) in South Africa launched the #YouthTube competition in 2016.

Aims: The objectives of this competition were to drive brand engagement, promote blood donation and provide a platform for young, aspiring filmmakers to show their talent by creating a short film promoting blood donation.

Methods: Successful South African YouTubers (Grant Hinds in 2016 and Anne Hirsch in 2017) invited the youth to create a short film between 30 s and 3 min promoting blood donation. A detailed brief and the competition T's & C's were found on YouthTube tab on the WPBTS website.

There were 2 entry categories: individual school learner and individual tertiary learner. The competition deadline was 3 months. Entries were reviewed and 3 finalists were chosen per category. The finalists' videos were uploaded on the WPBTS website and the public was encouraged to vote for their favourite within a month, after which the voting was vetted and the winners were announced.

An invitation e-mailer and poster was sent to all secondary and tertiary institutions with details about the competition, as well as to film schools in and around Cape Town. A text message was sent to all youth blood donors. Additional promotion for the competition was done through the quarterly youth newsletter, social media and a radio advertisement.

Prizes included camera equipment for the category winners and spot prizes for voters.

Results:
- 12 Individual school learner entries were received in 2016; 5 in 2017.
- 8 Individual tertiary student entries were received in 2016; 14 in 2017.
- The number of video views in 2016 was 2,579 and 3,272 in 2017.
- The number of votes received was 624 in 2016 and 619 in 2017.
- The campaign costs in 2016 were approximately R175,000 in 2016 and R110,000 in 2017.
- The Facebook reach was 130,912 in 2016 and 335,367 in 2017.
- The number of impressions on Facebook was 571,738 in 2016 and 734,530 in 2017.
- The number of YouTube views in 2016 was 7,434 and 28,821 in 2017.

Summary/Conclusions: The campaign met the objectives set. The number of entries, video views, votes received, Facebook reach and impressions and YouTube views illustrated that the public engaged with the WPBTS brand and that the campaign has grown. Blood donation was promoted through the fantastic final videos that will have a much longer lifespan than the competition itself. The prizes will also help the winners further their passion for filmmaking.

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ANALYSIS OF THE IMPLEMENTATION OF THE LOYALTY PROGRAMME "EVERY DROP IS VALUABLE" IMPLEMENTED IN THE BLOOD CENTRE IN POZNAŃ

L Guliński, M Sokołowski and K Olbromski
Blood Center in Poznan, Poznan, Poland

Background: In Poland, the blood service is based on voluntary blood donation. The units authorised for the collection, processing, storage and distribution of blood and blood components for treatment are 21 Regional Blood Centres, Military Blood Centre and Blood Centre of the Ministry of the Interior Affairs. The Regional Blood Centre in Poznań is one of the largest centres in Poland. Throughout the country, the National Blood Centre (NCK) is the national coordinator for the activities concerning blood donation, separation of blood components and managing blood supplies. The NCK's specific tasks include, among others, suggesting solutions for ensuring self-sufficiency of the Republic of Poland in blood, blood components and blood products, as well as carrying out tasks related to health programmes in the field of blood donation and blood therapy. On 22 December 2016 at the initiative of NCK, a loyalty program financed by the Ministry of Health "Every drop is valuable" was implemented in the framework of the health policy programme entitled "Ensuring self-sufficiency of the Republic of Poland in blood and its components in the years 2015–2020". The aim of this program is to encourage current and potential blood donors to promote socially positive attitudes and behaviours. By collecting stamps in the so-called loyalty cards in exchange for donated blood or its components blood donors have the opportunity to choose symbolic rewards related to promoting the idea of voluntary blood donation.

Aims: Analysis of the effectiveness of implementation of the Loyalty Programme "Every drop is valuable" in the Regional Blood Centre in Poznań

Methods: The survey involved a group of 100 blood donors randomly selected from users of the loyalty program who filled in an anonymous questionnaire. The results of the survey were analysed taking into account the following indexes:

CSI (Customer Satisfaction Index) – Customer Satisfaction Index = sum of points awarded by customers in each category/number of categories.

Retention Rate RR – maintenance rate = (number of blood donors registering to donate blood again over a given period/number of donors donating blood in the previous period)* 100%

Results:
1. From 22 December 2016 to 31 January 2018 total number of 6,061 donors signed up for the loyalty program. In the mentioned period the number of donations from the participants of the programme totalled 16,109.
2. Among the users of the loyalty program 4,942 donors donated blood more than once.
3. In the analysed group 25% were women and 75% were men.
4. In the analysed group 70% of people were aged between 25 and 44.
5. In the analysed group 86% of the donors signing up for the loyalty programme obtained information about the loyalty program during their visit to the Regional Blood Center in Poznań.
6. The customer satisfaction rate was: 97.
7. The retention rate of the blood donors was: 19.5.

Summary/Conclusions:
1. The implementation of the loyalty program brought the expected results and proved to be effective in promoting the idea of voluntary blood donation.
2. In order to increase the evaluation indexes additional forms of informing donors about the possibility of participating in the loyalty programme such as social networking sites or online advertising should be applied.
3. When analysing the positive effect of the loyalty scheme it should be noted that it is a useful tool of correlation between voluntary donating blood and individual elements of management within the blood collection system.

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IS DONOR GIVING BLOOD AT WOODSTOCK FESTIVAL A RELIABLE AND SAFE DONOR?

E Przybylska and K Olbromski
Blood Center in Poznan, Poznan, Poland

Background: Woodstock Festival in Poland is the biggest music mass event which takes place every year in summer in Kostrzyn n.Odrą, Poland and which is attended by people from different subcultures. It attracts approximately 750,000 people from various age groups: from very young to mature participants. This festival is accompanied by various events from cultural ones such as theatrical performances, dance workshops, tutoring for personal development as well as events organized by different religious groups. There is also opportunity to donate blood. The blood collection at the festival is of high importance as the levels of ...stock" in blood centres during the summer are relatively low. At the same, such an event makes it possible to promote donating blood and educate wider groups if current and potential donors.

Aims: The aim of the analysis was to estimate the virus safety of blood collected at the Woodstock Festival.

Methods: The analysis is based on the data from the computer system Bank Krwi by Asseco regarding first time and repeat donors that donated blood at Woodstock Festival in Poland in years 2013–2017 focusing particularly on the donors with confirmed positive virus results.

Results: In years 2013–2017 the total number of 250,953 donors donated blood in the area of activity of Blood Centre in Poznań, 3291 donated blood at the Woodstock Festival which accounts for ~1% of the total number of donors. The average number of donations per event is 658. Following positive confirmed test results were recorded: 1 in 2013, 1 in 2014, 1 in 2015, 0 in 2016 and 2 in 2017.

Summary/Conclusions:
1. The number of donors donating blood at Woodstock Festival counted for 1% of the total number of donations.
2. The average number of donations per one event was 658 which significantly restocks the blood supply in the time of summer holidays.
3. The infected donors were first time donors hence the conclusion that the first time donors did not possess knowledge regarding donating blood and the means of potential virus infection.
4. Further educational activities on a wider scale regarding responsible donating blood must be carried out.
5. Growing number of repeat regular donors was observed which shows that the awareness and responsibility of these donors is increasing.
6. Although participants of this event are generally (and mistakenly) perceived as the group of increased risk, applying thorough methods of medical qualification and verification of donors using means of virus tests (serological and NAT methods) allows to conclude that blood collected at this event is safe for its recipients.
7. For many of the repeat donors giving blood at Woodstock Festival this event is the only occasion in the year when the decide to give blood which at the same time proves that it is possible to combine entertainment with helping those in need.

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VOLUNTARY NON–REMUNERATED BLOOD DONATION IN THE RUSSIAN FEDERATION

A Chechetkin[1], V Danilchenko[2], A Makeev[3] and I Krobinets[4]

[1]Blood Component Department, Russian Research Institute of Hematology and Transfusiology [2]Blood Service Organization Department, Russian Research Institute of Hematology and Transfusiology [3]Blood Transfusion Department, Russian Research Institute of Hematology and Transfusiology [4]Immunohematology Laboratory, Russian Research Institute of Hematology and Transfusiology, Sankt-Petersburg, Russian Federation

Background: Voluntary non-remunerated donation of blood and blood components is the basis for the blood service to obtain safe and effective blood products. The governmental Program of blood service development, aimed at the development of non-remunerated donation system, the creation of a common information base of blood and blood components donations and technical re-equipment of the blood service establishments are implemented in the Russian Federation.

Aims: The aim of this work was to study the dynamics of indicators of voluntary non-remunerated donation of blood and blood components in the blood service establishments in the Russian Federation.

Methods: Indicators of activity of blood service establishments in the Russian Federation in sectoral statistical observations over the period 2007–2016 and the calculation of indices characterizing the level of development of voluntary non-remunerated donation of blood and blood components were analyzed. Data are presented according to the administrative division of Russian Federation into Federal districts (FD).

Results: For the period 2007–2016, the proportion of voluntary non-remunerated donors in blood service establishments in the Russian Federation increased by 8.4% and reached 98.0%. The proportion of voluntary non-remunerated donors in the Siberian, Volga, Southern and North-Western FD varied from 98.2% to 99.5%. About 37.0% of regions of the Russian Federation had only voluntary non-remunerated blood donation. In recent years, there has been a progressive increase in number of voluntary non-remunerated plasma donors. The percentage of plasma donation from voluntary donors increased by more than 19.0%. The greatest number of voluntary non-remunerated plasma donations was observed in the Volga, Siberian and Central FD. Over a 10-year period, the volume of blood collected from voluntary donors has increased by 19.0%. About 13.0% of blood was collected in mobile units. The blood service establishments in the Central, Volga and Siberian FD collected the largest volume of donated blood. The proportion of first-time donors was 28.4% in 2016. Various actions were held to recruit blood donors and to retain them as regular donors of blood and blood components. Public institutions and non-profit organizations played an important role in this activity. For this purpose, educational and informational programs are created and the media channels and social networks are used.

Summary/Conclusions: During 2007–2016, there were positive changes in the indicators of blood donation from voluntary non-remunerated donors of blood and plasma in the Russian Federation. The percentage of voluntary non-remunerated donors increased by 8.4%, the percentage of voluntary plasma donations – by 19.0%, the volume of blood collected from voluntary donors – by 19.0%.

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DONOR DEFERRAL RATES AT THE DONOR INTERVIEW AFTER FILLING OUT DONOR QUESTIONNAIRE

L Espensen, M Eis Lund and K Titlestad

Klinisk Immunologisk Afdeling, Odense Universitetshospital, Odense C, Denmark

Background: A self-administered computerized donor questionnaire has been in place since 2009. The implementation reduced the number of cancelled donations after initial accept from approx. 100 per quarter to approx. 15 per quarter. The deferrals after initial accept has been in focus as they involved staff and utensils at the blood bank. But a number of donors are also deferred at the donor interview after filling out the donor questionnaire, as they don't fulfill the current donor selection criteria. These numbers has not been followed on a regular basis. However they are important as donors donate on a voluntary basis, and if deferred in the blood bank, they already spend time on showing up, without getting to donate. This could lead to a loss of the donor as several studies showed that deferred donors are less likely to return. Furthermore the staff has spent time to look through the questionnaire and talk to the donors, who are deferred. To be able to educate the donors about the selection criteria and facilitate self-deferral it is important to know the actual number of deferral and the reasons for deferral.

Aims: The aim of this study is to assess:
- The number of deferrals
- The reasons for deferral
- Ways to reduce the deferral rates

Methods: Donor data are stored in a blood bank system (CSAM ProSang, Stockholm). The data from the donor questionnaire were withdrawn from the database to generate a report on the reasons for deferral. Data from 01-06-2017 to 31-12-2017 are included.

Results: The results are divided into whole blood donors, and plasma donors because the selection criteria are different.

Totally 21,865 whole blood donors showed up, 1,039 (4.9%) of them were deferred. The reasons were mainly:

Medicine – 281 deferred donors (27.0% of the deferrals)

Quarantine due to travel – 267 deferred donors (25.7% of the deferrals)

Disease and operation – 279 deferred donors (27.0% of the deferrals)

Minor deferral rates due to dentist examination (3.3% of the deferrals), tattoos (2.7% of the deferrals), piercing (2.9% of the deferrals) and some minor reasons.

Totally 9,975 plasma donors showed up, 131 (1.3%) of them were deferred. The reasons were mainly:

Medicine – 33 deferred donors (25.2% of the deferrals)

Disease and operation – 40 deferred donors (31.3% of the deferrals)

Less often we found deferrals because of quarantine due to travel (3.8% of the deferrals), tattoos (5.3% of the deferrals), acupuncture (5.3% of the deferrals), piercing (2.3% of the deferrals) and some minor reasons.

Summary/Conclusions: In conclusions the results shows that the donors self-awareness of the deferral criteria could be improved regarding drug administration, travelling and disease and operation.

Our blood bank could benefit from better information both in the blood bank and on the websites in order to save time for the staff and prevent donors to waste their time when they show up for a donation and are deferred.

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PREVALENCE AND ETIOLOGY OF ANEMIA IN BLOOD DONORS DEFERRED BY THE COPPER SULFATE TECHNIQUE HEMOGLOBIN ESTIMATION

K Myamon[1], S Hlaingoo[1] and Y Naing[2]

[1]Blood Bank, General Hospital, Mandalay [2]Clinical Laboratory, General Hospital, Pakokku, Myanmar

Background: Donor selection is critical to blood transfusion safety. Unnecessary deferral is also important for blood adequacy. Anemia is one of the major causes of temporary donor deferral, which is preventable and treatable. Iron deficiency is the world's most widespread nutritional disorder, especially in developing countries. Moreover, Myanmar has high prevalence of important haemoglobinopathies: alpha thalassaemia, Hb E, beta thalassaemia. The copper sulfate method is used to screen blood donors for haemoglobin measurement at blood bank, General Hospital, Mandalay. However, it cannot be detect the etiology of anemia. Investigation of the etiology will benefit the blood donors by the prompt correction of iron deficiency or by proper guidance for haemoglobinopathies. This prompted the current study that aimed to determine the prevalence and etiology of anemia in deferred blood donors.

Aims: The aims of the current study were to determine the actual prevalence of anemia in blood donors deferred by the copper sulfate technique haemoglobin estimation and the etiology of anemia in deferred blood donors regarding iron deficiency anemia and haemoglobinopathies.

Methods: The study was done at blood bank, General Hospital, Mandalay, Myanmar. The study included 130 prospective blood donors deferred by the copper sulfate technique of haemoglobin estimation. Haemoglobin estimation was compared with that of automated screening method. The blood samples with haemoglobin level less than target value were tested for etiology of anemia (<12.5 g% in male and <11.5 g% in female). Serum ferritin estimation was done by chemiluminescence immunoassay e411. The identification of abnormal haemoglobins was verified by quantitative hemoglobin electrophoresis.

Results: Among 2,811 potential blood donors, 2,306 (82.03%) were fit for donation and 505 (17.97%) were deferred. The prevalence of anemia among the total deferred donors was 25.74% (130). Fifty eight (44.62%) of initially deferred donors presented normal hemoglobin levels by the automated method. Male female ratio was 2.2:5 in anemia donors. Among actual anemic donors, iron deficiency anemia was identified in 54.17% and Hb E trait was 23.61%. Beta thalassemia trait was 15.2% and alpha thalassemia was 4.17%. Hb E beta was 2.78%. Iron deficiency anemia is more

common in male (61.53%) than female. However, haemoglobinopathies are more common in female (42.37%).

Summary/Conclusions: The rate of temporary deferred donors for anemia is high. The discrepancies observed between the copper sulfate method and automated screening method suggest the need for standardization and constant control of haemoglobin screening method. Iron deficiency anemia is still major cause of anemia followed by haemoglobinopathies in blood donor population. The prevalence of Hb E is slight lower than that of general population. The prevalence of beta thalassemia trait is higher than that of general population whereas that of alpha thalassemia trait is lower. By recognizing the types of anemia, we can provide a guide for future development of programmes to improve the blood donors health and to promote donor recruitment so that we can achieve blood safety, our ultimate goal.

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ESTABLISHMENT OF INDEX SYSTEM FOR INVESTIGATION AND EVALUATION OF BEHAVIOR INTENTION AND RELATED INFLUENCING FACTORS OF REPEATED BLOOD DONATION

L Pan and W Hu

Blood Center of Zhejiang Province, Zhejiang Provincial Key Laboratory of Blood Safety Research, Hangzhou, China

Background: The data of blood donors in Zhejiang Province, China from 2006 to 2015 were retrospectively analyzed. The proportion of repeat donors was 30.8%, while the global proportion of repeat donors was 50%. To meet the increasing demand of blood for clinical use, it is necessary to increase the proportion of repeat donors.

Aims: To establish a highly reliable index system for the investigation and evaluation of behavior intention of repeat blood donation and related influencing factors, so that the system can be used to analyze the factors affecting the blood donation and to develop the strategy of first blood donor recall.

Methods: 1) Based on the Theory of Planned Behavior, the evaluation index system framework of behavior intention of repeated blood donation and related influencing factors was formed through literature research, open discussion and focus groups. 2) The expert consultation on the evaluation index system was carried out by Delphi method. 3) A total of 15 experts and scholars were selected to carry out comprehensive evaluation from the aspects of attitude, cognition of behavior control and subjective norms, to identify and screen evaluation indexes and assign weights to them.

Results: 1) The positive coefficient of expert consultation was 100%. 2) The degree of authority of the expert (Cr) was determined by two factors: the expert's basis for judgment (from 10 point to 1 points, from practical experience to intuition, expressed by coefficient of judgment Ca) and the expert's familiarity to the subject (from 10 point to 1 points, from very familiar to unfamiliar, expressed by coefficient of familiarity Cs). In this study, the expert's authority coefficient to the index system Cr was 8.2, so the expert's authority was considered to be high and the result was credible. 3) The coordination coefficient of expert consultation (W_1) was 0.58, then it was analyzed by Chi-square test, $\chi^2 = 301.4$, $P < 0.01$, so it was statistically significant and the expert evaluation opinion was well coordinated. Of these, the primary indicator of attitude $W_1 = 0.51$, $P < 0.01$, the primary indicator of subjective behavior criterion $W_1 = 0.55$, $P < 0.01$, and the primary indicator of perceptual behavior control $W_1 = 0.59$, $P < 0.01$. 4) There are 44 secondary indicators in the preliminary system of indicators developed in this study, and finally 30 credible and effective secondary indicators are obtained.

Summary/Conclusions: The evaluation index system established in this study is reliable and can be used as a tool for evaluating the motivation of repeat blood donors.

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INVESTIGATION AND ANALYSIS OF REGULAR PLATELET APHERESIS DONORS IN HANGZHOU AREA FROM 2012 TO 2016

K Fuxian, Z Yue, Y Li, F Qing and L Haifeng

Zhejiang Blood Center, Hangzhou, China

Background: The retention of regular blood donors are the basis of blood safety. To strengthen the construction of regular blood donors team and explore a more scientific concept and a more effective operation mode of the voluntary blood donors is a challenging task of the blood center staff. Understanding the composition of blood donors helps define the key populations to be recruited in the future and the direction of work during the 13th national five-year plan.

Aims: The aim of this study was to analyze the platelet apheresis donors in Hangzhou and the status quo of the construction of platelet apheresis donors team and to discuss improvement strategies in order to provide a scientific basis for the construction of platelet apheresis donors team in the 13th national five-year plan.

Methods: The distribution of sex, age, blood type, educational background, and the number of donations of platelet apheresis donors in Hangzhou from 2012 to 2016 were studied. The data were analyzed by SPSS 19.0 statistical software.

Results: The number and the amount of platelet apheresis donation from 2012 to 2016 increased 41.5% and 56.1%, respectively. The number of regular platelet apheresis donors and the number of regular platelet apheresis donations increased significantly (P < 0.001).In 2016, the amount of blood donated by regular platelet apheresis donors accounted for 91.6% of the total amount of blood, and increased by 107.2% compared with that of 2012. The proportion of new regular platelet apheresis donation increased from 17.6% to 45.0% (P < 0.001).The number of regular apheresis donors was O type > A type > B type > AB type, with more males (76.7%) than females (23.3%).The highest education degree was university degree or above, accounting for 48.1% of the donors and 83.5% of the donors were between 21 and 45 years old. The 21 to 30-years-old group showed a descending and the 41 to 50-years-old group showed an ascending trend. The numbers and donations of regular apheresis donors who only donate once a year decreased, while the numbers and donations of regular apheresis donors who only donate twice a year was accounting for 63.1% and 90.3%. The largest number of donations was the three to five times a year, accounting for 38.3%. The numbers of regular apheresis donors who donate over ten times a year in 5 years increased from 152 in 2012 to 562 in 2016 (269.7%),and donations increased from 1,867 in 2012 to 8,537 in 2016 (357.3%),while donors for six to nine times a year increased by 45.0% and 46.6% respectively.

Summary/Conclusions: Although the construction of platelet apheresis donors has achieved remarkable results, but there is great room for improvement and development. Accurate recruitment, retention and maintenance to target group were important for healthy and sustainable development of the construction of platelet apheresis donors.

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DETERMINATION OF THE PROPORTION FOR REPETITIVE ALTRUISTS DONORS DEFERRED BY LOW HEMOGLOBIN IN A BLOOD BANK AT INTERMEDIATE ALTITUDE

DM Baquero[1], M Garcia[2], A Rodriguez[3] and F Palomino[4]

[1]National Blood Bank, Colombian Red Cross [2]Unidad de Fisiología, Escuela de Medicina y Ciencias de la Salud, Universidad del Rosario [3]National Blood Bank, Colombian Red Cross [4]Fundación Para Alternativas A la Transfusión Sanguínea (FUATS), Bogotá D.C., Colombia

Background: Low hemoglobin levels are one of the main causes of donor deferral.

Aims: Identify the proportion of repetitive altruistic blood donors which were deferred exclusively due to low hemoglobin at the time of selection.

Methods: Considering that the repetitive altruistic donor is the most important input for a Blood Bank, this population was defined as any person who made two or more donations in the last 365 days including whole blood, plateletpheresis and erythropheresis. The total number of registered donations was selected from 2.011 to 2.017, as well as the total number of deferred donors registered in the HEXA-BANK software (Tharsis). Subsequently, only repetitive deferred donors were selected, because they had hemoglobin lower than 13.0 g/dl (women) or 13.5 g/dl (men), by means of their unique identification number. The cut point of hemoglobin used, applies to the resident study population at 2,650 m.a.s.l. For comparisons between populations, a student T test, or chi-square test, were used using the Sigmastat 3.1 software.

Results: The 5,901 repetitive donors contributed 20,586 donations, that is, 11.4% of the total received, with men being the most abundant (61%, 0) in the period

analyzed. Each repetitive donor made an average of 3.5 donations (range of 2–99). However, 99.8% made <50 donations, 60.9% from men, while within the group of donors with more than 50 donations, 83.3% were men (P = 0.11). We identified 174 episodes of deferral for low hemoglobin in repetitive donors (71.8% in women), of which 27 occurred more than once in the same donor (P < 0.05). Of this population, 70 people had at least one previous donation in the last year. The remaining 104 were donors who had at least one donation after having had a low Hb deferral. In the period studied, a total of 179,851 donations were collected, of which 90.9% corresponded to whole blood, 5.0% to plateletpheresis and 4.1% to erythropheresis. Out of 48,418 deferred donations, 16.2% corresponded to low hemoglobin, with more frequent exclusion in women than in men (2.3 times, P = 0.02) and in first-time donors than repetitive ones. Based on the data obtained, it is estimated that a repetitive donor in the analysis bank is five times less likely to be deferred by low hemoglobin compared to a first time donor.

Summary/Conclusions: Although the population of repetitive donors for the blood bank in the period analyzed represents 1 in 10 people, and the frequency of deferred by low hemoglobin in the total donor population was 16 per 100 donations, it is deduced that it is the non-repetitive donors the ones that have the greatest impact in this cause of deferral. Therefore, the data suggest that repetitive donation does not seem to be the cause of the appearance of low Hb that is reflected in deferral and eventually in the loss of a valuable repetitive altruistic donor.

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TRUE TALE OF OUTDOOR VOLUNTARY BLOOD DONATION CAMPS IN RAJASTHAN: A DOCUMENTARY

A Bajpayee

Department of Transfusion Medicine and Blood Bank, AIIMS, Jodhpur, India

Background: After 32 years of World Health Assembly resolution (WHA28.72) to establish efficient national blood transfusion services based on voluntary non remunerated donations (VNRD), our country is still facing the deficit of safe blood to our patients.. In Our National Blood policy formulated in 2002 the first objective is to provide safe and adequate quantity of blood and components and recommended action plan to achieve this objective is monitoring of blood transfusion services. To achieve a goal of 100% VNRBD, even though number of outdoor voluntary blood donation camps are markedly increased in our region but actually collection of blood does not guarantee he provision of safe blood to our patients as well as our donor safety. The driving force behind these camps is equally important.

Aims: The aim of our study was to assess the quality and safety aspects of VBDC and the actual status of Donor screening and donor selection methods followed in the outdoor blood donation camps. Our objective was to understand the current barriers in collecting a safe blood without compromising a donor safety.

Methods: The study period was March 2015 to February 2018 in which we had witnessed 76 Voluntary blood donation camps in various regions of Jodhpur district. Out of these 74 were outdoor blood donation camps and two were indoor camps inside the blood bank. National AIDS control organization (NACO, India) and Central Drugs standard control organization (CDSCO, India) has given guidelines to define the minimum basic standards to follow during an outdoor voluntary blood donation camps We evaluated the camps by tracking compliance in Five parameters: 1. Safety and hygiene in handling Biomedical waste 2. Donor Hemoglobin screening 3. Completion of Donor questionnaire and consent form 4. Post donation care and 5. Role of Incentives in Voluntary blood donation. We also made a small documentary on Mega blood donation drives which is a very common practice in our country.

Results: In this region 92% of Outdoor blood donation camps were organized by local community (cast) based organizations and local leaders only 8% of camps were conducted by educational institutions and offices. Noncompliance was observed in 100% of private standalone blood banks in all the five parameters and 80% of state government blood banks. The noncompliance associated with individual parameters varies from 80–95%. The number of blood units collected in these camps by various participating blood banks varies from 50–600, which also increases wastage of units due to outdate. The driving force behind these camps was also non altruistic.

Summary/Conclusions: In Mega blood donation camps Donor screening and post donation care was seriously compromised. It needs urgent attention of our National health policies makers. Our National blood policy is only defined in papers but still needs implementation even after 15 years of formation, there is no mechanism to evaluate adherence to guidelines. There is no regular and strict monitoring of blood banks by licensing authorities.

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ASSOCIATION OF AWARENESS AND LACK OF OPPORTUNITY WITH LOW RATE OF VOLUNTARY BLOOD DONATIONS IN PAKISTAN

SJ Ansari[1], H Shabber[2] and Z Zehra[1]

[1]Biosciences, COMSATS Institute of Information Technology (CIIT) [2]Federal Government Services Hospital and Post Graduate Medical Institute, Islamabad, Pakistan

Background: Voluntary Non-Remunerated Blood Donation (VNRBD) is considered safest for the transfusion. In Pakistan, concept of voluntary donation is rare. Continuously increasing blood demand is met mostly by the replacement blood donors arranged by the family of recipient. Under the currently practiced replacement system, pressure on the attendants of the recipient to provide blood donors before transfusion creates a huge risk on blood safety. Danger of multiple donations by a family member of the recipient with few days, arranging paid donors or instigating blood bank staff for pilferage of blood cannot be excluded.

Pakistan is one of the signatories of the World Health Organization's (WHO) resolution to reach 100% VNRBD by 2020. WHO, Government of Pakistan and Government of Germany are spending a huge budget and technical services on re-organizing the blood transfusion system in Pakistan. There are around 60 private Blood Donor Organizations currently promoting and collecting voluntary donations in Pakistan and despite various efforts from the government and private organizations there is no significant increase in voluntary blood donations. This study was done to dig out the reasons for low rate of VNRBD in Pakistan.

Aims:
1. To document knowledge, attitude and practices among population eligible for donation.
2. To help policy makers setting a strategy to promote VNRBD.

Methods: This cross-sectional study was conducted from January to December 2017 in which 616 individuals responded to a well-structured questionnaire. The respondents were residents of 58 districts across Pakistan. The data was collected by visiting several blood camps and universities. Data analysis was performed using R.

Results: From the total participants 36.2% (n-223) donated their blood at least once and 63.8% (n-393) were non donors. None of the donors were regular voluntary donors and donated blood for their friends or family in the replacement of transfusion. The survey was taken by 60% females (n-372) and 40% males (n-245). From the 36.2% participants who donated at least once, only 20.2% (n-45) were female and 79.8% (n-152) were male. Common reasons for non-donors were no opportunity 52.9% (n-208), lack of awareness 40.9% (n-161) and 6% (n-24) had fear of donation. 39% (n-227) of the respondents thought that blood is not screened in Pakistan and 40% (n-246) were not sure about it. 35.4% (n-218) were willing to become regular donors, 20.9% (n-129) were not and 43.7% (n-269) were not sure. Participants were aware about some basic questions apart from the volume of blood donated each time which only 20% answered correctly.

Summary/Conclusions: The study highly endorses that the eligible blood donors are less aware about the process and importance of donating blood. Females who are more than 50% of the population need to be targeted for the blood donor campaigns. Awareness about blood donation can be added in the curricula at high school and graduation level and opportunities can be created for the eligible blood donor community in the form of blood camps.

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KNOWLEDGE AND ATTITUDE TOWARDS BLOOD DONATION AMONG NON-BLOOD DONOR RESIDENTS OF KUALA TERENGGANU AT HOSPITAL SULTANAH NUR ZAHIRAH, KUALA TERENGGANU

S Mat Noh[1], H Mohamed Fauzi[1], F Abdul Karim[2] and M Kambali[3]

[1]Advanced Medical and Dental Institute, Kepala Batas, Pulau Pinang [2]Pusat Darah Negara, Kuala Lumpur [3]Blood Transfusion Unit, Hospital Sultanah Nur Zahirah, Kuala Terengganu, Terengganu, Malaysia

Background: The increment in blood utilization and reduction in blood collection leading to blood supply shortage has been a worldwide problem including Malaysia. It was noted that Terengganu recorded the lowest blood donation rate among all states in Malaysia for five consecutive years, from 2011 until 2015, and still lagging far behind despite the increment in the yearly usage of blood.

Aims: To determine the knowledge and attitude score towards blood donation and their association, among non-blood donor residents of Kuala Terengganu at Hospital Sultanah Nur Zahirah (HSNZ).

Methods: This was a cross-sectional study using a self-administered questionnaire that includes demographic data, knowledge and attitude section. Three hundred and twenty (320) participants who are non-blood donor residents of Kuala Terengganu attending HSNZ were selected using systematic random sampling.

Results: Forty-two percents (42.2%) of the participants had heard of blood donation through social media, while another 26.3% heard it on television and radio. In general, 207 (64.69%) of the participants have good knowledge towards blood donation with a mean score of 5.19 ± 1.87 out of possible 8. As for the attitude, 297 (92.81%) of the participants have a good attitude with a mean score of 70.79 ± 8.19 out of possible 100. However, there is no significant association found between knowledge score and attitude score (P = 0.122). Majority of the participants agreed with the statement of 'I do not want my blood to be given to other religions' (73.1%), followed by the statement of 'I do not want my blood to be given to other races' with 67.8%. Statements of 'I do not donate because the fear of needles' and 'Blood donation is painful' were being agreed with 55.9% and 55.0% of the participants.

Summary/Conclusions: The participants recorded a good mean knowledge score and mean attitude score pertaining to blood donation. This could be explained by more knowledge is being shared in the internet and social media by the providers and each and every individual from all age group and different sociodemographic background has an open access to this platform. However, being knowledgeable in this population does not mean that it will be followed by a positive attitude which can also explain the lowest blood donation rate recorded previously. This situation could be masked by the myths and false beliefs regarding blood donation that always spread around without any intention to correct it by gaining knowledge from the proper channel, especially with regards to blood donation with different religion and race, depending on the culture and custom of heredity of the different population. This is supported by the results from barriers to blood donation where most of the participants refused to give their blood to other race and religion. Generally, the knowledge and attitude towards blood donation were good; however, they were not significantly associated and it was not translated into practice. Blood Transfusion Service must focus on the barriers to donating blood and take appropriate steps to overcome the myths and false beliefs regarding blood donation that suits the multicultural background of the population. Enlightenment from the religious department and full use of social media for a two-way interaction could help in correcting myths and subsequently raise the awareness towards blood donation among the non-donor population.

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KNOWLEDGE, ATTITUDE AND PRACTICE TOWARDS BLOOD DONATION AMONG GENERAL POPULATION IN LIMA, PERU

J Paredes[1], BR Cordova[1], B Collantes[1], G Aguilar[1], R Ortega[1] and S Loyola[2]
[1]Universidad Nacional Mayor de San Marcos [2]Universidad Peruana Cayetano Heredia, Lima, Peru

Background: In Peru, voluntary blood donation is a scarce practice and represents less than 5% of available blood in blood banks. The lack of voluntary blood donors is a major public health challenge. The blood demand is mainly covered by replacement donors. Therefore, it is necessary to identify factors that affect the voluntary donation of blood that comes from general population.

Aims: To explore the knowledge, attitude and practice of blood donation among people in the community.

Methods: During October 2016, we conducted a pilot cross-sectional study among adults. Health care providers and health science students were not eligible to participate in the study. The participants were selected using a nonrandom sampling technique. All participants underwent oral informed consent and were surveyed in a public place in Lima, Peru. A structured survey was applied for collecting demographics, and knowledge, attitudes and practices regarding blood donation. We assessed associations between the future intention to donate blood with potential explanatory variables related to demographics, knowledge, attitudes and practices. Prevalence ratios (PR) were estimated using general linear models. Data analysis was performed in Stata v14 considering P < 0.05 as significant.

Results: Among the 137 respondents, 71 (51.8%) were males, 72 (52.5%) were between 17 and 30 years old, and 70 (51.1%) were professional workers. The knowledge regarding how blood is used, eligibility criteria related to age and weight, minimum interval of time between donations and blood safety was varied and even inadequate among the participants. The needle phobia, the lack of information of the donation process, distrust of the sterility of the material used for blood extraction and the believe that blood is subsequently sold were the most frequent reasons reported for not donating blood. One-third of respondents (45/137, 32.8%) admit having donated blood. Interestingly, 91.2% (125/137) highlighted the importance of blood donation, however, 83.2% (104/125) of them could donate in the future mainly

motivated by a sick relative or friend, or in a national catastrophe. Being between 17–30 years old was significantly associated to a better attitude for a future blood donation, followed by the group of 31–40 (P = 0.006). People between 41–50 years old (PR=0.76, P = 0.040) and people older than 50 (PR=0.65, P = 0.039) had a lower predisposition for a future blood donation compared to young people. Sex, work status and knowledge were independent predictors for future blood donation.

Summary/Conclusions: Our findings suggest that the level of knowledge related to the blood donation process is scarce and frequently mistaken. Despite the good attitude for voluntary blood donation, it is possible that the lack of information and fears represent the main barriers that prevent voluntary donation. Young people (<41 years old) could represent the target public to promote voluntary donation. Inform the community of the requirements and the blood donation' process could potentially increase the voluntary donation.

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ASSOCIATION OF SMOKING WITH CONCENTRATION OF HEMOGLOBIN IN BLOOD DONORS

E Protopopova[1], N Filina[1], M Gubanova[2], E Shestakov[3] and E Zhiburt[3]
[1]Krasnoyarsk Regional Blood Center No. 1, Krasnoyarsk [2]Stavropol Regional Blood Center, Stavropol [3]Pirogov National Medical Surgical Center, Moscow, Russian Federation

Background: The toxic effect of tobacco smoking is influence on rheological properties of blood, coagulation activity, hematological score, the development of inflammatory reactions.

Impact of tobacco smoking on the blood donor organism and predonation testing of donor is discussed.

Aims: To evaluate the impact of tobacco smoking on concentration of hemoglobin in blood donors.

Methods: Predonation blood tests of 500 donors were studied, 339 males, 161 females, mean age 34.5 ± 10.5 years. Association of hemoglobin concentration with sex, height, weight, age, smoking experience and number of cigarettes smoked per day was estimated.

Results: The mean concentration of hemoglobin in men is 147.6 ± 1.2 g/l, in women 128.5 ± 1.7 g/l (P < 0.01).

Association between hemoglobin concentration and age was not revealed. However the concentration of hemoglobin correlates positively with growth (r = 0.46, P < 0.001) and weight (r = 0.39, P < 0.001).

Hemoglobin concentration is higher in a group of smoking donors than in a group of non-smokers (146.8 ± 2.3 and 140.0 ± 1.4 g/l, P < 0.01) and increasing with a smoking experience (Kruskal–Wallis test, H = 106.8 at a critical value of (11.1), P < 0.001).

Positive correlation between concentration of hemoglobin and number of cigarettes smoked per day was established (r = 0.31, P < 0.001).

Summary/Conclusions: Hemoglobin concentration in blood donors is not associated with the age of the donor.

Hemoglobin concentration is higher among smoking donors, increases with a smoking experience and correlates positively with growth, weight and number of cigarettes smoked per day.

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Abstract has been withdrawn

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DONOR DEFERRAL FREQUENCY, REASONS AND RATES OF RETURN IN AN URUGUAYAN BLOOD CENTER

Y Lopez[1,2], M Rodríguez[1,2], M Bangueses[1,2], G Arago[3], A Kiriakidis[3] and J Curbelo[4]
[1]Hemotherapy Technicians Career Department, Escuela Universitaria de Tecnología Médica-Hospital de Clínicas, Facultad de Medicina, Universidad de la República Oriental del Uruguay, Montevideo [2]Blood Banking and Transfusion Medicine [3]Information and Technology [4]Director, Hemocentro Regional Maldonado, Maldonado, Uruguay

Background: Blood donor selection is a key step in blood safety. Donor deferrals play a major role in the relation between the blood bank and the donor base, since

it impacts both blood quality and the process of keeping a loyal and educated blood donor base. Deferral rates may vary between blood centers and countries, 10% being the rate most reported.

Aims: To analyzed all blood donations at our center for the period of 2017 and assess the rates and reasons for deferrals, and return after deferral.

Methods: We performed a retrospective analysis of our blood center database, with descriptive statistics analysis, as well as chi-square tests to compare deferred donors subpopulations ($P < 0.05$). Statistical analysis was performed with SPSS v.20.0.

Results: In 2017, 12,315 persons concurred to our center to donate blood, of which 2909 (23.62%) were deferred. 9.89% of these tried to donate voluntarily, while the rest (91.1%) were either for replacement or blood donor enterprise agreement. 96.83% were temporarily deferred, and 43.9% were women; there were no differences between mean age of both sexes (33.17 years for women; 34.06 years for men). 53.55% of deferred donors have at some point donated blood at our center (12.07% after being deferred in this period), 25.46% have been deferred more than once, and 28.81% have return after being deferred on that occasion; this number can adjust higher since some donors have not completed their temporary deferral period. Of returning deferred donors in general, we found no difference between men and women ($P = 0.10$).

The most important deferral causes were: low hemoglobin (9.34%), hypertension (8.68%), being under relevant medication or treatment (7.91%), sexual risk behavior (6.9%), hypotension (5.58%), flu-like state (5.33%), and recent surgery (4.53%); others include getting a tatoo in less than one year (3.77%), recent use of marijuana (3.17%), low weight (2.79%), recent vaccination (1.77%) and travelling to endemic zones (1.36%).

Not all the most significant deferred donor subpopulations behaved the same. Some deferred donors exhibit better return rates than the expected from the general deferred donor population; these differences are statistically significant. They include: hypotension (46% return, $P = 0.000$), hypertension (37%, $P = 0.003$), flu-like state (43%, $P = 0.000$) and recent use of marijuana (43%, $P = 0.001$). The lowest return rates were from low weight (2.5%, $P = 0.000$), body piercing (9.43%, $P = 0.002$) and sexual risk behavior (10.61%, $P = 0.000$). Also, low weight and body piercing deferred donors repeat with the lowest rates of effective donation at any time (17.5% and 26.42%, respectively), compared with all deferred donors (53.55).

Summary/Conclusions: Our center deferred 23.62% of the persons that presented at the facility to donate blood in 2017, with 96.83% of them deferred temporarily. 53.55% of all deferred donors donated blood, either before or after, and 9.89% were trying to donate voluntarily. Some subgroups of deferred donors returned more consistently, the most important being those deferred due to hypotension, hypertension, flu-like state and recent use of marijuana. Other subgroups almost never return, with those deferred due to low weight, body piercing and sexual risk behaviour being the most prominent. Age was not a factor for returning deferred donors. The analysis of the deferred donor population characteristics will provide the institution opportunities of planning, intervention and education at the moment of deferral, which can couple with promotion efforts, so the impact of deferral itself can be better understood by the donor.

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ASSESSMENT OF KNOWLEDGE AND ATTITUDES REGARDING HIV/AIDS AMONG BLOOD DONATION CAMPAIGN ORGANIZERS IN UVA PROVINCE, SRI LANKA

D Akmeemana, S de Silva, D Dayarathne and S Perera
Blood Bank, Provincial General Hospital, Badulla, Sri Lanka

Background: According to the 2016 annual report of the National STD/AIDS Control Programme [NSACP] in Sri Lanka, 23 voluntary blood donors were confirmed as HIV infected. There is an upward trend in the number of blood donors detected with HIV each year, and the possibility of transmitting HIV to patients through window period donations cannot be discontinued.

Mobile campaign organizers are the main recruiters of blood donors and a sound knowledge on HIV/AIDS will help them in identifying and recruiting safe blood donors.

Aims: Mobile blood donation campaign organizers in Uva Province, Sri Lanka for the year 2017 were assessed on 1: Basic knowledge on HIV/AIDS 2: Identifying high risk persons and populations in society 3: Methods of transmission of HIV and treatment options available 4: Attitudes in society towards HIV infected persons 5: Knowledge relevance to blood donation and transmission of HIV through blood transfusion. The study will also analyze the answers in relation to the educational qualifications of the mobile organizer and first time versus repeat campaign organizers.

Methods: A prospective study using a structured self administered questionnaire was handed over to the mobile organizer for data collection. Statistical comparison

was performed using Chi-square test by SPSS. $P < 0.05$ was considered as statistically significant.

Results: 303 mobile campaign organizers consented and participated in this study. Among them, 67 [22.12%] had studied up to ordinary level [O/L], 141 [46.53%] up to advanced level [A/L] and 95[31.35%] were graduates. 90 [29.7%] were first time mobile organizers and 213 [70.3%] were regular organizers.

When analyzing their basic knowledge on HIV/AIDS 88.8% knew that HIV was transmitted by a virus but only 37.6% knew that HIV infection cannot be identified at early stages of the disease with specific symptoms. 88.8% were aware that NSACP has facilities for free HIV testing at its clinics.

When identifying high risk populations in the society 60.1% identified correctly all the high risk categories and 71.3% knew that people with other sexually transmitted diseases bear a higher risk for contracting HIV and 59.1% had a good knowledge on methods of transmission of HIV.

Regarding the knowledge on blood donation and transmission of HIV only 71.9% knew that all blood units collected are tested for HIV before transfusion and 88.4% thought screened blood is 100% safe, unaware of the risk of window period donations. 88.9% of the responders knew that one infected unit can transmit the disease to several patients through blood components and only 54.2% of organizers knew that HIV infected blood donations have been detected in Sri Lanka.

This study also shows that there is a positive attitude among the participants towards HIV infected persons regarding their welfare and treatment.

When analyzing the above data in relation to the organizers level of education of up to O/L and above O/L [A/L & Graduate], those who had a high education level had a higher basic knowledge on HIV/AIDS [P: 0.008], Identified better the high risk population groups for contracting HIV [P: 0.003] and were aware of the window period for HIV testing and its risks [P: 0.012]. There was no significance for the above when we considered the first time versus regular organizers.

Summary/Conclusions: This study shows clearly that campaign organizers who are educated have a relative sound knowledge on the subject of HIV/AIDS and will be better recruiters of safe blood donors and conducting educational programmes for recruiters will increase the quality of the transfusion service.

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FROM FIRST-TIME PLASMA DONOR TO ESTABLISHING A ROUTINE: HOW DO DONORS DECIDE HOW OFTEN THEY WOULD LIKE TO DONATE PLASMA?

N Van Dyke[1], R Thorpe[1], K Jensen[1], B Masser[1,2] and T Davison[1]
[1]Clinical Services & Research, Australian Red Cross Blood Service, Melbourne
[2]School of Psychology, University of Queensland, St Lucia, Australia

Background: Demand for plasma products, and therefore for reliable plasma donations, continues to grow in Australia. First time plasma donor retention, and frequency of subsequent donations are pressing issues. Plasma donors in Australia can donate every two weeks, as opposed to every 12 weeks for whole blood, yet only 59% of plasma donors return within four months of their first plasma donation. Moreover, average plasma donation frequency is only 4.3 times per year. Previous research has explored the motivators, facilitators, and barriers that affect conversion to plasma donation; however there is little understanding of the initial experience of plasmapheresis and how to encourage new plasmapheresis donors to return to donate on a regular basis.

Aims: To explore what prompted first-time donors to convert to plasmapheresis and to identify their intentions to return to donate plasma in the future, and at which frequency.

Methods: Telephone interviews were conducted with 26 donors who had given their first plasma donation within the preceding 7–14 days. These donors were sampled to represent a broad mix of ages, genders, locations, and prior whole blood (WB) donation experience. Each interview was approximately 25 minutes in length and was recorded and transcribed. Qualitative techniques were used to code the interviews to identify key themes.

Results: Most study participants (n = 21) had little or no prior knowledge of plasma, and donated because a blood service staff member had asked them to consider it. Blood centre staff were also reported as the primary source of plasma-related information, including about frequency of donation, and an important source of support during the donation process.

All participants identified being able to donate more frequently as a benefit of donating plasma as compared to WB, because more frequent donation would allow them to help people more often, and to more easily establish a donation routine. While they all expressed an intention to donate plasma again, most indicated that they did not intend to donate at the minimum inter-donation interval in Australia

(every two weeks) because of other responsibilities and priorities in their lives. Donors indicated that the frequency at which they donated plasma needed to be often enough to be a meaningful contribution but not so often as to be a chore. For most, the preferred frequency was donating every four weeks.

Summary/Conclusions: These findings indicate that first-time plasma donors are positively oriented towards establishing a donation routine early in their careers. Importantly, decisions about future donations were made in the context of wanting to help as many people as possible through their donations, while also actively assessing how to fit this behaviour into their lives. In meeting this balance, most donors do not intend to donate as often as the blood service allows them to (every two weeks in the Australian context), but more often than is the current average. This provides preliminary support for introducing initiatives early in plasma-donor careers to assist donors in establishing a donation frequency that is substantially higher than the typical donation experience in this country.

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A FOLLOW-UP SURVEY OF KNOWLEDGE, ATTITUDES AND PRACTICES SURROUNDING BLOOD DONATION IN UGANDA BLOOD TRANSFUSION SERVICE

J Kimera

Blood Donor Recruitment Department, Uganda Blood Transfusion Service, Kampala, Uganda

Background: Blood donation is a remarkably safe medical procedure. However, attitudes, beliefs, and levels of knowledge may affect it. A range of socio-demographic, organizational, physiological and psychological factors may influence peoples' willingness to donate blood. Education had positive influence on attitudes towards blood donation as well as blood donors' satisfaction to the time and location of donation. The most common misconceptions about blood donation were the risk of infection, selling donated blood to patients, and that blood donation believed to cause physical weakness.

Aims:
- To measure the level of knowledge regarding blood donation
- To find out positive and negative attitudes
- To suggest some motivational factors

Methods: A cross-sectional study was conducted at Nakasero Blood Bank. Participants were selected by convenient non-random sampling technique. A self-created questionnaire was used for data collection between August 2017 and November 2017.

Results: The study included 349 individuals. About 45.8% of the participants claimed that they have a history of blood donation. Reported causes for not donating blood were blood donation not crossing their mind (52.4%), no time for donation (45%), and difficulty in accessing blood donation center (41.3%). Reported motivating factors for donating blood were one day off (81.4%), mobile blood donation caravans in public areas (79.1%), and token gifts (31.5%).

Summary/Conclusions: People in the age group 18–35 years, males and females, higher education and military were more likely to donate blood as well as people who showed higher knowledge level and positive attitude towards blood donation. Anthropological studies into blood donation are needed to plan an effective revised, targeted blood donation campaign and also to focus on some motivational factors are recommended.

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FEAR OF BLOOD, INJECTIONS AND VASOVAGAL REACTIONS IN THE CONTEXT OF BLOOD DONATION IN BRAZIL

ML Zucoloto[1], T Gonçalez[2], N Menezes[3], B Custer[2], W McFarland[3] and E Martinez[1]

[1]*University of São Paulo, Ribeirão Preto, Brazil* [2]*Blood Systems Research Institute* [3]*University of California San Francisco, San Francisco, United States of America*

Background: Blood banks around the world are struggling with a permanent deficit of blood and despite efforts to comprise the psychosocial factors associated with blood donation, so far little is known about the reasons for non-donation and the impact of different barriers for on blood donating behaviors on in distinct populations. The fear and the anxiety due to fear associated with blood donation are considered relevant barriers to blood donation in scientific literature. However, the fear of blood, injections, and vasovagal reactions was had never investigated in blood donation context.

Aims: To investigate the fear of blood, injections, and vasovagal reactions and their association with blood donation attitude and practice, in a sample of primary healthcare users in a Brazilian municipality.

Methods: This is a cross-sectional survey with stratified and representative sample. The interviews were carried out in 12 randomly-selected healthcare facilities. Study variables were: lifetime donation profile (frequency of donation, never donated, unable to donate); attitudes regarding blood donation among non-donors (intention to donate in the future, never thought of donating); and current donation profile (currently unable, donation only when needed, and blood donation frequency). To assess fear of blood (FBG), fear of injections (FIG), and fear of vasovagal reactions (FFI), we used the Blood Injection/Fear Scale (BIFS). We tested associations between variables using regression models and conditional inference trees (CIT).

Results: A total of 1,055 primary healthcare users participated (79.7% females; mean age=40.6 years (SD=15.2)); 63.4% never donated blood, 13.3% claimed they are unable to donate, 6.1% donated only once, 9.2% donated 2 to 5 times, 2.4% donated 6 to 10 times, and 5.6% donated more than 10 times. Females exhibited higher scores for FIG and FBG. FFI was associated with middle socioeconomic status among all study participants. Those who never intended to donate exhibited the highest scores in the three dimension of fear. According to CIT, gender is the variable that best distinguishes donors from non-donors. Being female and presenting high scores of FBG are characteristics associated with decreased blood donation. Among males, blood donation frequency is low among those aged 33 years and under.

Summary/Conclusions: Fear of blood, injections, and vasovagal reactions were associated with blood donation attitude and practice, and can be considered important barriers in blood donation decision in the Brazilian sample of primary healthcare users.

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ESTABLISHING BLOOD DONOR REENTRY STRATEGY FOR ANTI-HCV OR HCV NUCLEIC ACID TEST SCREENING REACTIVE DONORS IN CHINA

L Li[1], Z Liu[1] and Y Wu[2]

[1]*Clinical Blood Transfusion Research Center, Institute of Blood Transfusion, CAMS & PUMC, Chengdu, China* [2]*Bloodworks Northwest, Seattle, United States of America*

Background: Screening of blood donors for antibody to HCV and HCV nucleic acid test (NAT) is a well established venue to prevent HCV transmitted disease. However, with the current available technologies, HCV testing may result in donor loss due to false positive results. This study intended to establish a donor reentry procedure for HCV screening reactive donors in China.

Aims: Establishing blood donor reentry strategy for anti-HCV or HCV nucleic acid test (NAT) screening reactive donors.

Methods: This study was a collaboration between the Institute of Blood Transfusion (IBT) of Chinese Academy of Medical Sciences and 12 blood centers. All samples of ELISA and /or NAT screening reactive were collected and sent to IBT between Jan, 2014 and Sept, 2016. After confirmation and tracking, identification the donors were HCV antibody true positive or false positive.

Results: There were 796 samples were collected from twelve blood centers in China. Of these, 528 donors could be classified successfully: 135 true positives, 393 false positives. 268 donors were abandoned for unsuccessful follow-up. HCV antibody positive rate was 17% for anti-HCV/HCV NAT screening reactive donors.

Summary/Conclusions: According to the experimental results, a blood donor confirmation strategy for anti-HCV/ HCVNAT screening reactive donors was formulated: (1) If the results were ELISA and ID-NAT reactive, the donors were determined HCV antibody positive; (2) If the results were ELISA reactive and ID-NAT non-reactive, the RIBA were positive, the donors were determined HCV antibody positive; (3) If the results were reactive on anti-HCV and ID-NAT non-reactive, but RIBA was negative, follow-up after three months; (4) If the results were non-reactive on anti-HCV and ID-NAT reactive, follow-up after three months; According to the reentry strategy, 135 donors were determined true positives, 393 donors were determined false positives who can be reentered safely.

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Abstract has been withdrawn

POST DONATION NOTIFICATION, COUNSELING AND RESPONSE RATE OF REACTIVE BLOOD DONOR: AN IMPORTANT STEP TO PREVENT REACTIVE DONOR FROM RE-DONATING BLOOD

SA Ali, S Usama and M Mirza
Laboratory, Patel Hospital, Karachi, Pakistan

Background: Provision of safe and adequate blood is a fundamental part of blood bank services. A crucial step in the prevention of transfusion transmitted infection is to notify and counsel reactive donors blood donors. Post donation notification and counseling of sero-positive blood donors not only protect the health of the donor but also prevent secondary transmission of infectious diseases.

Aims: The aim of the study was to determine the response rate of reactive blood donor after notification of their screening status

Methods: This is an observational study carried out in Patel Hospital Blood bank over a period of 05 months from July – November 2016 involving total 1,539 donors. All sero-positive blood donors were informed by the blood bank staff about an abnormal test result with an advice to report to blood bank for counseling and for referral to respective department/clinics of the hospital for further management. The response rate of reactive donors after notification of their abnormal test results was evaluated

Results: The total reactive donors were 82(5.3%). 54(66%) reactive donors could be contacted of which 39(72%) responded positively to the notification calls and attended counseling at the blood bank and 28(34%) reactive donors could not be contacted either due to incorrect/changed contact details or did not picked up call even after three attempts

Summary/Conclusions: The response rate of the reactive donors was found to be 72%. The response rate of reactive blood donors in developing countries is quite low suggesting insufficient health care knowledge and a poor understanding of screening tests.

Abstract has been withdrawn

STRUCTURE OF BLOOD DONORS IN THE REGIONAL CENTER TETOVO

E Kocovska[1], T Timova[2] and E Velkova[3]
[1]ITM, Tetovo [2]ITM, Strumica [3]ITM, Skopje, Macedonia

Background: Through the analysis of the socio – demographic structure of blood donors in the Regional Center Tetovo, we can achieve significant information about several crucial issues, such as plans for boosting the number of voluntary donors, as well as, programs for gaining new blood donors.

Aims: To prepare a plan for stimulating blood donation in the region, especially the young population, with an emphasis on high school students and university students, due to the fact that the population is aging.

Methods: The study covers a one – year period, starting from January 2017 to December 2017, in the Regional Center Tetovo, which includes the blood donation at the Department of Transfusiology, as well as the mobile team on field, outside the Department. The input material used for this study was data from local blood donor registry.

Results: During the analyzed period were collected 1,542 blood units. 862 (55.9%) blood units were collected at the Department of Transfusiology, while 680 units (44%) were collected on the field, by the mobile team. The majority of the blood units were voluntary, more precisely 1,542 units (100%). Male donors have dominant participation in the blood units, 1,406 (91%), while female donors 136 units (8.8%). Blood donors who have donated blood for the first time have participation of 290 units (18.8%), while blood donors who have donated blood for several times have greater participation in the blood units, 1,252 (81.1%). Employed blood donors have dominant participation of 1,116 units (72.4%), over unemployed blood donors with 93 units (6%). 171 units (11.1%) were collected by high school students, while 149 (9.7%) were collected by university students. Retired population participates with only 13 units (0.84%). 629 units (40.8%) were donated by Macedonians, 893 units (57.9%) by Albanians, and 20 units (1.3%) were donated by other nationalities.

Even though, the percentage of blood units donated by Albanians is higher than Macedonians and other nationalities, we must put an emphasis on the fact that Albanian population is approximately 80% in Tetovo. Therefore, their participation is insignificantly higher.

Summary/Conclusions: Blood units in the Regional Center of Tetovo have been collected by two sources, which have almost equal importance. However, the study concludes that units collected at the Department of Transfusiology prevailed. Analyzed units show that the vast majority of the blood collected is voluntary. Most of the units are donated by male population. The majority of blood donors are those who have donated blood for several times. Employed population is crucial for blood donation. In terms of nationalities, Albanians donate more blood units than other nationalities. Our future intentions are to implement promotion activities in order to increase blood donation by females, high school and university students, unemployed people, all nationalities, especially Albanians because they are majority of the population in Tetovo.

THE IMPORTANCE OF VARIOUS METHODS IN RECRUITING BLOOD DONORS

B Hermundstad, A Llohn, T Knutsen and S Mousavi
Blood Bank, Akershus University Hospital, Lørenskog, Norway

Background: Adequate blood supply depends on a stabile donor corps. There is always a need to recruit new volunteers to replace the outgoing donors due to various reasons; age limits, migration, travel and other deferrals. Every blood bank should know the best methods to recruit volunteer blood donors.

Aims: The aim of this study was to provide knowledge about various methods by which blood donors are recruited to the Blood bank. It was investigated whether methods of recruitment were influenced by demographics or if they were changed over time

Methods: Data was collected using a questionnaire given to 1,498 donors. Donors were stratified into 1 of 3 recruitment groups: recruited by friends/colleagues, recruited by family and recruited by other methods (Red Cross webpage, media, recruitment campaigns, Facebook). To assess changes over time, donors were grouped into five periods: 1978–1990, 1991–2000, 2001–2005, 2006–2010 and 2011–2015.

Results: Compared to the group that was recruited by friends/colleagues, the group that was recruited by family had a significantly higher percentage of men (53% vs 43%) a higher percentage in the 18–35 age group (60% vs 48%) and a higher percentage with RhD negative blood types (35% vs 14%). In a logistic regression model RhD negative blood type was the single most important predictor of being recruited by family (adjusted odds ratio 3.7; P < 0.001). The proportion of donors who registered at www.Giblod.no increased significantly from 19% in 2006–2010 to 37% in 2011–2015. Over this period, the mean age at recruitment has increased, from 27 years (1978–1990) to 36 years (2011–2015).

Summary/Conclusions: Our findings show that the most effective method is that Blood banks encourage blood donors to recruit family members and friends/colleagues. Recruitment by family member becomes more important when the donors have less common blood types.

The increase in the proportion of people who register at www.Giblod.no as blood donor is encouraging.

BLOOD DONOR PROFILE – IS THERE ANY CHANGE AFTER 10 YEARS?

E Petkovikj, G Andonov, M Blagoevska, K Dimitrovski, R Grubovic, S Useini and L Mitevska
Institute of Transfusion Medicine, Skopje, Macedonia

Background: Improving the blood donation process is one of the missions and goals of the Institute for Transfusion Medicine (ITM) in Skopje for continuous providing sufficient amounts of safe blood.

Aims: The aim of the study is to analyze the structure of the donors who donated blood during the blood donor's sessions, organized by the ITM in Skopje and in Republic of Macedonia, studying some variables like gender and profession as well as first time donors.

Methods: This is a retrospective study performed by using data from the official records of the mobile teams and the donations in the ITM, for the years of 2007 and 2016.

Results: There were collected 17,115 blood units in 2007 and 25,501 blood units in 2016. From the total number in 2007: 13,711 (80.1%) were males and 3,404 (19.9%) were females; 8,032 (46.9%) were employed, 3,237 (18.9%) were unemployed, 4,008 (23.5%) were high school students, 1,670 (9.8%) were university students and 168 (0.9%) were retired ones. First-time blood donors were 3,495 (20.4%). In 2016: 19,666 (77.1%) were males and 5,194 (22.9%) were females; 17,646 (69.2%) were employed, 2,429 (9.5%) were unemployed, 2,977 (11.7%) were high school students, 1,690 (6.6%) were university students and 118 (3%) were retired ones. First-time blood donors were 3,304 (19.5%). Discussion: Around 80% of the blood donors are men, with increase of the women blood donors in 2016. The employed are the largest group among the blood donors with high percentage increase of 23% in 2016 vs 2007. There is double reduction of the unemployed blood donors and the high school students in 2016 vs 2007.

Summary/Conclusions: Development of better strategy for motivating and recruiting new blood donors among the youth especially, and keeping the regular donors is needed.

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ANALYSIS OF DONOR DEFERRAL FREQUENCY AND REASONS IN SOUTH OF IRAN

A Khosravi[1], M Jalalifar[1], A Salah[2], M Karimzadeh[3] and P Salehi-fard[4]

[1]Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran [2]Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Shiraz [3]Medicine Faculty, Shahid Beheshti University of Medical Sciences, Tehran [4]Medicine Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background: The main goal of the blood transfusion organizations is to provide a safe and adequate blood supply. To ensure that, stringent eligibility blood donor selection criteria must be implanted along with sensitive laboratory screening tests. Evaluating the donor deferral reasons can be useful in designing efficient donor selection strategies.

Aims: Evaluation of the blood donor selection and deferral pattern in the south of Iran.

Methods: This retrospective study was carried out on all volunteers who were admitted to Fars blood transfusion organization (FBTO) in the south of Iran, between the years 2016–2017. The total deferral rates of donors were analyzed within demographic characteristics and donor status. Thereafter, deferral reasons were calculated.

Results: Overly 451,932 blood donor volunteers were admitted during the study period. Among them, 115,014 (25.4%) were deferred from donation (11.57% permanently and 88.43% temporarily). Deferral rate in male and females were 90.2% and 9.8%, respectively. Moreover, the rates in regular, lapsed and first-time donors were 19.7%, 32.9%, and 47.35%, respectively. Seventeen percent of donors were deferred on physical examination. The most common causes of donor deferral were unsafe sexual contact (16.6%) and "tattooing, acupuncture, or ear piercing" (10.3%).

Summary/Conclusions: Our findings indicated that deferral rate in our country is slightly higher than other regions that may be caused by strictly donor selection criteria. Usually, the deferred blood donors will not return to donate blood and consequently high donor deferral rate leads to decreased blood donors' pool. Hence, the national guideline of blood donor selection should be reconsidered to decrease unnecessary deferrals.

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METHODS TO PREVENT MEDICAL WITHDRAWAL FROM BLOOD DONATION

BB Bakhovadinov[1], S Edalieva[2], M.A. Kucher[1], D Ernazarva[2] and D Pevtsov[1]

[1]Raisa Gorbachev Memorial Institute for Children Oncology, Hematology and Transplantation, St. Petersburg State Medical University, Saint Petersburg, Russian Federation [2]Republican Scientific Blood Center, Dushanbe, Tajikistan

Background: Medical withdrawal from blood donation remains relevant problem, which negatively affects the overall state of donation. One of the most frequent reasons is a decreased hemoglobin level associated with iron deficiency, which is revealed in 40–45% of blood donors. The determination of donor's ferritin concentration in serum allows identifying iron reserves.

Aims: To determine reasons of low hemoglobin levels in regular blood donors and to develop methods to reduce the number of medical withdrawal from blood donations.

Methods: For the assessment of tissue iron stores in blood donors, concentration of serum ferritin (SF) was determined by immunoradiometric assay method with "Immunotech" test-systems and routine hematological parameters were analyzed. The content of SF was determined in 2,000 blood donors, of which male were 51.4%, female – 48.6%. Similar parameters were examined in 100 female blood donors after 4 regular blood donations and in 100 male blood donors after 5 regular blood donations during one year. The comparison group consisted of blood donors (n = 200, including 100 men and 100 women) who underwent additional treatment with bivalent iron after each blood donation – 100 mg once a day for 3 days orally. Donor age ranged from 18 to 63 years (M±m = 28 ± 0.7).

Results: The content of SF, hemoglobin, erythrocytes and hematocrit differed in primary, regular blood donors and regular blood donors, with additional iron supplementation (Table 1).

Frequency of medical withdrawal from blood donation in primary donors due to low serum blood parameters was 18.4% – in men 4.2% and 14.2% in women. In donors with additional iron supplementation, the number of medical withdrawal due to low hemoglobin was in 4 cases and in 28 cases in regular donors who did not take iron, mostly female.

Summary/Conclusions: Regular blood donation in a hot and dry climate leads to depletion of iron reserves and an increase in the number of medical withdrawal from blood donation. Prophylactic use of iron prevents the development of iron depletion and reduces the likelihood of withdrawal from blood donation.

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UNDER–REPRESENTATION OF IRANIAN WOMEN IN BLOOD DONATION

L Kasraian[1], N Naderi[2], M Karimi[1] and L Tahmasbi[1]

[1]Blood Transfusion Research Centre, High Institute for Research and Education in Transfusion Medicine [2]Shiraz University of Medical Science, Anesthesiology Department of Shiraz University of Medical Science, Shiraz, Iran

Background: The under-representation of women in blood donation can create a blood shortage. This study was aimed at determining factors which encourage or impede blood donation in women.

Aims: The findings can help us to design effective recruitment strategies that could encourage women to donate blood to cover patients' need

Methods: This cross-sectional study was conducted in Shiraz, Iran between 1st January 2017 and 1st August 2017 on women aged 18–60 years old. The demographic characteristics of the participants were surveyed as well as the reasons that motive blood donors and the factors that deter non-donors .Reasons for lapses in donors were also mentioned.

Results: The most frequent reasons for blood donation were altruistic reasons (94.5%), moral and personal obligation (92.3%), a feeling of responsibility to help people (86.5%), and awareness of the positive effect of blood donation on their health (77.4%).The most common deterrents to blood donation in non-donors were the fear of developing anemia (68.4%),the fear of weakness and dizziness (66%), unsuitability due to certain medical conditions (62.4%), and had never been in a situation in which they were asked to donate blood(61.8%).

Summary/Conclusions: In spite of the figures which indicate altruistic reasons as the chief motivating factors for women to donate blood and assuming blood donation as a worthy act, the overall female contribution in blood donation remains low. Therefore, it is necessary to implement measures aimed at informing women about the importance of blood donation and steps must also be taken to allay fears based on misinformation. Confidence in the blood donation organization must be a major consideration in future recruitment strategies to reassure women about the safety of blood donation. Finally, further measures to prevent and correct anemia must be implemented.

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THE STUDY OF MEDICATIONS DEFERRAL RATE AMONG KHOUZESTAN BLOOD TRANSFUSION SERVICE (6 YEARS EXPERIENCE)

M Ehtiati[1], M Jalali Far[2,3], J Torabi Zadeh Maatughi[4] and F Fayezi[5]

[1]Vice-Chancellor in Treatment Affairs, Shahid Beheshti University of Medical Sciences [2]Blood Transfusion Research Center, High Institute of Research & Education in Transfusion Medicine, Tehran [3]Thalassemia and Hemoglobinopathy Research Center, Ahvaz Jundishapur University of Medical Sciences [4]Blood Transfusion Research Center, High Institute of Research & Education in Transfusion Medicine [5]Secondary Education, Ministry of Education, Ahwaz, Iran

Background: Provide safer and adequate blood supply is the main goal of all blood transfusion organization. That goal achieved by selecting appropriate blood donors. The medication is one of causes of exclusion of blood donors due to their effect on donor and/or recipient's health. Medications affect the donations by two mechanisms: showed the disease that donor take medication for it and the second mechanism is the drug metabolites that exist in blood circulation and in some situation maybe teratogenic and affect the health of recipients. As that reason the blood organization take strict strategies for guarantee safety both of the blood donor and recipients.
Aims: Study the deferral rates among our blood donors is helpful in evaluating the success of our donor counseling and identification the rate and at-risk donations.
Methods: Our retrospective study was included the blood donor that referred to Khuzestan blood transfusion service (KHBTS) for six years (2011–2017) and excluded from blood donation due to medications. Donor's information analyzed by statistical software.
Results: The total deferral blood donors were 247,991 people. Total temporary and permanents deferral rate showed irregular variation, it was 92.5% and 7.5% in first year of study and 90.95% and 9.05% in the sixth year respectively. The exclusion rate due to medication showed significantly decrease from 18.3% (8,562/47,494) to 9.52% (3,424/35,970) in beginning and the end of our study. Most of deferred donors was males. The deferral rate among donation type showed fluctuation during our study period. At the beginning was 45.19% (3,869), 20.15% (1,725) and 34.66% (2,968) among firs time, lapsed and regular blood donors and the pattern changed at last year as the follow: 33.86% (1,053), 30.66% (1,050) and 35.48% (1,215) respectively.
Summary/Conclusions: Our finding showed effective strategy in reduce the rate of medication deferral. The high number of medications in lapsed and regular donors need the corrective action. The informative materials should be provided and available based on updated list of the common drugs that causes in deferral for lapsed and regular blood donors. Because the easy access to drugs in our country without physician's prescription, enhancement the blood donor's knowledge about self-therapy effects on health of donors and recipients is highly recommended. Due to general tendency to traditional and herbal medicine and because the most of donors don't account the herbal medicine as medications, the blood transfusion should updated the deferral causes by considering the herbal as medication.

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A QUALITATIVE EXPLORATION OF THE MOTIVATING FACTORS FOR BLOOD DONATION IN REGULAR DONORS AND UNIVERSITY STUDENTS

H Wang[1], P Huang[2], K Chen[3] and S Sun[4]

[1]Technology Division, Taichung Blood Center, TBSF [2]Sociology, Tunghai University [3]Component Processing, Taichung Blood Center, TBSF [4]Director, Taichung Blood Center, TBSF, Taichung, Taiwan

Background: Many studies showed that altruism has been the most important motivating factor for blood donation. This study examines in what sense and to what extent altruism motivates blood donation in regular donors and university students with qualitative exploration.
Aims: A generic concept of altruism is unable to capture diverse motives behind a variety of altruistic behaviors. Drawing on focus group interviews, this study tries to identify different situations of and motives for first-time and repeated blood donation in young and regular donors.
Methods: 19 participants recruited from data bank of Taichung Blood Center were arranged into four focus groups, including three of regular donors and one of university students, and were asked semi-structured questions concerning their respective situation and experience of blood donation. Interviews were audio-taped, transcribed and then using content analysis to specify patterns of situation and motivation. Four focus groups were conducted from April to October, 2017.
Results: The study found that generational subculture plays a significant role in blood donation behavior. It seems that calling-up is quite common for younger people in many social activities including blood donation. This implies that altruistic motives may not be a major motivating factor for altruistic behaviors in younger generation. Moreover, we identify two types of altruistic motives in regular blood donors. Interviewees view blood donation as good deed or benefaction in a belief that it might bring retribution in return, either to themselves or to their families in the future, or to health statues. Inspired by evolutionary biology, we conceptualize such culturally-influenced altruistic motives as reciprocal altruism.
Summary/Conclusions: Our findings showed that altruistic behaviors might not motivated by concern for the welfare of others. Altruistic motives may also involve reciprocal or self-interest motives. Our findings may be heuristic in developing effective strategies for recruitment and retention of blood donors among different generations.

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Abstract has been withdrawn

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CUPPING AS A MAJOR CAUSE OF BLOOD DONOR DEFERRAL RESULTING DONOR LOSS IN IRAN

M Jalali Far[1,2], A Salah[3], A Khossravi[1], M Shirmohammadi Esfeh[3], M Paridar[4] and M Ehtiati[5]

[1]Blood Transfusion Research Center, High Institute of Research & Education in Transfusion Medicine, Tehran [2]Thalassemia and Hemoglobinopathy Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz [3]Blood Transfusion Research Center, High Institute of Research & Education in Transfusion Medicine, Shiraz [4]Deputy of Management and Resources Development, Ministry of Health and Medical Education [5]Vice-Chancellor in Treatment Affairs, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background: To provide a safe blood supply, select suitable donors with the lowest risk is critical. Many of blood donors are deferred each year, do not return to donate blood and resulting loss of donors. Wet cupping therapy (WCT), called Hijama, is common in Muslim countries and lead to many donor deferrals. Many strong reports have shown that WCT significantly increased the risk of bloodborne infections, including HIV, hepatitis B, and hepatitis C infections.
Aims: To evaluate of cupping as a cause of blood donor deferral
Methods: This retrospective study was carried out on all volunteers who were admitted between the years 2016–2017. The total deferral rates of donors were calculated. Thereafter, deferral caused by WCT were analyzed.
Results: Totally 115,014 (25.4%) were deferred from blood donation. Out of that 9,848 (8.5%) were deferred because of WCT history. WCT caused deferral in 6.1%, 10.03% and 8.53% of regular, lapsed and first-time donors, respectively. The rate of donor deferral because of WCT increased from 7.89% in 2016 to 9.2% in 2017.
Summary/Conclusions: In the spite of the high risk of bloodborne pathogens infections and also an absence of evidence supporting the efficacy of WCT, its practice is increasing in our country. The national standard should be designed for licensing of WCT practitioners to decrease the risk of infection. Moreover, people must be informed about the risks of WCT thorough mass media.

BLOOD DONATION ACTIVITIES IN THE REGION OF STRUMICA DURING THE FIVE-YEAR PERIOD FROM 2012 TO 2017

T Timova[1], E Kocovska[2] and E Velkova[3]

[1]Strumica, Institute of Transfusion Medicine of Republic Of Macedonia, Strumica [2]Institute of Transfusion Medicine of Republic of Macedonia, Tetovo [3]Institute of Transfusion Medicine of Republic Of Macedonia, Skopje, Macedonia

Background: Today blood is a powerful means of treatment which brings the hope back to the ill and the injured. We cannot imagine modern health care of the population without enough blood and blood components reserves. The Department of Transfusion medicine, as a specialized branch of medicine, serves as a mediator between the humane blood donors and the patients.

Aims: In order to obtain blood that will satisfy the need and secure minimal reserves of blood in our country, it is necessary to motivate citizens to donate blood. The aim of this study is to conduct a review of blood donations in the region of Strumica, and to show the efficiency of the Department of Transfusion medicine - Strumica, in obtaining enough blood and blood components necessary for the treatment of the ill and the injured patients in Strumica. At the same time it will conduct an analysis and a review of the profile of the blood donors by sex, age, profession etc.

Methods: The data were obtained from the Department of Transfusion medicine-Strumica. In this retrospective study, a period of 5 years (2012–2017) has been analyzed, and the number of blood donors has been recorded by year and structure.

Results: The number of blood units during the last five years has been oscillating, so that in 2012 were obtained 1701 blood units, 2013–1819, 2014–2042, 2015–1900, 2016–1830, 2017–1705. The total number of blood units collected at the Department of Transfusion medicine – Strumica during this five-year period is 10,997 units. According to the profile of the blood donors, most of them are voluntary blood donors 10,463 (95.19%), relatives 504 (4.81%). Of the total number of blood donors 6,411 (58.3%) are employed, 2,782 (25.3%) are unemployed, 1,210 (11.0%) are high school students and 561 (5.1%) are university students. According to sex, 9,281 (84.4%) are male donors and 1,716 (15.6%) are female. With blood group A were 4,311 (39.2%) blood donors, with blood group O were 3,706 (33.7%), with blood group B were 2,078 (18.9%) and with blood group AB were 869 (7.9%) blood donors.

Summary/Conclusions: Although all patients' blood requirements are satisfied, in order to achieve and keep positive atmosphere for donating blood it is necessary to carry out regular activities for informing, educating and motivating people to donate blood, starting with the youngest population with special attention to those target groups who have not showed enough interest for donating blood. The aim of these activities is to increase the number of new young blood donors and to keep the regular blood donors.

Abstract has been withdrawn

DOES THE ONGOING REPLACEMENT/FAMILY DONOR SYSTEM IN LEBANON RESPECT THE ETHICAL VALUES OF DONATION?

A Haddad[1,2], T Bou Assi[3,4] and O Garraud[5,6]

[1]Clinical Pathology and Blood Banking, Sacré-Coeur Hospital, Lebanese University, Beirut, Lebanon [2]Faculty of Medicine of Saint-Etienne, University of Lyon, Saint-Etienne, France [3]Laboratory Medicine and Blood Bank, Saint Joseph Hospital, Dora [4]Laboratory Medicine, Psychiatric Hospital of the Cross, Jaledib, Lebanon [5]Institut National de la Transfusion Sanguine, Paris, France [6]Faculty of Medicine of Saint-Etienne, University of Lyon, Saint Etienne, Lebanon

Background: Lebanon have a decentralized/fragmented transfusion system in which blood supply system is mainly based on replacement/family donation (around 80%) followed by compensated and voluntary donations. This current system doesn't meet the World Health Organization (WHO) recommendation which firmly advise all countries to establish a blood supply based exclusively on Voluntary Non Remunerated Blood Donation (VNRBD) and consider such donors as the only safe and sustainable mode of supply. According to the WHO, VNRBD is the only mode that respects all ethical values of blood donation. These values were defined by the International Society of Blood Transfusion (ISBT) code of ethics that was later endorsed by the WHO and includes mainly: volunteering with absence of coercion or financial incentives, sense of responsibility of donor towards releasing information during the pre-donation interview, anonymity between donors and recipients, protection and respect of the individual's rights (confidentiality), protection of donor's health and safety, adequate information regarding potential risks or adverse events provided for donors, respect of internationally scientific standards and donation under the responsibility of a suitably qualified, registered medical practitioner.

Aims: To describe the features of the replacement/family donor system in Lebanon in order to determine whether this predominant mode of donation respects the ethical values of VNRBD.

Methods: An analysis of all the published work in Lebanon related to the recruitment and motivation of replacement/family donors was initially conducted then followed by a deep interpretation of the current situation based on our personal experience as specialists in transfusion medicine.

Results: Volunteering is not completely free since donor undergoes family or social (friends/acquaintances) coercion; thus, the motivation for donation is not based on pure altruism but on restricted solidarity. While answering the questions of the pre-donation interview, the awareness of responsibility might be affected too by the social coercion. Even though the donor receives no payment or any other financial substitute, the moral profit of "debt of gratitude" towards the receiver is always present. The anonymity is not fully respected since patient might know the donor or vice-versa and despite the fact that the donation itself will not mandatorily be transfused to the recipient. However, donor's rights are usually respected since there is no discrimination of any kind, including gender, race, nationality or religion. All information's are adequately provided with respect of international standards despite the fact that the blood bank staff in around half of the facilities is not always qualified with an available qualified registered medical practitioner.

Summary/Conclusions: Despite that replacement/family donor system is the major blood supply in Lebanon that repeatedly proved its efficiency especially in emergency situations; however, its features don't fully respect the ethical values of VNRBD and places in addition the transfusion environment under some form of pressure because of the replacement supply. Moreover, the safety of this type of donation is debatable. Consequently, there is no doubt that Lebanon needs to transform its current replacement based blood supply to VNRBD based system in order to respect the ethical values of donation and increase its blood safety level.

Blood Collection Incl. Apheresis

COLLECTION EFFICACIES OF A NEW APHERESIS SYSTEM FOR DOUBLE DOSE PLATELET COLLECTION

P Kitpoka, W Thienphopirak, S Chanthet, S Chiawchan and P Phattanachak
Pathology, Ramathibodi hospital, Bangkok, Thailand

Background: New generation apheresis systems enable a multiple unit collection of platelets from the one eligible donors in a single procedure. The advantages of this procedure are to maximize donor resources, minimize risk of transfusion transmitted diseases and reduce production costs.

Aims: The aims of this study is to evaluate the performance and collection efficacy of the AmiCORE Apheresis System, Fresenius Kabi AG, Germany for collection of double dose platelet (DDP). The platelet quality characteristics and donor safety were also evaluated.

Methods: Eighteen repeated donors were recruited for DDP. DDP were collected in 100% plasma for the target of 5.6×10^{11}. Donor pre- and post-donation parameters, procedure and platelet quality characteristics were measured. Donor reaction were observed.

Results: Prior to platelet collection, Donors for DDP collection had an average platelet count of $313 \pm 43 \times 10^3/\mu l$. None of the donors have post-donation platelet count less than $100 \times 10^3/\mu l$. Red cell loss from DDP collection averaged 21 ± 1 ml. Collection times averaged 87 ± 21 min. The DDP collections had an average platelet collection efficiency of $82.59 \pm 5.56\%$, producing a total average platelet yield of $6.50 \pm 0.44 \times 10^{11}$. The average actual to targeted platelet yield ratios was 1.16 ± 0.08. All of DDP had residual white blood cells $‹1 \times 10^6$/unit. No adverse events were reported from any donors.

Summary/Conclusions: The efficiency and safety of DDP collection by the AmiCORE Apheresis System has been revealed in this evaluation. Leukoreduced platelets had acceptable characteristics and passed international standard requirement.

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THE EFFECT OF PLATELETPHERESIS FREQUENCY ON DONOR COAGULATION AND PLATELET FUNCTION

Q Feng, F Kong, J Chen, J Ye and C Li

Donation, Zhejiang Blood Center, Hangzhou, China

Background: Single-donor platelets (SDP) transfusions are effective for the prevention and treatment of bleeding in patients with platelet number and/or function disorders. The demand for SDP has been growing steadily in China. However, due to the limited number of plateletpheresis donors, the imbalance between the clinical demand and supply of SDP becomes increasingly prominent. To alleviate the shortage of supply, the plateletpheresis interval was modified from 28 to 14 days and the annual donation frequency from 12 up to 24 in 2011 according to amendments of the national blood donation law. After the adjustment, plateletpheresis frequency of donors was significantly increased in our center, yet it was not well known whether the adjustment affected the coagulation and platelet function of donors.

Aims: The aim of this study was to systematically evaluate the effect of plateletpheresis frequency on donor coagulation and platelet functions using thromboelastogram (TEG).

Methods: We selected 117 cases of regular plateletpheresis donors in Zhejiang blood center from 1 August 2016 to 31 July 2017. According to the frequency of plateletpheresis, donors were divided into 3 groups: 6–11, 12–17 and 18–24 times annually. We also selected 32 cases of first time plateletpheresis donors as control group. The blood samples were collected before donation. Coagulation and platelet functions were tested using TEG (Haemonetics company, Braintree, MA, USA). Platelet counts were tested by a SYSMEX XS-800i blood cell analyzer. The results were statistically analyzed using SPSS (version 19.0). Comparisons among different groups were analyzed using one-way analysis of variance and $P < 0.05$ was set as significantly different.

Results: Results: The values of R, K, α-Angle, MA, PLT, MPV and PDW of the four groups were all in the normal ranges. All parameters were not statistically significant among the four groups (F = 0.164, 0.065, 0.165, 0.697, 0.239, 0.204 and 0.273, respectively, P > 0.05). There was also no significant difference between any two groups. The correlation between plateletpheresis frequency and R, K, α-Angle, MA, PLT, MPV, PDW values was not statistically significant (R = −0.053, 0.067, −0.097, −0.099, −0.043, −0.002 and −0.005, respectively, P > 0.05).

Summary/Conclusions: The frequency of plateletpheresis ranging from 12 to 24 donations annually does not affect PLT counts and function, nor does it affect coagulation function in plateletpheresis donors.

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IMPROVEMENTS OF PLATELET YIELDS AND COLLECTION EFFICIENCY IN A NEW APHERESIS SYSTEM DURING EVALUATION BY OPTIMIZING DEVICE PARAMETERS

AK Tiwari, D Arora, G Bhardwaj, G Sharma, G Aggarwal, S Pabbi, A Ratan and D Setya

Transfusion Medicine, Medanta-The Medicity hospital, Gurgaon, India

Background: Institutional Quality Assurance (QA) program requires any new equipment in the facility to be evaluated for performance before putting them into routine use. AmiCORE Apheresis System is a new generation of continuous-flow centrifugation apheresis device, which uses a one-time use, single-needle disposable kit with ACD-A, as the anticoagulant and saline volume replacement for single-dose platelets (SDP) and double-dose platelets (DDP). During the initial evaluation of the AmiCORE (Fresenius Kabi AG, Germany) it was found that the platelet yields and collection efficiency were sub-optimal. The manufacturer was apprised and they in turn made changes to the parameter settings of the device for improving the Operational Performance (OP).

Aims: The aim of the study was to evaluate the OP before and after the "device parameters optimization" by the manufacturer.

Methods: All donors were healthy and met the statuary donation criteria. Each donor was given 1,000 mg oral calcium just prior to the procedure as part of institutional Standard Operating Procedure (SOP) and adverse reactions, if any, were noted. The device was set up with the basic default settings of 8:1 whole blood: anticoagulant ratio, a citrate infusion rate of 1.25 mg/kg/min, inlet flow rate of 100 ml/min and return flow rate of 120 ml/min. 15 consecutive SDP procedures were performed with a target yield of 3.5×10^{11}. OP data of these procedures was collected and analyzed. This included donor pre-and post-donation platelet counts, red-cell and plasma loss, volume of whole blood processed, collection time, flow rates and platelet product quality characteristics (actual platelet yield, swirling, pH and residual WBC count). Primary performance parameters such as Platelet Yield, Actual vs.

Targeted (A: T) ratio and Collection Efficiency were assessed. As these parameter results were sub-optimal, the manufacturer was informed of the results along with the data. The manufacturer analyzed the submitted data as well as the data downloaded from the device. In order to optimize the device performance, they made three changes in the machine; Set-point, Yield Adjuster and Input Hematocrit.

Another 15 SDP procedures were performed with the same target platelet yield of 3.5×10^{11}. OP data of these procedures was also collected and analyzed as done for the earlier procedures.

Results: Primary performance of the device was similar pre- and post-optimization except for platelet yield, ratio of actual vs. targeted yield and CE. Donor vitals and procedure details did not vary with statistical significance. Device optimization did change the Platelet Yield, A: T ratio and Collection Efficiency in a statistically significant manner. Platelet yield was 2.77×10^{11} and 3.88×10^{11} pre- and post-optimization, respectively a percent increase of 40.4% with a P-value of 0.00027. A: T was 0.791 and 1.110 pre and post-optimization, respectively a percent increase of 40.4% with a P-value of 0.00027. Collection Efficiency was 56.7% and 76.5% pre- and post-optimization, respectively a percent increase of 34.8% with a P-value of 0.00064.

Summary/Conclusions: This study shows how initial operational qualification of equipment as part of a QA program and partnership with the manufacturer can play an important role in the successful implementation of new devices for an institution.

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IMMUNE ADHERENCE CLEARANCE PROVIDES A GENERIC APPROACH TO DEPLETE PATHOGENS FROM THE BLOOD STREAM OF SEPTIC PATIENTS

DZ de Back[1], S Nezjad[2], B Beuger[3], M Veldhuis[4], E Clifford[4], F Ait-Ichou[4], J Berghuis[4], E Gouwerok[4], S Meinderts[3], H Vrielink[1], W de Kort[5], D de Korte[6], M van Kraaij[7] and R van Bruggen[3]

[1]Department of Transfusion Medicine [2]Department of Donor Affairs [3]Department of Blood Cell Research [4]Department of Red Blood Cell Diagnostics [5]Department of Donor Studies [6]Department Product and Process Development [7]Department of Transfusion Medicine and Donor Affairs, Sanquin Blood Bank, Amsterdam, Netherlands

Background: Apheresis is increasingly being applied to collect cells or plasma, even allowing the collection of multiple blood components during one procedure. Although the quality of the cellular and plasma products that are obtained by apheresis have been extensively studied and shown to be of high quality, the impact of apheresis on the red blood cells (RBCs) that are returned to the donor has not been thoroughly investigated.

Aims: The aim of our blinded prospective study was to investigate the impact of plasma-/ plateletapheresis on RBCs that are returned to donors using the devices that are currently in use by the Dutch National Blood Bank Sanquin: MCS+, PCS2, Trima Accel, and Auto-C.

Methods: The effect of the plasma,- or plateletapheresis procedures by four different devices: MCS+ (Haemonetics), PCS2 (Haemonetics), Trima Accel (Terumo BCT) and Autopheresis-C (Fresenius Kabi), on the RBCs that are returned to the donor was tested in a blinded, prospective trial in a cohort of 25 donors.

Results: A rheologic analysis of donor RBCs prior to and after plasma-/ plateletapheresis showed no differences in outcome. However, a strong increase in hemolysis was found in samples from the Trima Accel devices after plateletapheresis, compared to all other machines tested. Furthermore, an increase in complement deposition on RBCs was seen after all plasmapheresis procedures. Lastly, a significant decrease in the expression of the complement regulating protein CD59 was seen in all post apheresis samples as well as a significant decrease of the adhesion molecule CD147.

Summary/Conclusions: The increase in complement deposition and the decrease in the expression of CD59 suggests that RBC clearance might be enhanced after return to the donor. Possible effects on the donor due to an increase in hemolysis after Trima Accel plateletapheresis should be further investigated.

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THE UTILITY OF PRE-DONATION DONOR WHITE CELL COUNT AS A RELEASE CRITERION FOR APHERESIS PLATELETS

K Van Den Berg[1] and U Jentsch[2]

[1]Medical, South African National Blood Service, Port Elizabeth [2]Special Laboratory Services, South African National Blood Service, Constantia Kloof, South Africa

Background: Combined apheresis and pooled platelet utilisation in the South African National Blood Service (SANBS) increased by 25% from 2010 to 2016. Apheresis donations accounted for almost 44% of platelet products issued in 2016. Collecting sufficient apheresis products in a vast, largely rural country such as South Africa remains challenging. Availability of safe, sufficient products are dependent on among other factors, local eligibility and release criteria for individual products. At SANBS, apheresis donors have a pre-donation white cell count (WCC) performed; a normal WCC ($\leq$10, 8 $\times$ 10^9/l) is required for product release. In addition, a randomly selected subset (20%) of apheresis products is submitted for bacterial culture for quality control purposes. A negative culture is a requirement for product release. Pooled platelet products are not subject to these requirements.

Aims: We aim to assess the impact of WCC as a release criterion for apheresis platelets and the association of raised WCC and positive bacterial culture.

Methods: Apheresis platelets are collected using cell separators and may, dependant on the total platelet count, be split in to multiple products. Release criteria for apheresis products includes inter alia a normal pre-donation WCC and for a subset of collections, a negative bacterial culture. Pooled platelets are produced from the buffy coats of 5 regular donors and while subject to some release criteria, these do not include WCC or bacterial cultures.

Collection, demographic, WCC and bacterial culture results for all apheresis platelets collected at SANBS from 1 January 2013 to 31 December 2016 were extracted from the SANBS Business Intelligence Database. Summary statistics were used to describe the data and chi-squared test use to assess significance of associations.

Results: A total of 36,158 apheresis platelet donations were performed at SANBS from 2013 to 2016. Of these 61% (22,006) were from male donors and 90% (32 452) from White donors. The mean overall WCC was 6.4 $\times$ 10^9/l. Raised pre-donation WCC were noted in 442 donors (1.2%) with an average WCC in this group of 11.8 $\times$ 10^9/l. Maximum recorded WCC was 18.2 $\times$ 10^9/l. Of the 8 375 units submitted for bacterial testing, 331 (4%) tested positive. There was no significant difference (P-value 0.909) in the proportion of units with a raised WCC among units which had either a positive (1.2%) or negative (1.3%) bacterial culture.

Summary/Conclusions: Our data indicates that there is no association between a raised pre-donation WCC and a positive bacterial culture among apheresis platelet donors at SANBS. During this period, there were no reported cases of transfusion transmitted bacterial infection, albeit that haemovigilance in South Africa is hampered by under-reporting. The use of pre-donation WCC as a release criterion for apheresis platelets resulted in the loss of 327 collections, which translates to ~700 products in an environment plagued with chronic shortages. To our knowledge, South Africa is one of the only countries who uses pre-donation WCC as a release criterion for apheresis platelets. These findings, in conjunction with the differing practice for pooled platelets, supports a review of the use of pre-donation WCC as a release criterion for apheresis platelets.

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DOES PLASMAPHERESIS AFFECT THE OUTCOME OF HEPATITIS B VACCINATION?

R Norda[1], O Berseus[2], G Edgren[3], K Nilsson Ekdahl[4], B Nilsson[4], J Pink[5], J Struwe[6] and O Akerblom[1]

[1]Clinical Immunology and Transfusion Medicine, Uppsala University Hospital, Uppsala [2]Research and Development, Örebro University Hospital, Örebro [3]Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm [4]Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden [5]Australian Red Cross Blood Services, Kelvin Grove, Queensland, Australia [6]Folkhälsomyndigheten, Stockholm, Sweden

Background: Plasmapheresis donations have increased in numbers of donors and collections. A higher frequency and increased volumes are also practiced. Previously unpublished observations have therefor been summarized. 1992 the level of anti-HBs in the plasma pool in Örebro was below the European Pharmacopoeia requirements for source plasma for immunoglobulin preparation. Thus, registered plasma donors were offered hepatitis B vaccination according to a schedule used in Stockholm for vaccination of health care workers.

Aims: To increase the anti-HBs antibody content of the plasma pool by immunization of plasma donors.

Methods: Anti-HBs antibody negative plasma donors were offered vaccination at 0, 1–2 and 6–12 months. Samples were taken at donation about one month later after each vaccine injection and after another 12 months of follow-up. Vaccination and blood sampling was performed prior to the plasmapheresis procedure. Plasma collection was performed using the PCS 2 (Hemonetics, USA). Quantitative anti-HBs antibody determination was performed by Ausria II (Abbot, USA).

Results: Donors were enrolled between September 1992 through April 1994. Altogether 130 donors completed the vaccination scheme, but 12 did not complete the follow-up scheme. Altogether, 118 donors (67 women and 51 men) completed the whole scheme. A protective antibody level of >10 IU/l was observed in 95% of the women and 90% of the men. The geometric mean titer (GMT) was 211.3 IU/l for the women and 180.7 IU/l for the men. At follow-up, 26.7% of the responding donors had an antibody level that was $\geq$90% of their maximum titer. At follow-up, there was a higher anti-HBs titer in the women (P = 0.043). The number of plasma donations prior to or during the vaccination or the follow-up periods did not correlate with the maximum or follow-up titer of the donor.

Summary/Conclusions: There were no more comments on the level of the anti-HBs in the plasma pool. There was an expected development of a protective (anti-HBs >10 IU/l) antibody response in the vaccinated plasma donors. Compared to outcome of other vaccination studies, including the series in Stockholm, the GMT was lower than expected.

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IS ORAL SUPPLEMENTATION WITH CALCIUM OF ANY BENEFIT TO PREVENT BONE METABOLIC CHANGES IN PLATELETPHERESIS DONORS?

SA Sanchez-Guerrero[1], E Barrientos-Galeana[1], M Tolentino-Dolores[2], R Samano[2], G Chico-Barba[2] and E Fernandez-Sanchez[1]

[1]Blood Bank, Instituto Nacional de Cancerologia [2]Clinical Nutrition Lab, Instituto Nacional de Perinatologia, Mexico City, Mexico

Background: Apheresis donation produces several metabolic changes in donors due to the chelation effect of sodium citrate infused as an anticoagulant during the whole donation procedure. A secondary hyperparathyroidism phenomenon is conspicuous but long-term effect of these metabolic changes has been scarcely explored as well as the potential preventive measures to be taken.

Aims: To assess if oral supplementation of calcium either as pills or enriched-diet before plateletpheresis donation could be of any benefit to prevent metabolic changes such as divalent cations, hormones and bone markers.

Methods: This is a prospective study which included 134 plateletpheresis donors who were divided amongst four different groups: those who received oral supplementation with calcium carbonate + vitamin D (CC); those supplemented with calcium carbonate +minerals +vitamin D (CMD); those receiving calcium-rich diet (Dt); and a control group of donors who received no supplementation (Ctrl). Either way of oral supplementation was started 48 h before plateletpheresis donation. The following serologic tests were performed: calcium (Ca) and magnesium (Mg) levels by colorimetric assays; zinc (Zn) and copper (Cu) by atomic absorption spectrophotometry; 25-OH vitamin D, parathyroid hormone (PTH), osteocalcin (OC) and C-terminal telopeptide of collagen type 1 (CTX-1) by EIA. Blood samples were drawn at three different stages: before and immediately after donation as well as 15-days after plateletpheresis. Statistical analysis: Kruskal-Wallis, U-Mann Whitney and Wilcoxon tests. This protocol was approved by the Ethics and Research Committees of both participant institutions.

Results: All cations (Ca, Mg, Zn and Cu) as well as 25-OH vitamin D levels significantly decreased immediately after apheresis donation. In contrast, PTH increased more than 100% compared to the predonation levels. These changes were observed in all study groups. However, donors who received oral supplementation belonging to those CC and CMD groups had a trend to recover homeostasis in the following 15 days. Regarding the metabolic bone changes the Ctrl, CC and CMD groups increased their OC levels by 37%, 28% and 9%, respectively, being these changes statistically significant. Finally, the levels of CTX-1 increased 200% but just in the Ctrl group.

Summary/Conclusions: Even though there is no way to prevent the metabolic changes produced by the infusion of sodium citrate in apheresis donors, we found a trend to accelerate the homeostasis in those donors receiving oral supplementation of calcium assessed by PTH, OC and CTX-1. We believe that the development of new anticoagulants which do not chelate cations would be desirable but in the meantime,

we suggest to increase the 15-day gap between each consecutive donation as well as to supplement with CMD to any of our plateletpheresis donors.

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IN THE SEARCH FOR ECONOMICALLY EFFICIENT AND FLEXIBLE SINGLE DONOR PLATELET COLLECTION: COMPARISON OF FOUR PLATELETPHERESIS DEVICES

L Bonstein, P Abu Shkara, E Goldshtain, Z Malkis, E Dahan, EJ Dann and L Shapira

Blood Bank and Platelet Donation Unit, Rambam Health Care Campus, Haifa, Israel

Background: The need for platelet donations is well-recognized. Despite suggested advantages of single donor platelets (SDP), derived by apheresis, over platelet concentrates (PC) derived from whole blood of several donors, SDPs were previously used only as a second option at our institution due to their higher cost. In order to reduce patient exposure to multiple donors, increase platelet transfusion efficacy, while decreasing associated adverse effects, we have established at our medical center a plateletpheresis donation unit capable to meet our need of about 4,500 therapeutic units $(2.5–3 \times 10^{11}$ Plt/unit) annually. This collection unit relies on donors recruited by patients' families; most of them are first-time donors, some with borderline venous access. Hence, we have searched for an apheresis collection device adaptable to a wide range of donors and economically efficient, implying its ability to produce maximal amounts of double-dose SDP units within a short time period from most recruited donors.

Aims: To compare the efficacy of four plateletpheresis devices, including, the newest Trima Accel-7, in a unique pool of first-time donors.

Methods: Collection efficiency (CE) and rate, processing time, adaptability to a wide range of donors, percentage of double-dose units/donor and exposure to anticoagulant (ACDA) were retrospectively compared using four apheresis devices: Amicus (Fresenius) and Cobe Spectra (Terumo BCT) using double-needle collection sets as well as Spectra Optia (Terumo BCT) and Trima Accel-7 (Terumo BCT) using single-needle sets. To evaluate device applicability to a variety of donors, they were categorized into four groups according to the venous access, group 1 being the most difficult to manage (smallest venous diameter).

Results: This retrospective analysis included results of 800 procedures, 200 performed on each device. Males comprised 98% of the donors, 93% were first-time donors with an average age, TBV, hematocrit and platelet pre-count of 34 years, 5,376 ml, 43% and 232×10^9/l, respectively. Overall CE was highest with Trima Accel-7 (64.6%) followed by Spectra Optia (62.8%), Cobe Spectra (48.4%) and Amicus (47.5%). Trima Accel-7 was also significantly more economically efficient, with 72.6% of collections yielding double-dose units compared with 61%, 54% and 50.4% by Cobe Spectra, Spectra Optia and Amicus, respectively. Additionally, the collection rate (yield/duration) of Trima Accel-7 was significantly higher $(7.1 \times 10^9$ Plt/min) than that of the other devices (6.3, 5.9 and 5.6×10^9 Plt/min for Spectra Optia, Cobe Spectra and Amicus, respectively). The ACDA volume used with Amicus was significantly greater than with the other assessed systems (P < 0.0001). While Spectra Optia was suitable solely for donors in groups 3 and 4 (37% of donors), Cobe Spectra and Amicus, using double-needle sets, were adaptable to a wider range of donors from groups 2–4 (88%). Only Trima Accel-7, although using a single needle set, could be adapted to 100% of donors due to its ability to adjust to both low and high venous resistance.

Summary/Conclusions: Of the four evaluated systems, Trima Accel-7 is found to be the most efficient and donor-friendly device, yielding a maximal number of double-dose SDP units from a diverse donor population, providing the highest collection rate using reduced ACDA volume.

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USEFULNESS OF THROMBOELASTOGRAPHY IN THE EVALUATION OF COAGULATION FUNCTION IN PLATELETPHERESIS DONORS

Q Feng, Y Zheng, F Kong and C Li

Donation, Zhejiang Blood Center, Hangzhou, China

Background: Plateletpheresis is a relatively safe technique that is commonly used nowadays for donating platelets. Donors undergoing repeated plateletpheresis might have certain proportion of complications including thrombosis and haemorrhagic disorders, a minority of which even being fatal. These complications might be related to the abnormal coagulation function of the donors. Currently, plateletpheresis donors do not undergo any coagulation function test, which is replaced by physical history and platelet count. This is because that traditional coagulation function test is time-consuming and laborious. Thromboelastography(TEG) is a rapid and dynamic method for monitoring platelet & coagulation functions, which has been widely used in the clinic but rarely in plateletpheresis donors.

Aims: The aim of this study was to evaluate the proportion of coagulation dysfunction in plateletpheresis donors by thromboelastography (TEG), and to investigate the relationship between TEG index and routine platelet index.

Methods: A total of 134 plateletpheresis donors(male=106, female=28) who were eligible for plateletpheresis in Zhejiang blood center were tested by TEG and routine platelet tests before plateletpheresis. TEG index(R time, K time, α-Angle and MA) and routine platelet index(Plts, MPV, PDW)were tested. R > 10 min, K > 3 min, α-Angle<53° or MA<50 mm were defined as hypocoagulation, and R < 5 min, K < 1 min, α-Angle>72° or MA>700 mm were defined as hypercoagulation.

Results: 23.1% (31/134) of plateletpheresis donors had abnormal TEG index. Among them 13.4% (18/134) was found with hypocoagulation, and 9.7% (13/134) donors with hypercoagulation. The ratios of hypocoagulation in male and female donors were 16.0% (17/106) and 3.6% (1/28), respectively (χ^2=1.98, P > 0.05). The ratios of hypercoagulation in male and female donors were 5.7% (6/106) and 25.0% (7/28), respectively (χ^2=7.38, P < 0.05). The Plts were negatively correlated with R time and K time(r = 0.256,0.441; p < 0.001),and positively correlated with α-Angle and MA (r = 0.410, 0.390; p < 0.001). We found no significant correlations among MPV, PDW and TEG index.

Summary/Conclusions: In summary, this study showed that almost a quarter of plateletpheresis donors had abnormal TEG index, with male donors having higher ratio of hypocoagulation and female donors higher ratio of hypercoagulation. The PLTs had significant correlation with TEG index.

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EVALUATION OF SIDE EFFECTS OF PLATELETPHERESIS FROM YEAR 2015 TO SECOND HALF OF 2017 IN IRAN

S Sharifi, A Pourfathollah, K Shams Asanjan, A Ali Balazadeh and M Asadi

High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: With the advance of transfusion medicine, the method of platelets production was gradually shifted from centrifugal methods toward plateletpheresis .

Aims: Plateletpheresis has many advantages over traditional methods. Therefore, platelet donor's care is very important. Donors care program begun in 2015 at the Iranian Blood Transfusion Organization.

Methods: This study was conducted on plateletpheresis donors, who were apheresised with Trima and Hemonetics machines from the year 2015 to the second half of the year 2017. Firstly, guidelines were prepared. Side effects were monitored, using monthly follow-up forms from 29 provincial centers which performed apheresis.

Results: Out of 6,850 Platelet donations by Trima and Hemonetics, 96 (1%)side effects were reported. The most side effects respectively were 52 cases of vascular injury (54%), 42 cases (43.7%) of vasovagal shock followed by 8 cases (8.3%) citrate toxicity.In this study, there was no correlation between the side effect - vasovagal - and history of donation. There was no correlation between type and incidence of side effects with the kind of Apheresis machine. Reactions in the majority of cases were mild (78.1%), and 20.8% were moderate.

Summary/Conclusions: Considering this fact that hematoma was the most side effects, it was recommended to train the phlebotomists.

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COMPARATIVE EVALUATION OF THE IMPACT OF TRIMA ACCEL 7 ON DONOR COMFORT AND DONOR EXPERIENCE

JA García-Erce[1], E Rodríguez Segura[1], E Aramburu[1], M Ayape[1], R Garbayo[1], M Antelo[2], M Antoon[3], L Simon-Blum[3] and B Pirson[3]

[1]Banco de Sangre y Tejidos de Navarra [2]Servicio de Hematología y Hemoterapia, Complejo Hospitalario de Navarra, Pamplona, Spain [3]Terumo BCT, Zaventem, Belgium

Background: Terumo BCT's Trima Accel software version 7 (TA7) is an enhancement in all aspects of performance. With the new version it is expected that donors will spend less donation time connected to the machine and that they will encounter fewer venous access pressure alarms during the collection. These improvements should ameliorate the average donor experience. If target yields and split rates are

kept constant, it is expected that procedure times will be reduced compared to earlier Trima versions. An improvement in the baseline leukoreduction performance and the introduction of new insights in leukoreduction chamber management should procedurally be reflected in a decrease in leukoreduction failures as well as in a reduced number of runs flagged for residual leukocyte verification.

Aims: The objective of this evaluation was to evaluate the impact of the new software features introduced with TA7 by comparing its procedures retrospectively with those of Trima Accel version 6 (TA6).

Methods: Eight-hundred twenty-two (822) TA6 procedures spanning the period from 4th January 2016 to 10th October 2017 were compared to 233 TA7 procedures covering the period from 18th October 2017 to 29th January 2018. Data were extracted from the machine data loggers that record all relevant procedural parameters during each individual run. The primary outcome were the number of machine access pressure alerts per procedure. T-testing (StatSoft, Inc. (2012). STATISTICA (data analysis software system), version 12. www.statsoft.com.) was used to compare the data sets.

Results: Both donor populations (TA6 vs. TA7 respectively) were comparable and were characterized by: TBV – 5,207 vs. 5,217 ml; Donor platelet count pre-procedure – $252 \times 10^3/\mu l$ vs. $243 \times 10^3/\mu l$; Donor hematocrit pre-procedure – 44% vs. 45%. The gender distribution was 11.2% female with TA6 vs. 5.6% with TA7. Venous access pressure alerts were significantly improved by TA7 with an average of 0.4 ± 2.4 alerts per procedure as compared to 2.0 ± 6.2 ($P < 0.05$). Procedure time was reduced from 49 ± 11 to 47 ± 11 min for TA6 and TA7 respectively ($P < 0.05$). The number of white blood cell verification flags decreased slightly from 2.8 to 2.6% (TA6 vs. TA7).

Summary/Conclusions: In comparable donor populations, implementation of TA7 decreases the number of access pressure alerts significantly (>50%) compared to previous Trima versions. It does so without increases in procedure time. The average procedure duration was also found to be slightly but significantly reduced. These improvements are expected to offer more donor comfort and overall a more satisfactory donor experience.

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OVERVIEW OF BLOOD DONATION IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF REPUBLIC OF MACEDONIA

G Andonov, RM Grubovic Rastvorceva, K Dimitrovski, M Blagoevska, S Useini, E Petkovikj, O Damevska Todorovska, B Todorovski and M Grubovic

Institute for Transfusion Medicine of RM, Medical Faculty – Skopje, Skopje, Macedonia

Background: Republic of Macedonia has around 2,000,000 inhabitants and at least 3% of them should donate blood according to the estimated need for the treatment of sick and injured patients. We still do not have these 60,000 blood donations per year and we have around 50,000 donations.

Aims: The aim of the study was to evaluate the blood donation in the Institute for Transfusion Medicine of RM from January 2017 till January 2018.

Methods: This is a retrospective analysis of the monthly blood donation registries in the Blood Donation Department in the Institute and the registries of donations on the mobile sites.

Results: There were 23,683 donations in 2017 in the Institute for Transfusion Medicine of RM. Mobile teams collected 17.758 (75%) blood units across the country, of which 13,285 (74.8%) were donated by males and 4,473 (25.2%) by females. The highest peaks with mobile teams were in March – 2120 donations, July – 1,797 donations and November – 1,828 donations. There were 5.925 (25%) blood donations in the ITM, 4,977 (84%) donations by males and 948 by females (16%). The peaks were in March – 589 donations and December – 569 donations. There were 2,100 (8.9%) first time blood donors, of which 1,701 (9.6%) donated blood on the mobile sites and 399 (6.7%) who donated blood in the ITM. There were 3,338 (14.1%) deferred donors in total, of which 2,534 (14.3%) were deferred on the mobile site and 804 (13.6%) deferred donors in the ITM. The number of university students that donated blood was 1,458 (6.16%) and the number of high school students was 2,797 (11.8%).

Summary/Conclusions: In order to increase the blood donation rate some updated methods of motivation should be introduced, especially for the young people to be able to overcome the gap in the donation age, due to the aging of the population in the country.

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ELIGIBILITY OF BLOOD DONORS WITH CORONARY ARTERY DISEASE

P Lesley[1], M Tak ShengYan[2,3], D Howard-Cordi[2,4] and T Butler-Foster[5,6]

[1]*Medical Affairs, Canadian Blood Services, Ottawa* [2]*Medical Affairs, Canadian Blood Services* [3]*Department of Laboratory Medicine and Pathobiology, University of Toronto* [4]*Department of Health Studies, Ryerson University, Toronto* [5]*Arthur Labatt School of Nursing, Western University* [6]*Medical Affairs, Canadian Blood Services, London, Canada*

Background: Current Canadian Blood Services' (CBS) donor criteria defers all allogeneic donors with any degree of coronary artery disease (CAD), even if asymptomatic, non-obstructive, or medically optimized. However, autologous donors with uncomplicated stable CAD are permitted to be phlebotomized on clinic. Donors and their physicians have challenged CAD deferrals and question any evidence supporting these decisions.

Aims: Given an aging donor population, the threat of blood shortages, and CAD deferrals estimated at 1,000 per year, an internal and external review was performed to determine the evidence supporting or refuting the eligibility of stable CAD allogeneic donors.

Methods: A PubMed search using the key words "whole blood donor complications" and "high risk autologous blood donors" was performed to find evidence of complications in individuals with low and high risk CAD undergoing blood donation or phlebotomy. Additionally, the CBS post-donation reaction database and the CBS autologous program was reviewed for reports of CAD complications. International blood operator CAD policies were also reviewed.

Results: Myocardial infarctions (MI) and deaths have been rarely reported post-donation worldwide. At CBS, 12 reaction reports secondary to potential or probable CAD symptoms have been recorded over a period of 11 years yielding 1.09 possible cardiac symptom reports per 900,000 annual donations on a 400,000 donor base. There has been no litigation arising out of these reports. Review of the CBS autologous program indicated no serious CAD complications from donors bled on clinic or in a hospital high risk program over many years.

Internationally, in the literature only four CAD-related hospitalizations were reported following 4.1 million American Red Cross (ARC) donations. International operators of hospital autologous high risk programs reported an adverse event rate of 0.7% but with no causal relationship demonstrated. Adverse complications from CAD autologous donors were not more frequent compared to allogeneic donors. Phlebotomies secondary to iron overload in high risk individuals did not demonstrate an association with CAD complications. Donor CAD complication rates at CBS are lower than predicted CAD rates in the general population.

Among international blood operators surveyed, only ARC was determined to accept stable CAD allogeneic donors. Australian Red Cross, United Kingdom's National Health Services, German Red Cross, Hema Quebec, and Italy all defer allogeneic donors with any evidence of CAD. Council of Europe recommends deferral for any CAD history, yet under autologous standards stable CAD is not an absolute contraindication, and donation may be subject to a Cardiologist assessment.

Summary/Conclusions: There is no significant evidence for post-donation related CAD complications in blood donors except rare (0.7%) unproven events in an in-hospital high-risk autologous program. ARC has screened millions of allogeneic donors while accepting all stable CAD donors for many years without any major events. Low risk CAD allogeneic donors (i.e. asymptomatic, no new treatments, no physical restrictions) can be safely bled on clinic. CBS plans to revise its CAD criterion accordingly.

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DONATION OF SINGLE DONOR PLATELETS IN THE INSTITUTE FOR TRANSFUSION MEDICINE OF REPUBLIC OF MACEDONIA – 8 YEAR SURVEY

S Useini, RM Grubovic Rastvorceva, K Dimitrovski, G Andonov and E Petkovikj

Institute for Transfusion Medicine of RM, Medical Faculty – Skopje, Skopje, Macedonia

Background: Single donor platelet concentrate derived by plateletpheresis is preferable in terms of reducing the risks of adverse reactions in platelet transfusion when compared to random donor platelet concentrates.

Aims: The aim of our study is to present our experience in collection of single donor platelets with apheresis.

Methods: This is a retrospective study performed in the Institute for Transfusion Medicine of Republic of Macedonia from 2010 till 2018. All donors were fully

informed on the donation procedure and signed an informed consent for donation. The optimal platelet count that we want to achieve was $\geq 3.0 \times 10^{11}$ equal to 12 random donor platelet doses. Minimum preapheresis platelet count in donors requested to start the apheresis collection was 150.000/µl. Platelet collection was performed using flow cell separators Haemonetics MCS+ and Trima Accel. Acid Citrate Dextrose formula A was used for anticoagulation.

Results: There were 831 apheresis platelet collections for the mentioned period, median 104 per year. There were 49 apheresis collection in 2010, 66 collections in 2011, 78 collections in 2012, 97 collections in 2013, 105 collections in 2014, 108 collections in 2015, 120 collections in 2016 and 208 collections in 2017. The number of apheresis collections is increasing from year to year with almost double increase in 2017. Median precollection platelet count of donors was 273,000/µl, with range from 182,000/µl to 397,000/µl. Male were 78% of the donors and females were 22%. The single procedure usually took 45–70 min. The median platelet count collected was 4.0×10^{11}, range 2–6.5×10^{11}. The median processed blood volume was 3,215 ml and median used ACD-A was 352 ml. Mean total volume of collected product was 312 ml. The adverse effects included vein perforation and the numbness of the extremities as reaction of ACD-A (hypocalcemia), which occur rarely and was very mild.

Summary/Conclusions: The apheresis collection of platelets is an effective and safe procedure. The collected platelet count was more than the wanted optimum platelet count. The number of apheresis donors is increasing and we are working on expanding our Voluntary Platelet Donors Registry.

P-192
MEDICAL ENQUIRY DOES NOT ADVERSELY IMPACT DONOR RETENTION

T Butler-Foster[1,2], Z Solh[3,4], B Neil[5], B Chin-Yee[6], P Lesley[7], D Howard-Cordi[8,9] and I Chin-Yee[1,3,4]

[1]Medical Affairs, Canadian Blood Services [2]Arthur Labatt School of Nursing [3]Pathology and Laboratory Medicine, Schulich School of Medicine, Western University [4]London Health Sciences Centre [5]Resource Management, Supply Chain, Canadian Blood Services [6]Department of Medicine, University of Toronto, London [7]Medical Affairs, Canadian Blood Services, Ottawa [8]Medical Affairs, Canadian Blood Services [9]Department of Health Studies, Ryerson University, Toronto, Canada

Background: Canadian Blood Services (CBS) assesses donor eligibility by medical enquiry (ME) when suitability to donate blood cannot be determined without further medical evaluation. ME donors are temporarily deferred while the medical office assesses their eligibility. The impact of the ME on donor retention compared to donors not involved in this process has not been evaluated, yet significant resources are expended on these enquiries.

Aims: This study assessed donor retention in donors who are accepted after ME compared to donors who are never deferred (ND) and to those who are temporarily deferred (TD).

Methods: We retrospectively reviewed CBS national donor base using Business Intelligence (BI) warehouse data analyzing whole blood donations, repeat deferrals, and non-return frequency for ME, ND, and TD groups. The TD group consisted of donors deferred for six months or less, and the ME group included donors accepted by MEs initiated and resolved between October 1, 2015 and April 1, 2016. Data were collected for all groups from April 1, 2016– October 1, 2017. Apheresis plasma and platelet donors were excluded. Statistical differences were analyzed with the Chi-Square test (P value <0.05 significant) using GraphPad Software and 95% confidence intervals were calculated between groups.

Results: 2,220 MEs were initiated and resolved during the study period. 1,535 (69%, CI 67.2–71.1%) were accepted and 685 (31%, CI 28.9–32.8%) were deferred or abandoned for non-response. Of the 1,535 donors accepted by ME, 948 (62%, CI 59.3–64.2%) returned to attempt donation and 584 (38%, CI 35.6–40.5%) did not return during the study period. In the TD group 54,557 (64%, CI 63.9–64.7%) returned to attempt donation and 19,476 (36%, CI 35.3–36.1%) did not. A difference between eligible donors returning to attempt donation in these groups could not be detected (P = 0.38).

The ND group consisted of 190,884 donors who gave 354,306 donations (1.86/donor) 808 ME group donors gave 2,531 donations (3.13/donor). 27,602 donors in the TD group gave 85,447 donations (3.10/donor).

Donors accepted by ME were significantly less likely than the TD group to be deferred a second time (n = 143 or 9.3%, CI 7.9–10.8% and n = 7,479 or 13.7% CI 13.4–14.0% respectively, P = 0.0001).

38.8% (CI 38.6–39.0%) of the ND group donated more than once during the 18-month study period. In comparison, 85.4% (CI 85.2–85.7%, P = 0.0001) of the TD

group and 84.2% (CI 82.4–86.1%, P = 0.0001) of the ME group donated more than once.

Summary/Conclusions: TD and ME donors make up a small but important source of regular committed blood donors. The majority return after a deferral and donate more regularly than the ND group. These differences may be due to recruitment efforts to bring in new and lapsed donors or related to motivational differences in the ME and TD groups that should be further studied. The ME process is more effective at preventing future donor displacement as evidenced by decreased repeat deferrals in this group. These data demonstrate the overall effectiveness of the ME process in retaining and preventing future donor displacement and highlight its value to blood center operations.

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BLOOD DONOR DEFERRAL DURING AN EIGHT- YEAR PERIOD IN ZLATIBOR REGION WESTERN SERBIA

M Perisic-Bozic, D Djenadic, R Smiljanic, V Divac, D Drndarevic, I Filipovic, B Tesovic and M Jankovic

Department of Transfusion Medicine, General Hospital Uzice, Uzice, Serbia

Background: Transfusion is an irreversible event, which means that blood donation has to be pleasant for the donor and safe for the patient. The selection of blood donors is the first step towards transfusion. The criteria for the selection are based on national legislation on transfusion medicine and recommendations of the European Union.

Aims: Analysis of the reasons for donor deferral in the Zlatibor region.

Methods: Retrospective analysis of the reasons for donor deferral from January 2010 until December 2017, based on a completed questionnaire, determining the haemoglobin level from capillary blood by the copper sulphate method, Haemocue or by an automated haematology analyzer and by physical examination by a specialist in transfusion medicine.

Results: In an eight-year period, the total number of potential donations was 59,266, of which deferral occurred in 9,063 or 15.29 percent of cases. We collected blood in our Department at the General Hospital and in our mobile units. In our population, we have more male donors, 86.5 percent, while female donors accounted for 13.5 percent, and among all deferred donors, there were more males, 63.15 percent than females, 35.85 percent of the total number of total number of donors. The reasons for permanent deferral, (2.4 percent) were: HBV; HCV infection and other severe health problems. The most common reason for temporary deferral is low haemoglobin level, 41.12 percent, then low blood pressure, 10.47 percent, any sort of infection, 10.29 percent, high blood pressure, 7.12 percent and taking drugs, 6.17 percent.

Summary/Conclusions: Our deferral rate is within the acceptable percentage for deferral, according to international standards, which should not exceed 20 percent of donors or less. Donors who have been temporarily deferred need to be encouraged to donate again because they will always be necessary for safely treating patients.

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MITIGATING NEGATIVE EXPERIENCES FOR TRANS DONORS: LESSONS FROM OTHER HEALTH DISCIPLINES

T Butler-Foster[1,2], B Neil[3], I Chin-Yee[2,4,5], M Huang[6], T Sivananth[1,5] and K Jackson[1]

[1]Arthur Labatt School of Nursing, Western University [2]Medical Affairs [3]Resource Management, Supply Chain, Canadian Blood Services [4]Pathology and Laboratory Medicine, Schulich School of Medicine, Western University [5]London Health Sciences Centre, London [6]Medical Affairs, Canadian Blood Services, Toronto, Canada

Background: Trans is an umbrella term for individuals whose gender identity differs from the sex assigned to them at birth i.e. transgender, transsexual, gender non-conforming, non-binary individuals.

Trans blood donors report distressing donation experiences which may indicate staff difficulties in culturally sensitive care provision. These negative experiences can harm these donors and the reputation of blood agencies. Discourse regarding best practices in culturally sensitive care provision for trans donors is currently absent in transfusion medicine literature.

Aims: To address this knowledge gap, a systematic scoping review was undertaken to explore and understand the extent and range of research related to culturally sensitive care provision for trans individuals as investigated in other health care disciplines.

Methods: Electronic databases (CINAHAL, PubMed, and Scopus) were searched from October to November, 2017. Initial search terms included "trans", "healthcare",

"delivery", "knowledge", and "disparities" and were modified according to database requirements. English language North American studies published and using data collected within the last five years were included to capture recent societal trans-inclusive discourse in North America. Studies regarding medical interventions and population subsets were excluded.

Results: Among the 256 eligible studies, 8 met inclusion criteria. Studies spanned a variety of health care disciplines (nursing, gynecology, psychiatry, internal medicine, etc.) with varying degrees of trans patient exposure.

Thematic analysis revealed systemic and practice gaps. Systemic gaps included rigid binary intake processes, uncertainty regarding how trans individuals are identified in the practice setting, and difficulties knowing when to ask and use pronouns. These deficiencies can hinder the therapeutic relationship and also dilute data for institutions and for broad public health interventions and research. Evidence based recommendations in this review included a two-step intake process asking all individuals their sex assigned at birth and their gender identity and asking all individuals their pronouns at the outset of the therapeutic relationship.

Practice gaps identified a lack of education to assist in caring for trans individuals. Frequent confusion and conflating of key terms and pathologizing trans patients was identified. As well as confusion regarding prevalence of gender affirming surgeries and when discourse with patients was required about such interventions. Moreover, there was a lack of understanding of stigma generated by the health care system for trans individuals and how stigma can elevate patient health risks. Recommendations included institutional and purpose built or job specific training on trans sensitivity, however, there was no consensus on the optimal medium to deliver this education and further research is required regarding the best way to implement these interventions.

Summary/Conclusions: In the absence of transfusion medicine specific research this scoping review identified key knowledge gaps and highlighted evidence based recommendations in the literature across several health care disciplines. Systemic and practice gaps were identified that if investigated by blood agencies could improve provision of culturally sensitive care for trans donors. This review provides a call to action for transfusion medicine research on this topic to improve donor relations and the overall efficacy of the blood program.

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THE UPWARD TREND OF NONINFECTIOUS BLOOD DISCARDING CALLS FOR ATTENTION TO THE QUALITY OF BLOOD COLLECTION PROCESS

X Rong[1], S Li[1,2], F Feng[2] and J Chen[2]

[1]Institute of Transfusion [2]Department of Blood Collection, Guangzhou Blood Center, Guangzhou, China

Background: Guangzhou is the medical center of Southern China, where concentrated medical resources attracted the patients in the surrounding areas. The growing number of medical services had increased the demand of blood transfusion, resulting in the gradual increasing pressure of blood supply. To meet clinical transfusion needs, we should increase blood collection while decrease blood discarding. The two main reasons cause blood discarding are infectious reasons (ALT, Hepatitis, HIV, etc) and noninfectious reasons (physical examination, expiration, etc). We reviewed the data of blood collection and blood discarding in Guangzhou Blood Center 2011–2016, and analyzed the reasons for blood discarding.

Aims: To obtain the causes of blood donation discarding and the trend during 2011–2016, find out the improvements to minimize wastage of blood.

Methods: The data on blood collection, blood testing, blood preparation, and blood discarding of the targeted years were reviewed and analyzed. The discarded blood was divided into infectious and noninfectious reasons. Infectious reasons included ALT greater than 50 units, HBV/HCV and HIV not qualified for ELSA and/or NAT, and ELSA detection of infectious markers of Treponema pallidum not qualified. Noninfectious reasons were physical reasons(including lipemic, hemolysis, clot, etc.), and expiration, confidentiality of blood abandonment. Statistical analysis were performed by using SPSS19.0 software.

Results: 1. A total of 5 533 166 units of blood were collected and prepared from 2011–2016, of which 348 355 blood units were discarded, with a total blood discard rate of 6.29% 0.2. The main reason for blood discarding was infectious reason, owing to which 193,281 units (3.49%) were discarded. ALT accounting for the largest proportion 41.51% (80 227/193 281) of those infectious blood discarding. 3. The blood discarding due to infectious showed a steady decline from 4.51% in 2011 to 2.57% in 2016, (χ^2 = 6,140, P < 0.01). 4. A total of 155 074 units(2.80%)of blood were discarded owing to noninfectious reasons, and the rate increased significantly from 2.22% in 2011 to 3.14% in 2016, (χ^2= 9,168, P < 0.01) 0.5. The majority of

noninfectious discarding was physical unqualified donations accounting for 97.13% (150 619/ 155 074), among which Lipemic blood accounted for 87.27% (131,442/ 150,619), other causes accounted for 6.85% including hemolysis, clot, nonstandard quantity, etc., and the rate of damaged packaging was 5.88%.

Summary/Conclusions: Infectious factors were the primary reasons for blood discarding at present and it is steadily declining while noninfectious reasons are increasing yearly. We should pay attention to the process of blood collection, especially consultation before blood donation to exclude high-fat diet blood donors, and strictly follow the standard operation procedures to improve the quality of blood collection, thus minimize the wastage of blood caused by noninfectious factors and ensure the supply of blood.

Donor Adverse Events

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CALCIUM IN DRINKING WATER – EFFECT ON IRON STORES IN DANISH BLOOD DONORS: RESULTS FROM THE DANISH BLOOD DONOR STUDY (DBDS)

AS Rigas[1], B Ejsing[1], E Sørensen[1], O Pedersen[2], H Hjalgrim[3], C Erikstrup[4] and H Ullum[1]

[1]Copenhagen Blood Transfusion Service, Copenhagen Oe [2]Næstved Blood Transfusion Service, Næstved [3]Statens Serum Institut, Copenhagen [4]Århus Blood Transfusion service, Århus, Denmark

Background: Studies confirm that calcium inhibits iron absorption. Danish tap water comes from groundwater, which contains varying amounts of calcium depending on the subsoil.

Aims: We investigated the association of calcium in drinking water with iron levels in Danish blood donors.

Methods: We used data on Danish blood donors including dietary and lifestyle habits, blood donation history and physiological characteristics including measures of ferritin levels along with information on area of residence from The Danish Blood Donor Study. Data on calcium levels in groundwater ('water hardness') was obtained through GEUS (the Geological Survey of Denmark and Greenland). We performed multiple linear and logistic regression analyses to evaluate the effect of water hardness on ferritin levels and risk of having iron deficiency (defined as ferritin levels <15 ng/ml), stratified by sex.

Results: There was a statistically significant negative association between water hardness and ferritin levels in both men and women. Risk of iron deficiency was correspondingly increased in both men (OR=1.55; 95% CI: 1.14–2.12) and women (OR=1.20; 95% CI: 1.03–1.40) with increasing water hardness. In analyses restricted to individuals who received supplemental iron tablets no statistically significant association between groundwater hardness and ferritin levels was observed.

Summary/Conclusions: As measured by ferritin levels, residential drinking water calcium content is associated with blood donors' iron levels and risk of iron deficiency. Calcium levels in drinking water may need to be considered when advising blood donors and other populations at risk for iron deficiency.

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STABILITY OF FERRITIN TESTING IN BLOOD DONATIONS IN A HIGH THROUGHPUT LABORATORY. COMPARISON OF THREE SYSTEMS: ARCHITECT I2000SR, COBAS E801 AND LUMIPULSE G1200

A Van Weert, L Wirht, G Gunarso, M Gorissen-Schutter and E Bakker

National Screening Laboratory Sanquin, Sanquin Blood Supply, Amsterdam, Netherlands

Background: Regular blood donation is known to be a cause of iron loss. For the detection of possible iron depletion, ferritin is used to monitor the iron stores of blood donors. Whereas in a clinical setting ferritin is mostly tested within 24 h, in blood donation testing within the same day of blood collection is not always feasible. Therefore, the National Screening laboratory Sanquin assessed the stability of ferritin measurement within the workflow of a centralized high-throughput screening facility.

Aims: In this study the stability of ferritin measurements in blood donation samples and a dilution series of the WHO 3rd International Standard was evaluated during 7 days using three different platforms: Architect i2000sr, cobas e801 and Lumipulse G1200. The results were aimed to provide insight in the effect of time on measuring ferritin towards determining the operational efficiency for blood donation testing without compromising quality.

Methods: From the WHO 3rd IS two dilution series (4.92–630 ng/ml) were made in PBS and serum, and serum samples from 95 whole blood donors were collected. The WHO 3rd IS series diluted in serum was measured at day 1 and 5 (data corrected for serum ferritin concentration), the series diluted in PBS and the donation samples were measured on day 1, 2, 5, 6 and 7. Donation samples were measured at day 1, 4 and 7 after blood donation. Samples were stored at 4–8°C. The measurements were done in duplicate. The systems are calibrated against the WHO 1st IS (80/602 human liver; Architect and e801) and WHO 3rd IS (94/572 recombinant; Lumipulse G1200).

Results: For all systems the WHO 3rd IS dilution series in both PBS and serum showed values that were consistent at all time points. The values measured on the Lumipulse and e801 were in line with the values of the expected concentration, the Architect showed higher values for both series.Comparing serum and PBS data, the Architect showed more constant data in the range of about 10–630 ng/ml; for Lumipulse and e801 this was in the range of about 30–630 ng/ml. In contrast to the WHO 3rd IS data, in donation samples the value of the ferritin concentrations were consistently the highest on the e801, intermediate on the Architect and the lowest on the Lumipulse.

Summary/Conclusions: Ferritin can be measured stably up to 7 days after blood collection as shown by measuring dilution series of the WHO 3rd IS in PBS and serum and by measuring donation samples on the Architect i2000sr, Lumipulse G1200 and cobas e801. This provides the required flexibility of testing without compromising quality if measurement is not possible within 24 hours due to logistical constraints. The ferritin concentrations varied among the systems, which can be explained by the heterogeneity of ferritin and differences in the antibodies used on these systems, and because systems are calibrated against different WHO IS standards.

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IMPACT OF CHANGES IN MINIMUM HEMOGLOBIN (HB) LEVEL AND INTERDONATION INTERVAL ON DONOR HB DEFERRALS

M Goldman[1,2], Q Yi[3,4] and S O'Brien[4,5]

[1]Donor & Clinical Services, Canadian Blood Services [2]Deparment of Pathology & Laboratory Medicine, University of Ottawa [3]Epidemiology & Surveillance, Canadian Blood Services [4]Deparment of Epidemiology & Community Medicine, University of Ottawa [5]Epidemiology & Surveillance, Canadian Blood Services, Ottawa, Canada

Background: Iron deficiency is common in whole blood (WB) donors. In our donor population, males with borderline Hb levels and females donating at high frequency are at particularly high risk. As a partial mitigating strategy, we changed our minimum Hb level from 125 to 130 g/l for males and increased the minimum interdonation interval from 56 to 84 days for females.

Aims: We aimed to assess the impact of these changes on Hb deferral rates, performing extra analysis on donors self-identifying as black, and donors known to be Fy(a⁻b⁻), to evaluate impact on rare phenotyped units.

Methods: Predonation Hb was measured on a fingerstick sample using a portable hemoglobinometer. In fall 2016, messaging to female donors to reduce donation frequency started, followed by a change in minimum interdonation interval in the donor appointment booking system (Dec 2016) and a change in criteria (March 2017). Minimum Hb for females remained at 125 g/l. For male donors, minimum Hb increased to 130 g/l in March 2017, and minimum interdonation interval remained at 56 days. We compared Hb deferral rates and frequency of donation from July-Sept, 2016 (period 1) to July-Sept, 2017 (period 2) for all donors, and donors who self-identified as black (available only for fixed site donations). For Fy(a⁻b⁻) donors, we assessed Hb deferral rates from May 1, 2016 to March 4, 2017, and March 5, 2017 to Dec 31, 2017.

Results: For females, the Hb deferral rate was 13.5% in period 1, and 9.6% in period 2 (P < 0.001). The number of successful WB donations/female donor in the previous 12 months decreased gradually from 1.68 in period 1 to 1.25 in period 2. For males, the Hb deferral rate was 1.4% in period 1 and 2.3% in period 2 (P < 0.001). The number of WB donations/male donor was unchanged (2.5 in period 1 vs 2.4 in period 2). The overall Hb deferral rate (males and females combined) decreased from 7.1% to 5.6% (P < 0.0001). The Hb deferral rate for Fy(a⁻b⁻) donors increased in males from 3.2% to 5.1% (P = 0.09) but decreased in females from 21.9% to 12.3%

(P < 0.01), resulting in an overall decline in Hb deferrals from 9.6% to 7.4% (P = 0.10). The deferral rate for black males (3.3 vs 3.2, P = 0.94) and black females (13.7 vs 11.3%, P = 0.38) was unchanged statistically, partly due to small numbers, however the net trend for males and females combined (7.3 vs 6.4%, P = 0.49) was similar to donors overall. Overall WB collections decreased by 1.8% from period 1 to period 2; donations from new donors increased from 9.9% to 12.9% (P < 0.001).

Summary/Conclusions: Deferrals increased in males but decreased more substantively in females, resulting in an overall decrease in Hb deferrals for all donors, self-identified black donors, and Fy(a⁻b⁻) donors. There was likely better Hb recovery in females with the longer minimum interdonation interval as seen in the UK INTER-VAL study. The donation shortfall was addressed by recruitment of new donors, demonstrating the importance of a coordinated campaign to offset operational impacts of donor health initiatives.

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PREVENTION OF ANAEMIA IN BLOOD DONORS IN FRANCE: ROOM FOR IMPROVEMENT?

F Bigey[1], A Szyika-Gravier[2] and C Gachet[3]
[1]Production [2]Blood Collection [3]Direction, EFS, Strasbourg, France

Background: Prevention of anaemia in blood donors is based on two methods, in France. Pre-donation haemoglobin testing, performed by photometric measurement in a limited population of donors (new donors and donors over two years after last donation) only detects a quarter of anaemic donors as revealed by the post-donation blood count systematically sampled at the beginning of donation. The minimum haemoglobin level is 120 g/l for females and 130 g/l for males for whole blood donations, which is 5 g/l below the threshold defined by the European Directive. Thus, some donors are allowed to give blood despite pre-donation haemoglobin levels close to anaemia.

Aims: To evaluate current methods of anaemia prevention in blood donors in France.

Methods: A retrospective study was conducted in Alsace (about 150,000 donations per year) in 2013, including 1,925 donors who presented with a low haemoglobin level. We characterized the donors' profiles, their medical follow-up and their obstacles for returning to donate. Simultaneously, a prospective study was conducted in 93 female donors, aged 19 to 40, with no history of anaemia. During a 14 months follow-up, the development of anaemia and iron deficiency was investigated.

Results: The retrospective study showed a prevalence of anaemia of 3.7%; 75% were females aged 18 to 45 years. The annual whole blood donation frequency was 2.75 vs 1.95 in global donor population (P < 0.001). Half of them did not come back to donate 2 years after the detection of anaemia. Among them, half did not benefit from any medical follow-up. The recurrence rate of anaemia after a subsequent donation was 26% within 2 years.

The prospective study revealed an incidence of anaemia of 27% and iron deficiency of 84%. A minimum donation interval of 93 days has been deduced as a protective factor to prevent anaemia (P < 0.009).

Summary/Conclusions: These data are consistent with international studies prescribing several methods for prevention of anaemia in blood donors: reduction of the donation frequency, increased donation interval, ferritin testing or iron supplementation. A computerized monitoring of the haemoglobin concentration kinetic should help to anticipate the anaemia occurrence, by defining at-risk patterns. A personalized counselling of these donors would allow to increase the donation interval, preventing them to donate once too much. Of note, with these values, adopting the European threshold for haemoglobin levels would raise the donor deferral rate up to 10% for anaemia the year of implementation.

P-200
HAEMOGLOBIN REGENERATION IN A FRENCH POPULATION OF NEW DONORS

J Py[1] and M Barnoux[2]
[1]Directeur Médical [2]EFS Centre Pays de la Loire, Saint Jean de la Ruelle, France

Background: In 2008, France has established specific regulations about anaemia prevention in blood donation: lower haemoglobin (Hb) thresholds (120 and 130 g/l for women and men), targeted predonation Hb measurement, systematic blood count sampled before donation, 8 weeks interval between whole blood donations (WBD), and a maximum number of WBD per year of 4 for women and 6 for men.

Aims: Published studies about these regulations are scarce. We were interested about their consequences in donor Hb regeneration. Knowing there are underlying individual characteristics able to bias donor's return, we chose to work specifically on a large base of new donors.

Methods: We extracted from the French national donor database all donors doing their first WBD during 2015. We then followed every WBD made until the end of 2017, hence a survey period of 2 to 3 years. Main studied criteria was the ratio of donor achieving a recovery of their initial Hb level after a delay varying from the mandatory time interval between donations until one year.

Results: The study population contains 167,750 women (W) and 136,702 men (M) with mean Hb at their first donation of 136.2 and 153.8 g/l.

Nearly half of them never made a second donation (W 45%, M 49%) and only 21% of both sexes made at least 4 WBD in the study period. There is strictly no correlation between Hb level at the first donation and the maximum number of donations during the study.

On the second donation, 35% of women have recovered Hb level of the first donation after 8 weeks, and this proportion rises slowly with a greater interval but never reached 50%, even after one year. Comparatively, half of the men have recovered their initial level at 8 weeks, but this ratio remains stable afterwards.

This pattern is similar for men when they came for their third or fourth donation. But it is different for women with an acceleration of Hb recovery, reaching the 50% threshold after 28 weeks on the third donation and 24 weeks on the fourth. Women also have a recovery ratio which continues to rise when the delay between donations grows.

Non recovery is cumulative when donations are rapidly consecutive, peculiarly for women with a ratio of 21% when the third donation occurs 16 weeks after the first one and 17% if the fourth donation is done in a total delay of 24 weeks (respectively 41% and 38% for men).

Analysis taking in account age of the donor shows clearly a bad recovery for young women compared with oldest ones, not really observed with men.

Summary/Conclusions: Our work confirms that Hb recovery is better with men than with women after the first WBD. But it shows that some kind of adaptation occurs with women during following donations, not observed with men. Besides, these results are "mean" results, and they show that a significant number of donors, including men, never recover their initial Hb. A personalized follow-up, with the introduction of ferritin measurement, is a necessity.

P-201

FRENCH ORGANISATION TO PREVENT DONATIONS FROM ANAEMIC DONORS IS QUITE EFFECTIVE

J Py[1] and M Barnoux[2]

[1]Directeur Médical [2]EFS Centre Pays de la Loire, Saint Jean de la Ruelle, France

Background: In 2008, France upgraded its organisation to prevent anaemic donors' donation. A predonation haemoglobin (Hb) measurement (PM) became mandatory, but only for new donors, donors having no donation since two years at least, and donors with a recent low Hb. An invasive method was chosen, performed first on capillary blood, with a venous duplicate in case of a value below thresholds of 120 and 130 g/l in women and men. Besides, a full blood count (FBC) was added to mandatory tests, in order to survey regular blood donors.

Aims: This study wants to evaluate the efficacy of this organisation nearly ten years after its implementation, with a specific focus upon the invasive method practice.

Methods: A data extraction from all blood donation candidatures during August 2017 was done in the French national database. FBC Hb values were analysed as the gold standard, and compared with PM ones when they were done.

Results: 113,255 FBC Hb for women and 123,052 for men were usable. Among them, respectively 5.9% and 1.7% were below 120 and 130 g/l. But donor selection was quite effective, as an anaemic value was only found for 3.1% and 0.9% of whole blood donations. 52% of anaemic donors were prevented from donation and anaemia was present in 61% of non-accomplished donations.

3,673 whole blood donations were done with anaemic donors (most of them only slightly below thresholds). Among them, 64% were not tested for Hb PM and 36% were tested.

Correlation between FBC and capillary PM was quite good (0.741), but far less than between FBC and venous PM (0.871). In Bland-Altman plots, venous PM has a better difference against mean than capillary PM (−0.16 versus −0.26) and a lower standard deviation (0.50 versus 0.73).

Summary/Conclusions: French organisation to prevent donations from anaemic donors is quite effective, especially for higher anaemic state. A systematic Hb PM would be able to detect two thirds of the failures, but extension of invasive methods is very heavy and non-invasive methods are not precise enough nowadays. Other failures would be improved by doing venous PM right away, but this choice may be more binding for blood donors.

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STABILITY OF FERRITIN TESTING: EVALUATION OF TESTING STRATEGIES FOR HIGH THROUGHPUT ROUTINE DONATION SCREENING

A Van Weert[1], I Ebbing[1], M Kok[1], M Janssen[2] and E Bakker[1]

[1]National Screening Laboratory Sanquin [2]Department of TTA, Sanquin Blood Supply, Amsterdam, Netherlands

Background: Because blood donors may develop increased iron loss due to regular blood donation, ferritin testing is used to monitor their iron status. However, within the workflow of blood donation and screening ferritin testing within 24 h is not always possible and extra handlings for testing as required by the assay insert effect the efficiency of donation screening. Therefore strategies for efficient and reliable ferritin testing of blood donation samples have to be developed.

Aims: To study ferritin measurements in serum and plasma EDTA samples from blood donors in order to establish a testing strategy for ferritin measurement in routine screening without conceding quality and efficiency.

Methods: Ferritin testing was validated on the Architect i2000sr by establishing the precision in a dilution series of 6 concentrations in between 10–150 ng/ml. Measurements were done in 6-fold at two fixed time points during three days. To define the testing methodology, 50 serum tubes and 50 plasma EDTA tubes stored at room temperature or at 4–8°C, were centrifuged and tested at different time points in between 1–96 h after blood drawing in order to mimic the time between blood drawing and testing. Next, plasma EDTA and serum samples from 726 donations were tested in duplicate for up to 7 days. Statistical analyses were done in the R-package for statistical computing.

Results: The coefficient of variation of the average ferritin concentration over time is <3% at all concentrations of the dilution series. In the samples, the measured ferritin concentration increased with at the average 0.87 ± 0.11 (EDTA) and 0.52 ± 0.09 (serum) per day, which is a relative change of 2.3% and 1.1%, respectively. The variance of the difference in value as compared to the first ferritin measurement after blood collection (t = 1–5 h) increased with a standard deviation of 7.1% (plasma) and 7.4% (serum). Postponing centrifugation as well as storage of samples at 4–8°C resulted in a delay measuring higher ferritin concentration values over time in the same sample. Ferritin testing (n = 726) in daily routine confirmed the increase of the measured ferritin value relative to the value measured within 24 h, but that ferritin testing can be done consistently even if done >24 h after blood donation.

Summary/Conclusions: Ferritin measured in plasma EDTA and serum tubes for ≤96 h after blood collection revealed higher values when comparing with measurements within 1–5 h of blood drawing. This increase was less for samples stored at 4–8°C versus room temperature, as well as by postponing centrifugation. This may be explained by the heterogeneity of ferritin isoforms and its commutability. Taking into account time needed for transport of donation samples to the laboratory, a testing strategy can be to centrifuge samples <24 h after blood collection, first complete routine screening, and subsequently use the same tube for ferritin testing. Even though ferritin is measured later than 24 h after blood collection, efficiency and quality can be maintained as verified by implementation of ferritin testing in routine daily practice for high throughput donation screening.

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Abstract has been withdrawn

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DELAYED DONOR REACTIONS TO BLOOD DONATIONS – ANONYMOUS ELECTRONIC SURVEY

R Procházková[1,2], Z Kráľovská[1], P Suchý[3] and P Papoušek[1]

[1]Transfusion, Regional Hospital Liberec [2]Faculty of Health Studies, Technical University of Liberec, Liberec [3]Department of Rock Structure and Mechanics, Academy of Science of the CR, Praha, Czech Republic

Background: Incidence of undesirable delayed blood donation reactions that appear only after leaving a donation centre (off-site) is not so thoroughly observed unlike early reactions.

Aims: The aim of the study was to determine the incidence of delayed complications to blood donations using a method of the electronic survey.

Methods: The studied population comprised voluntary, and non-remunerated donors who gave whole blood, and apheresis donors in the Regional Hospital Liberec during the last 12 months. 5,497 donors were addressed via a short mobile phone text message with a link to an anonymous electronic questionnaire located on the Regional Hospital Liberec website. Donors filled in the possible troubles regarding only the last finished donation.

Results: 1,792 questionnaires were used for the definitive analysis (32.6% of all addressed donors). The donor average age was 38.5 years. Some of the complications were present in 35.3% donors (26.8% males, and 46.7% females, P < 0.001). The most frequent trouble was fatigue (21.2%), then hematoma after the donation (13.1%), weakness, faint, and dizziness (5.3%), and pain in a limb from which blood was taken (4.8%), shortness of breath on exertion (3.4%), manifestation of infection (cold, elevated temperature, muscle and joint pains, chills) during the seven post-donation days (2.0%), late venipuncture bleeding (1.5%), phlebitis (0.6%), nausea, and vomiting (0.4%), collapse (0.4%), and unconsciousness (0.3%). The adverse reactions occurred more frequently after whole blood donation (36.8%) than after plasmapheresis (24.4%), P < 0.001. Tired male donors had 17 times higher risk of weakness, or dizziness than non-tired donors (P < 0.001), and also tired women had 2.5 times higher risk of weakness, or dizziness than non-tired female donors (P < 0.001)

Summary/Conclusions: More than 1/3 of the donors with the majority of them being women reported some troubles after donations. Fatigue was the dominant difficulty among them. The study provided detailed data for working out educative material for donors.

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STANDING ENHANCES VASOVAGAL SYMPTOMS ELICITED BY STIMULI ASSOCIATED WITH BLOOD BUT NOT OTHER EMOTIONAL STRESSORS

P Gilchrist[1], A Coopersmith[2], M Li[2], V Woroniak[2] and B Ditto[2]

[1]Public Health & Primary Care, University of Cambridge, Cambridge, United Kingdom [2]Psychology, McGill University, Montreal, Canada

Background: Various stimuli (orthostatic stress, blood-related stimuli, fear, haemorrhage, etc.) are capable of triggering a vasovagal response (VVR). It remains unclear to what extent these represent identical or just similar physiological reactions.

Aims: This study examined the specificity of VVR in response to stimuli involving Blood/Injury when compared to other emotional stimuli, and built upon the idea of 'simulated' blood loss by hypothesizing that VVR are based on the prevention of excessive blood loss and thus triggered by stimuli that suggest as well as produce actual loss. As a result, the effects of certain emotional, blood-related stressors should interact with certain postural stressors.

Methods: 48 healthy young adults completed a questionnaire assessing medical fears (Medical Fears Survey –MFS-SF; Olatunji et al., 2012) and watched five 5-minute stimulus videos with different emotional content. All participants watched the Neutral video followed by 4 subsequent videos presented in counter-balanced orders: a Blood/Injury video depicting an open heart surgery, and three additional videos (Medical, Chase/Fear, and Loss/Sadness). Participants were randomly assigned to watch the videos either standing or sitting in an arm-chair. Vasovagal symptoms, blood pressure (BP), and heart rate (HR) were assessed during each video.

Results: The primary analyses were 2 Posture (sitting/standing) x 4 Video (Loss/Chase/Medical/Blood-Injury) x Medical Fear (treated as a continuous measure) repeated-measure general linear models (GLMs) with sex and a Neutral video value as covariates. As predicted, there was a significant Posture x Video interaction, $F(3, 129) = 3.53$, $P = 0.040$, $\eta^2_p = 0.076$, due to a specific enhancement of symptoms during the Blood/Injury video by standing. This effect was moderated by fearfulness leading to a significant Posture x Video X Medical Fear interaction, $F(3, 129) =$

5.30, $P = 0.010$, $\eta^2_p = 0.11$. Standing significantly increased symptoms experienced by more fearful participants during Blood/Injury but not other videos. This pattern was corroborated by SBP and HR with significant Posture x Film interaction effects, $F(3, 117) = 2.84$, $P = 0.048$, $\eta^2_p = 0.068$, and $F(3, 117) = 4.20$, $P = 0.011$, $\eta^2_p = 0.097$, respectively. As expected, this was due to notable decreases among those who watched the surgery film while standing.

Summary/Conclusions: Blood-related fears play a key role in eliciting VVR and orthostatic stress enhances this effect. These findings provide support for the theory that VVR may have developed as a means to facilitate the survival of animals who were injured and experiencing significant blood loss. Clinical implications include the management or reduction of blood-related stimuli for blood donors.

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DOES ANTI–HYPERTENSIVE MEDICATION POSE A RISK FOR THE DONOR?

K Johnsen[1,2], K Magnussen[3], L Malerstuen[1], C Erstad[3] and L Nissen-Meyer[1]

[1]Immunology and Transfusion Medicine, University Hospital of Oslo, Oslo [2]Center for Transfusion Medicine, Østfold Hospital Trust, Kalnes [3]Blood Center and Medical Biochemistry, Innlandet Hospital Trust, Innlandet, Norway

Background: In Norway blood donors taking any hypertensive medication were previously permanently deferred, on the assumption that they might have a higher risk of adverse reactions, due to reduced responsiveness of the vascular system. During 2014 and 15 this policy was changed in several blood banks in Norway, and since then a growing number of blood donors on anti-hypertensive medication has been accepted for donation. Approval criteria included stable dose of anti-hypertensive medication for at least 3 months, normal blood pressures, and no experience of side effects from the therapy. According to the lab information system, approximately 350 donors in the Blood Bank of Oslo have been registered to take anti-hypertensive medication, and 270 have donated blood within the last year.

Aims: In this quality study we wanted to validate the new criteria by testing if these donors experience a higher rate of adverse effects (AEs), like dizziness or fainting, compared to their previous experience and to other donors. Is it safe to use this group of people as blood donors? What is the added number of donations acquired from donors on anti-hypertensive medication?

Methods: Information about the blood donors using anti-hypertensive drugs was collected in a questionnaire presented to them upon arrival in the blood bank. Two blood banks are currently participating, the Blood Center of Oslo and the Blood Center in Innlandet Trust.

The questionnaire and the informed consent form were approved by the data protection officer, Oslo University Hospital. We are planning to gather information from as many donors as possible, within a 3–4 months period.

Results: Within the first 4 weeks of the study period, 44 donors taking anti-hypertensive medication were recruited to the study, 26 men and 18 women with a mean age of 56 years (range 27–67). Eighty-four % use angiotensin II antagonists, 32% use calcium blockers, 7% use ACE-inhibitors and 36% use combined therapy. Of these, none experienced severe post-donation episodes outside the blood bank. Two had experienced weak reactions connected to blood donation, e.g., dizziness and shortness of breath. Ninety-three % follow the recommendation to drink > 0.5 l fluid before/during donation. The acceptance of these blood donors has led to a welcome extra supply of altogether 225 units of whole blood to our blood centers.

Summary/Conclusions: Preliminary results from our study suggest that it is safe to accept blood donors despite anti-hypertensive drug therapy, as they don't experience more frequent AEs. In part, this can be explained by this group having on average higher blood pressures than other donors. Most of them also have experience with previous donation, and exhibit good compliance to advice from blood bank personnel.

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SURVEILLANCE OF BLOOD DONOR ADVERSE EVENTS AT RAWALPINDI INSTITUTE OF CARDIOLOGY, PAKISTAN

SJ Ansari[1], S Dad[2] and H Shabber[3]

[1]Biosciences, COMSATS Institute of Information Technology (CIIT) [2]Blood Bank, Rawalpindi Institute of Cardiology [3]Federal Government Services Hospital and Post Graduate Medical Institute, Islamabad, Pakistan

Background: Blood donation is a safe procedure and generally does not involve any complications. However, some blood donors may experience various Adverse Events (AEs) of variable severity. In Pakistan, the blood transfusion system relies predominantly on 'Family Replacement Donors" with very little contribution from Voluntary Blood Donors. However, in times of emergencies and crises, tremendous response from voluntary blood donors is observed. The adverse events during blood donation are not documented due to lack of proper documentation system and lack of awareness of the staff involved. The current study was initiated to improve the safety standards of blood donation by monitoring all adverse events in the blood donor section at Blood Transfusion Services, Rawalpindi Institute of Cardiology, Rawalpindi.

Aims: The study was carried out to estimate and compare the number and type of AEs, assess practices which would minimize AEs and strengthen the donor vigilance at Blood Transfusion Services, Rawalpindi Institute of Cardiology.

Methods: This retrospective single centre study was carried out from January 2016 to December 2016. All whole blood donors attended at the Rawalpindi Institute of Cardiology were included in the study. All AEs occurring during or at the end of donation were noted on a pre-tested standardized reporting form developed before conducting the study.

Results: In 44,553 blood donations, 299 blood donors were reported with adverse reactions, resulting in event rate of 0.7% which is 1 in about every 154 donations. All adverse events were of mild intensity and no severe complication, medical emergency or life threatening adverse reactions were observed. The adverse events included slow pulse 14.5% (n = 264), low BP 13.1% (n = 238), sweating 12.1% (n = 221), fainting 12.0% (n = 218), pallor skin 11.4% (n = 207), nausea 10.7% (n = 195), drowsiness 6.9% (n = 125), vomiting 6.4% (n = 117), cold extremities 5.2% (n = 94), hematoma 1.5% (n = 28), feeling warmth 1.5% (n = 27), multiple pricks 1.4% (n = 25), shortness of breath 1.0% (n = 19), headache 0.5% (n = 9), bruising 0.5% (n = 9), weakness 0.4% (n = 8), falling 0.3% (n = 6), restlessness 0.3% (n = 6) and anxiousness 0.2% (n = 4).

Summary/Conclusions: Donor haemovigilance systems allow monitoring of donor safety and assessment of the success of interventions designed to further improve donor safety. The study underlines the fact that blood donation is very safe procedure which could be made event-free by following proper physical and behavioral screening before blood donation and applying haemovigilance tools on collected data. There is need to provide specific information cards to donors at the time of an adverse event detailing immediate management and preventative actions relevant to subsequent donations. Adequate hydration, proper physical screening and comfortable environment at donation place reduce frequency of adverse reactions. It is crucial that all blood banks adopt a systematic approach to monitor the rates of donor adverse reactions. The current study needs to be emulated in other blood banks to bring about a general improvement in the functioning of the blood transfusion services in Pakistan.

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STUDY ON SLEEP QUALITY AND DONOR VASOVAGAL REACTION: A MATCHED CASE-CONTROL STUDY

C Yu[1], Y Chen[1], J Chen[1], H Tsai[2], Y Wang[1], S Wei[1] and S Hou[1]

[1]Taiwan Blood Services Foundation [2]Taipei Blood Center, Taiwan Blood Services Foundation, Taipei, Taiwan

Background: Insufficient sleep is one of the risk factors of vasovagal reaction (VVR), but a few study evaluated the association between sleep quality (SQ) and VVR.

Aims: To investigate the relationship between SQ and VVR among blood donors.

Methods: We conducted a case-control study recruited 104 whole blood (WB) donors with VVR (case group), who were identified during or after their blood donation, and 309 WB donors without VVR (control group), who were 1:3 in frequency and matched with age, gender, and donation site, during 2016–2017. A questionnaire through telephone was used to collect the risk factors of VVR and the Pittsburgh Sleep Quality Index (PSQI). The demographic characteristics, the information of blood donation, and the results of pre-donation medical examination were obtained.

Body mass index (BMI), estimated blood volume (EBV) and the percentage of blood loss (defined as the volume of blood collected divided by EBV) were calculated. Logistic regression was adopted to evaluate the association between SQ and VVR with adjustment of confounding factors.

Results: The averaged PSQI score was 5.91 ± 2.92 and 4.34 ± 2.62 in case group and control group, respectively. And it was showed a significant difference on the proportion of poor SQ between the two groups (51% in case group vs. 30.4% in control group, P < 0.001). After adjusting confounding factors and stratified by gender, the impact of SQ on VVR was significant in male donors who had poor SQ (OR= 4.99, 95% CI: 2.02–12.3), less than 6 hours of sleep (OR=4.62, 95% CI: 1.78–12.0) and sleep disorders (OR=3.46, 95% CI: 1.33–9.01). In female donors, the influence of blood loss was more important than SQ on VVR. Although female donors who had less than 6 hours of sleep or sleep disorders had a higher risk of VVR, the difference was not significant. However, a significant increased risk of VVR was observed in female donors with a blood loss of 8.5% or more (OR=5.30, 95% CI: 1.16–24.1).

Summary/Conclusions: To our knowledge, this is the first documented study to analyze donor SQ for the development of VVR. We found that poor SQ is an important factor for VVR in male donors but not in female donors. Female donors should evaluate the percentage of blood loss rather than SQ. Moreover, appropriate percentage of blood loss should be considered in individual to ensure donor safety.

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EFFECTIVENESS OF WATER AND SALTED SNACKS ADMINISTRATION AT TIME OF BLOOD DONATION ON RATES OF VASOVAGAL REACTIONS

P Robillard, Y Gregoire and M Antar

Hema-Quebec, Montreal, Canada

Background: Vasovagal reactions (VVR) are common in blood donors. Having donors to drink water and eat salted snacks before donating is a recognized preventive measure but is not easy to obtain and monitor.

Aims: To measure the effect of implementing a structured process to administer water and salted snacks to donors on rates of VVR.

Methods: Pre-implementation donors were simply informed at registration to drink water before donating. Amount was not mentioned and supply varied from an empty glass the donor had to fill, a 200-ml juice box, a 500-ml water bottle or nothing at all. Snacks were offered after donation and were sugary. On June 11th 2017 a program was introduced at all collection sites with leaflets, posters and pictograms to inform donors on importance of drinking water and eating salted snacks and all donors were provided with a 500-ml water bottle and a bag of salted pretzels at registration. They were told to drink the whole bottle before donating and to eat pretzels. Three check points monitored consumption at interview, venipuncture and recovery area. All severities of VVR were to be reported on a standardized form. Rates of all VVR and VVR without loss of consciousness (LOC) per 100 donations in the 6 months PRE (11 Dec 2016–10 Jun 2017) and POST (11 Jun–10 Dec 2017) implementation were compared using chi-square tests.

Results: There was a significant reduction in number (PRE: 7004; POST: 6081) and rates of all VVRs (PRE: 4.90; POST: 4.22) for a risk reduction of 13.9% (95% CI: 11.1–16.7). For VVRs-LOC risk reduction was 23.9% (95% CI: 13.1–33.4) (rates PRE: 0.33; POST: 0.25). Rates of VVRs significantly declined in both first-time (18.84 vs 16.92) and experienced donors (3.21 vs 2.84), in female (7.99 vs 6.81) and male donors (2.88 vs 2.41). For VVRs-LOC, risk reduction was 26.6% for female and 22.1% for male donors. Risk reduction was significant in all age groups being the greatest in the 40–49 (20.8%) and 30–39 (13.5%) yo. Although rates were lower in apheresis donors, risk reduction was as important as in whole blood donors for females.

Summary/Conclusions: Having a structured program for water and salted snacks delivery at blood collection sites significantly reduces the incidence of VVRs and more importantly of those with LOC. It improves donor safety and makes donation experience better, making it more likely for donors to return.

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PREVENTION OF VASOVAGAL REACTIONS IN BLOOD DONORS: A RANDOMIZED DOUBLE-BLINDED CONTROLLED COMPARISON OF EFFICACY AND HAEMODYNAMIC EFFECTS OF ORAL PREHYDRATION FLUIDS – A PRELIMINARY REPORT

C Cheung[1], W Lee[1], K Khaw[2] and C Chu[3]

[1]Department of Health Technology and Informatics, The Hong Kong Polytechnic University [2]Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong [3]Blood Collection and Donor Recruitment Department, Hong Kong Red Cross Transfusion Service, HA, Hong Kong, Hong Kong

Background: Vasovagal reaction (VVR) is an adverse effect that may occur during and after blood donation. Most symptoms are mild, however, serious consequences as a result from these symptoms after donation have been reported. VVR is a major factor accounting for the reduction of both first time and repeated blood donors. Even with extensive research targeting risk factors such as age, gender and weight in blood donors, there seems to be no definitive solution to address the issue.

Aims: VVR is associated with abrupt cardiovascular challenges leading to haemodynamic decompensation. The aim of this study was to investigate the haemodynamic effects of different methods of fluid prehydration in an attempt to minimize immediate and delayed VVR among young and healthy blood donors.

Methods: 63 blood donors with age <23 were recruited to participate in this randomized double-blinded controlled study. Subjects were assigned to one of the three groups prior to blood donation: 1) No prehydration (Control); 2) 500 ml water prehydration (Placebo) or 3) 500 ml oral rehydration salt (ORS). Haemodynamic measurements were recorded using transcutaneous Doppler ultrasound at five time points - before and after pre-hydration, followed by intervals at the start, mid-point and completion of the blood donation procedure.

Results: Data were analysed for 58 subjects. 20, 20 and 18 subjects were allocated to control, placebo and ORS group respectively. There was no difference in the incidence of immediate or delayed VVR among the 3 groups. Immediate VVR was recorded in 3 subjects (4.76%), with two in placebo and one in the ORS group. Delayed VVR was also reported in 3 subjects (4.76%), with two from control and one from the placebo group. Post-hydration measurements revealed a significantly higher stroke volume (SV) (74 vs 64 ml), higher cardiac output (CO) (5.32 vs 4.24 l/min) and lower systemic vascular resistance (SVR) (1,390 vs 1,731 mmHg min/ml) in the ORS group than the control group (P < 0.05). A reduction in SV and CO were detected regardless of group allocation during blood donation. After blood donation, the ORS group showed a significantly higher SV (67.94 vs 57.70 ml) and CO (5.33 vs 4.02 l/min) with lower SVR (1,455 vs 1,825 mmHg min/ml) than the control group. Blood pressure parameters did not show clinically significant changes across all groups before and after blood donation.

Summary/Conclusions: Preliminary findings suggested that prehydration with ORS may provide a better preservation of the haemodynamics, although it may not necessarily reduce the incidence of VVR. The cause of VVR is multifactorial, and ORS may exert a positive effect on one of the important contributing factors to VVR.

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SEVERE ADVERSE TRANSFUSION REACTIONS IN SLOVENIAN HAEMOVIGILANCE NETWORK FROM 2013 UP TO 2016

I Maric[1], K Petrusa[2], K Zeleznik[2] and I Bricl[1]

[1]Haemovigilance Office [2]Blood Transfusion Centre of Slovenia, Ljubljana, Slovenia

Background: Severe adverse transfusion reactions (SATR) are all adverse effects of blood or blood components which can be potentially fatal or could cause a long term illness. Analysis of adverse transfusion reactions (ATR) should raise the awareness and could allow their early recognition and prevention. National Slovenian hemovigilance office collects information about all ATR from 12 transfusion departments which supply blood components for 26 Slovenian hospitals. It is mandatory by the law to report all the severe adverse transfusion reactions to the Slovenian competent authority which at the end of the year has to produce an annual report and submit it to the European commission.

Aims: We are aiming to raise awareness about ATRs, especially by encouraging physicians to report more often mild ATRs.

Methods: We have retrospectively analyzed reports of all SATR in Slovenian hemovigilance system, from January 2013 up to December of 2016.

Results: In observed period there were 481 cases of ATR of which 45 were SATR. SATR were 9% of all cases. In the same period we issued 475,412 of blood components. For simplicity we assume that all the issued components or high majority of them were actually transfused. We calculated that the incidence of ATR in the period

we analysed was 1 in 1,000 transfusions or 1 in 10,500 in case of SATR. Most frequent adverse reactions were volume overload (TACO) with 22 reported cases; incidence of TACO was 1 in 16,671 transfusions of red blood cells. Second most common was severe allergic reactions with 10 cases or incidence of 1 in 47,512 transfusions. We also had 4 cases of transmission of hepatitis B virus with incidence of 1 in 118,853 transfusions, 3 hypotension reactions with incidence of 1 in 158,470 transfusions, 2 TRALIs with incidence of 1 in 237,706 and 2 cases of delayed haemolysis with incidence of 166,713 (calculated just on transfused red blood cells and not all the components). We didn't have a case of a death caused by transfusion or any cases of TA-GvHD, thrombocytopenic purpura or acute haemolysis.

Summary/Conclusions: Slovenia has a hemovigilance system which is determined by law. Because of strict testing regime combined with surveillance system and quality control safety of blood products is at a high level. We do realise that some of ATRs are underreported especially those with mild or all most no signs transfusion reactions for which physician is not sure that if it is related to transfusion. On the other hand we believe that vast majority of SATRs are reported because it is very hard to overlook and not to report life treating complication of transfusion. Reporting all ATRs is of great importance since it represents an opportunity for learning and system improvement. Being more aware of transfusion complications, recognising them faster and taking swift action will benefit our patients. Making transfusions safer, from the vain of the donor, up to vain of recipient, is in all our best interests and it is the responsibility of everyone involved in the transfusion chain.

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A STUDY TO EVALUATE THE USEFULNESS OF POST DONATION BLOOD PRESSURE MONITORING IN REDUCING VASOVAGAL REACTION

S Wong, K Iskhak, A Ho, L Li, D Pennefather, H Tan, L Tan and P Thant

Blood Resources, Health Sciences Authority, Singapore, Singapore, Singapore

Background: It was noticed in recent years, there was a rise of donor vasovagal reaction (VVR) in our national blood banks. Serious VVR may cause injuries or fear for future donation. A group of donors identified most prone to VVR were those aged between 16–25 years old. Thus, a small study to monitor donor's blood pressure (BP) post donation to reduce VVR were recommended.

Aims: To determine if implementation of post donation BP monitoring and only discharge donors after the BP is ≥ 100/60 could reduce the incidences of VVR.

Methods: The study were conducted in September and October 2017 on 200 whole blood donors at 3 local universities blood mobiles where their age range were within our study group. Of the 200 donors participated in this study, 100 donors were in the control group where donors drank at least 300 mls of isotonic drink. The other half of the donors were in the study group which they had their post donation blood pressure taken as an additional preventive measure coupled with at least 300 mls of isotonic drink consumed. The participants in control and study groups were equally divided amongst 3 universities to ensure consistency in other variables (Both groups had same physical and social environments).

Then a comparison between both groups was done to ascertain which group has a higher number of reaction rates.

Results: Out of the 200 participants, 2 participants dropped out from the study group because they could not wait for the BP monitoring and had to rush back for their classes. Another 7 donors in the study group had to terminate their donation half way during donation and were out of the study.

7 donors in the control group had adverse reactions while 13 donors in the study group was noted to develop adverse reaction after completing their donation.

The result has a P value of 0.100493 which is not significant at significance level of 0.05 using Chi-square test.

There were 24 donors in the study group completed their donation, had low BP (< 100/60) but had no adverse reaction. They rested in donation room and were encouraged to drink more fluid. They were allowed to leave the donation room when their BP readings reached ≥ 100/60. This group of donors could potentially develop VVR if they were not monitored closely in donation room.

Summary/Conclusions: This study showed higher rate of VVR despite post donation blood pressure monitoring. However, the P value result was insignificant. In this group of donors, lack of sleep, food and water insufficiency and higher level of activities could be the contributing factors for the cause of VVR. Therefore, monitoring blood pressure alone is ineffective in the prevention of reaction. Continuous education for this group of donors in preventing adverse reactions and what to do in the event of adverse reaction during and post blood donation are the more practical approach. We can conclude that taking BP post donation do not help in reducing VVR.

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Abstract has been withdrawn

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ADVERSE REACTIONS AMONG BLOOD DONORS IN KURDISTAN PROVINCE AND ITS EFFECT ON BLOOD DONOR RETURN RATES

S Ferdowsi, S Babahajian, K Khaledian and M Karimian
Blood Transfusion Research Center, Tehran, Iran

Background: Blood donation is widely considered to be safe with a low incidence of adverse reactions (ARs); however, ARs occasionally occur during or at the end of the blood collection. On the other hand, ARs can negatively affect donor retention.
Aims: The aim of this study was to assess the frequency of ARs in Kurdistan blood transfusion center, west of Iran, in 2015. We also determined the impact of ARs on donor return rates.
Methods: We performed a cohort study on whole blood donations, using data extracted from the blood service information. ARs were recorded using internationally agreed standard definitions. All donors were observed during and following donation for possible adverse events for 20 min. In addition, donors who had ARs were evaluated for return donation within 12 months and subsequent reactions.
Results: A total of 25,891 blood donors were enrolled. Of these, 20,476 (79.08%) were repeat donors and 5,415 (20.9%) were first time donors. Of the total number of donors, 170 (0.65%) experienced ARs; of these, 164 (96.4%) developed vasovagal reaction (VVR), 1 (0.5%) had arterial injury, and 5 (2.9%) developed hematoma. The mean age of female and male donors who experienced ARs was 31.4 and 30.73 years, respectively. In 87.05% (148/170), the donor was a man and in 58.8% (100/170) a repeat donation. Donors with hemoglobin less than 15 gr/dl was significantly associated with VVR (P = 0.004). The return rate within 1 year was 18% (32/170) and all of them were repeat doors. In all, 78.1% (25/32) of donors who experienced ARs at the first donation had an uncomplicated second donation.
Summary/Conclusions: The incidence of reactions was low at our center. In addition, our results showed donation experience strongly influences on donor return and reduced donor return was seen following ARs.

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NATIONAL DONOR VIGILANCE SYSTEM, AN EXPERIENCE TO REDUCE THE SEVER DONOR REACTIONS IN IRAN

K Shamsasenjan, A Sedaghat, S Aminikafiabadi, M Maghsoodlu, B Rabbani and A Pourfathollah
High Institute for Research and Education in Transfusion Medicine, Iranian Blood Transfusion Organization, Tehran, Iran

Background: Adverse reactions of blood donations have a main role for improving donors' satisfactions accordingly increasing blood donation frequency and retaining regular blood donors. These adverse reactions, especially the severe ones are very important as blood donors' care and the ethical issues for blood donations as well. A standard National Donor Vigilance System could be able to monitor the adverse reactions among blood donors carefully, to reduce the frequent and severe adverse reactions, and also to improve the quality and safety of blood donors.
Aims:
1. To improve donor satisfaction
2. To increase donation frequencies
3. To reduce the frequency of sever adverse events
4. To reduce donor injures
Methods: "National Donor Vigilance System" has been scaled up in 2016 in IRAN. After strengthening the national donor vigilance reporting system, a plan of interventions designed and implemented based on 4 categories as following: the national protocol for donor vigilance revised and updated based on WHO last version guideline on standard definitions for donor vigilance, the national donor vigilance reporting system and recording forms revised and updated, a national training manual about prevention methods for severe reactions developed, and a national training workshop conducted for all qualified physicians and all donor vigilance staff in all blood collection centers. Based on this experience the proportion of severe adverse donor reactions reduced from 7% of all adverse donor reactions in the year 2016 to 4% in the year 2017.
Results: In 2016 National Donor Vigilance System has been scaled up. The national donor vigilance reporting system showed that the proportion of severe adverse reactions was about 4% of all adverse reactions in 2017, while this percentage had been recorded about 7% for the year 2016, and this experience showed about 3% reduction in severe adverse donor reactions index in the years 2016 to 2017, by scaling up the national donor vigilance system.
Summary/Conclusions: Donor Vigilance has an essential role in blood donors' safety, in recruitment and retention of blood donors, also in ethical issues for blood donors. An accurate system for recording and reporting of blood donors' adverse reactions, especially with standard preventive interventions for severe reactions, could be very effective. In our national experience, training of staff had important role for reducing the donors' severe adverse reactions.

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INCOMPLETE FILTRATION OF RED BLOOD CELL UNITS AT CANADIAN BLOOD SERVICES

S Al Khan[1], T Butler-Foster[2,3], N Rickards[4], H Aljedani[4], M Bigham[1], R Skeate[5] and E Kahwash[4]

[1]*Canadian Blood Services, Vancouver, British Columbia* [2]*Medical Services, Canadian Blood Services, London, Ontario* [3]*Arthur Labatt School of Nursing, Western Ontario, London* [4]*Canadian Blood Services, Halifax, Nova Scotia* [5]*Canadian Blood Services, Toronto, Ontario, Canada*

Background: Incomplete filtration (IF) occurs when a red blood cell or whole blood (WB) unit does not completely filter due to blockage. Canadian Blood Services (CBS) implemented a policy of managing donors with WB donations resulting in IF. As per this policy, if the donor's WB donation resulted in ≥ 2 consecutive or ≥ 3 intermittent IF, medical office is notified and evaluates the donor for possible deferral. The published literature showed that some of the donors who have IF might not have an associated health issue. However, these donors are still lost to deferral in the current policy.
Aims: The aim of this study is to retrospectively examine data on donors with IF and to identify any associated factors found among the deferred donors.
Methods: We retrospectively reviewed the national CBS donor base using Business Intelligence (BI) warehouse data and ePROGESA data analyzing all deferred blood donors due to the IF for the period of January 1st, 2015 to December 31st, 2017. Data collected included donor's gender, age at deferral, blood group, total number of donations prior to deferral due to IF, production method of the unit associated with IF (B1 versus B2 collection bags), and type of filters used by CBS.
Results: There were 353 donors deferred due to IF during the study period. Among those 188 (53%) were males and 167 (47%) were females. Distribution of the ABO blood group of these donors included group O donors 57% (201/353), group A donors 27.5% (97/353), group B donors 10.8% (38/353) and group AB donors 4.3% (15/353). Among the deferred donors, 313 were regular donors with variable total donations (range: 3 to 270). IF was associated with B2 collection bags (242/353) at more than double the frequency compared to B1 collection bags (110/353). However, the total B1 collections by CBS are around 80% of whole blood collections and only 20% are B2 collections. Of note: B1 production method uses a different filter than B2. Also, the filtration step takes place at different stages of component production.
Summary/Conclusions: We observed no apparent association between age, gender, blood group, number of donations, and the IF events in the deferred donors. IF was associated more with the B2 method of production than B1 method. This may be

because we manufacture the RBC, PLT and plasma from B1 method first before the RBCs are filtered, while in B2 the whole blood is filtered before it is separated into RBCs and plasma. Other factors may include distance from clinic, or donor factors. Creating a robust system to investigate donor factors such as obtaining a medical history and results of follow up testing could identify any donor related factors. CBS does not currently follow up with donors deferred for IF. Implementing a more robust donor follow-up would provide a better line of sight into the donor causal factors of IF.

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ALTERATION IN BIOCHEMICAL PARAMETERS DURING PLATELETPHERESIS IN HEALTHY DONORS AND THEIR ASSOCIATION WITH ADVERSE DONOR REACTIONS

K Garg and P Kaur

Government Medical College and Hospital Sector 32 Chandigarh, Chandigarh, India

Background: Increasing demand for platelet transfusions and shrinking donor pool has led to a shift towards automated blood collections. The newer generation apheresis platforms provide high quality platelets in a short time. Apheresis procedures are associated with unique complications due to citrate infusion. Citrate induces hypocalcaemia and hypomagnesaemia, which are usually transient and self-limiting, but they can lead to significant donor discomfort and affect donor retention. The present study was conducted to analyze changes in biochemical parameters during plateletpheresis and their association with donor adverse reactions.
Aims: To determine the effect of citrate infusion on biochemical parameters during plateletpheresis in healthy donors and to correlate changes with adverse donor reactions.
Methods: The study was conducted from September 2017 to January 2018 on 45 healthy replacement plateletpheresis donors after written informed consent from the donor and approval by Institute Ethics committee. All the donors included in the study met eligibility criteria laid down by Director General of Health Services India. Plateletpheresis procedures were performed on continuous flow machine Fenwal AMICUS or Trima Accel Automated Blood Collection System depending upon venous access as per the department Standard Operative Procedures using closed system apheresis kits. Blood samples were drawn from each donor on three occasions, which included baseline pre-donation sample, 30 min after start of procedure and 30 min after completion of procedure. 2 ml sample was taken in heparinized syringe on each occasion to measure ionized calcium and 5 ml sample in plain vacutainers. Further, plain sample was subjected to measure serum calcium, serum magnesium, parathyroid hormone, total protein and serum albumin using P800 Hitachi Model analyzer.
Results: Forty-five healthy replacement donors aged between 29 ± 7 years and mean weight 74 ± 11.2 kg underwent plateletpheresis. There was statistically significant decline in mean total calcium 9.31 ± 0.66 mg/dl to 8.72 ± 0.93 mg/dl and ionized calcium from 3.7 ± 0.51 mg/dl to 2.8 ± 0.71 mg/dl ($P < 0.0001$) from baseline levels until 30 minutes after the start of procedure respectively. Using paired t-test; similar significant fall was observed in serum magnesium levels (1.83 ± 0.19 mg/dl to 1.6 ± 0.17 mg/dl), total protein (6.7 ± 0.60 g/dl to 5.8 ± 0.84 g/dl) and serum albumin (4.8 ± 0.39 g/dl to 4.1 ± 0.58 g/dl). The levels restored to near baseline levels within 30 minutes post-plateletpheresis. The parathyroid hormone showed significant increase from baseline levels of 21 ± 13 pg/ml to 95 ± 41 pg/ml during procedure and the levels remain elevated 30 minutes post-plateletpheresis. Out of 45 donors, 4% (n = 2) experienced symptoms of citrate-induced toxicity in form of perioral tingling and numbness over the extremities. Both the donors were managed with oral calcium supplementation.
Summary/Conclusions: Plateletpheresis induces marked reduction in biochemical parameters particularly ionized calcium, and magnesium levels. Moreover, alteration in parathyroid hormone levels could result significant impact on bone and mineral metabolism in regular repeat donors. In addition, decline in total protein and serum albumin may be a concern in donors also participating in plasmapheresis. Prophylactic calcium and magnesium supplements may be considered to prevent donor reactions in regular plateletpheresis donors.

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POST DONATION TELEPHONIC INTERVIEW: A TOOL FOR ACTIVE FOLLOW UP OF VOLUNTARY WHOLE BLOOD DONORS FOR ANALYSIS OF FREQUENCY AND PREDISPOSING FACTORS OF ADVERSE REACTIONS

AA Navkudkar, P Desai and S Rajadhyaksha

Transfusion Medicine, Tata Memorial Hospital, Mumbai, India

Background: Blood donation by healthy volunteers assures the availability of blood components for transfusion. Blood donation is well tolerated by most of the donors; however a few may experience adverse reactions. Reactions which occur at donation site are documented while those which occur after the donor has left the donation site may go unnoticed and thus are unreported. Hence, post-donation follow-up is important to get information about these adverse reactions.
Aims:
1. To analyze frequency and type of adverse donor reactions and its correlation with contributory factors if any
2. To add to the donor hemovigilance data for better understanding of the adverse donor reactions through analyzing data with other blood centers.
3. To develop a predictive model for the donors with a goal to define target groups to recommend best practices to improve donor care and safety.
Methods: This was a prospective observational study of 1,000 voluntary whole blood (WB) donors who consented to participate in it. Donors were contacted by the telephonic interview on two occasions; first after 24 h of donation and second after 2 weeks of donation. Donors were asked structured questionnaire, and information was documented according to gender, age, weight, place of donation, donation status and occupation. Statistical analysis was done by SPSS (Statistical Package for the Social Sciences) software.
Results: Of the 1,000 voluntary WB donors, 926 responded to phone calls on both the occasions. Of these 926, 79 (8.5%) donors experienced adverse reactions. All these donors experienced reactions within 24 h of donation while none experienced reactions beyond 24 h to 2 weeks. Of the 79 donors, 26 (33%) reactions occurred at the donation site while 53 (67%) reactions occurred after donor left the donation site. Total of 94% onsite reactions was vasovagal reaction (VVR) while 57% offsite reactions were hematoma. Of the 79 donors, 60% experienced VVR and 40% experienced hematoma including 2 donors experiencing both. VVR was higher in low weight donors, female donors and the first time donors ($P < 0.05$). Of the 49 VVR, 76% were mild, 18% were moderate and 6% were severe. Of the 49 donors with VVR, 27% donors complained of fear and anxiety of donation and all these were first time donors, 18% gave the history of inadequate water/fluid intake while in 55% donors, no associated factors were reported. Of the 32 hematoma reactions, 94% occurred at offsite while 6% occurred at onsite. Majority of hematoma took more than 7 days to recover.
Summary/Conclusions: Post donation interview proves to be an effective tool to acquire information about adverse donor reactions. Follow-up after 24 hours was helpful as all the reactions had occurred within this time period and donor recall of the reactions was better, which would otherwise have gone unreported. All these donors were advised for its management. This can also be used as a valuable tool for donor hemovigilance which is presently not mandatory in India. This will help in improving donor safety and satisfaction and will have a positive impact on national blood supply by improving donor return rate.

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POSTDONATION INFORMATION MANAGEMENT AND TRANSFUSION SAFETY

MI Puppo, V Cabrera, G Castelli, L Giunta and S Kuperman

Hospital Nacional De Pediatria "Prof Dr Juan P Garrahan", Caba, Argentina

Background: The postdonation information (PDI) is any fact reported by the blood donor, another person or disclosed at the blood center after blood donation, which could put at risk the safety of the blood products stemming from this donation. This occurs when a donor fails to report a risk that would have resulted in deferral or exclusion during the screening process.
The blood center implemented in November 2014 a standard operating procedure for homogeneous decision-making process, and put into practice an internal document to register all data about PDI.
Aims: This study analyzed the "post donation information forms" registered since 2014, and investigate the number, type and the main sources of PDI. It also took into account the actions taken as the result of PDI.

Methods: This is a descriptive and retrospective study, performed between November 2014 and December 2017. The following data were collected from the PDI form: kind of blood donor (first time or repeated) reception time (before or after seven days from donation) source (blood donor or third person) and type of PDI. It was also analyzed the decision adopted with the blood components from the involved donation.

Results: During the study period, there were 45,009 blood donations, and 142 (0.3%) IPD were registered, 84% during the first week of blood donation and 77% was reported by the own blood donor, 59% were from first time donor. When the types of PDI were analyzed, 77% was related to medical reasons (respiratory infection, fever, diarrhea) and 18% was associated to risks factor (risk sexual contact or blood exposition) Analyzing the actions taken with blood components associated with IPD it was detected that although the majority was discarded, 34% of the components have been sent to blood transfusion service at the moment of PDI, 3% of which related to a risk sexual factor.

Summary/Conclusions: The current donor screening process uses precautionary questions to guard against theoretical or potential risks, but has limitation and is error-prone. In this context PDI management is important in terms of blood safety. Even though, in this study the most commonly reported PDI were fever, respiratory infections and diarrhea, eighteen percent were related to a risk factor, most commonly sexually risk factor.

The blood centre has to discard all components related with PDI, but If the information is discovered or reported after the components have been distributed, the blood bank may attempt to retrieve them because they do not meet all quality standards. This study detected that 3% of the components related risk sexual contact have been sent to transfusion service. In this cases the blood center notified the potential risk.

The IPD process need blood donors informed about potential risk of blood transfusions. This achieves with voluntaries and repeated blood donors. Is important to frame the IPD in a quality program in order to ensure the training all the personnel involved, from the PDI reception to the decision making regarding the affected blood units.

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ANALYSIS OF TIME CHARACTERISTICS ASSOCIATED WITH THE OCCURRENCE OF ADVERSE REACTIONS IN FIRST-TIME DONORS

Y Gao

Blood Donation Service Department, Wuhan Blood Center, Wuhan, China

Background: Nowadays, the occurrence of adverse reaction is still an important problem. At the time of or after blood donation, still many blood donors are easy to have adverse reaction, especially first-time blood donors. According to the research before, mental stress is the main cause of the adverse reaction and psychological care can effectively alleviate the anxiety emotion, so that the adverse reactions can be preventable. With the increasing amount of blood collection in the world, it is difficult to give full attention to every blood donors. So, it is a good way to investigate the time characteristics associated with the occurrence of adverse reaction in first-time blood donors.

Aims: To investigate the time characteristics associated with the occurrence of adverse reaction in first-time blood donors, to explore the appropriate time to give psychological care to prevent adverse reactions, to enhance the proportion of fixed blood donors and to ensure blood supply to meet clinical use demand.

Methods: A retrospective analysis was conducted on the data of 200 blood donors. According to the time donors came to donate, 8 h working time was divided into 4 time periods (9:30–11:30, 11:30–13:30, 13:30–15:30, 15:30–17:30). The time of the occurrence of adverse reactions were evaluated in 110 first-time blood donors and 90 repeat blood donors.

Results: The incidence of adverse reaction in first-time blood donors group was significantly more frequent than repeat group (P < 0.05). The incidence of adverse reaction in second and fourth time period significantly more frequent in first-time blood donors group than repeat group (P < 0.05). The incidence of adverse reaction in first and third time period did not show a significant difference between two groups (P > 0.05).

Summary/Conclusions: The incidence of adverse reaction is more frequent from 11:30 to 13:30 and from 15:30 to 17:30. Therefore, first-time blood donors are closely monitored and cared by nurse, especially blood donors who come to donate blood in these time periods, so that most of the adverse reactions can be preventable. Timely, psychological care should be given according to the time period of donation to alleviate the anxiety emotion and the incidence of reverse reaction of volunteers. It is necessary to establish a scientific and effective mode of psychological counseling in different time period for voluntary blood donation.

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RHD VARIANTS AMONG BLOOD DONORS IN NORTHERN UGANDA: THE CURRENT LABORATORY TESTING AND CLINICAL CONSEQUENCES

TI Mugisha, O Polycarp, O Caesar, M Bashir and W Fred

International Health Sciences University, Kampala, Uganda

Background: RhD variants are of clinical importance owing to their high immunogenicity, and potential to cause alloimmunisation among RhD negative individuals following transfusion of D-positive red blood cells.

Aims: To determine the prevalence of RhD variant phenotypes among voluntary non remunerated blood donors at Gulu Regional Blood Bank (GRBB), Northern Uganda.

Methods: We conducted a cross sectional study, in which the first 4.0 ml of Ethylene di-amine tetra acetic acid (EDTA) blood sample was collected from voluntary non remunerated blood donors and typed for their ABO and RhD blood group status using IgG/IgM monoclonal typing antiserum. Blood samples that tested as RhD negative were further investigated for RhD variant phenotypes using indirect antihuman globulin haem-agglutination technique.

Results: We assayed 138 RhD negative blood samples obtained from voluntary non remunerated blood donors. Of these, 66.7% (n = 92) were males. Their median age was 24.4 (range, 14–33) years. Majority of the participants were of ABO blood group O (62.8%, n = 86), followed by A (19.7%, n = 27), then B (13.9%, n = 19) and least were AB (3.6%, n = 6). The prevalence of RhD variant phenotypes occurred among 0.7% (n = 1, 95% CI; 0.5–0.9). There was no statistical association of RhD variant phenotypes with donor gender, tribe and their ABO blood groups.

Summary/Conclusions: This study has revealed a high prevalence of RhD variant among blood donors at Gulu Regional Blood Bank in Northern Uganda. It further highlights a potential risk of alloimmunisation, as the present blood typing practices does not identify RhD variant phenotypes.

Blood Products – Blood Processing, Storage and Release

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IMPACT OF RED BLOOD CELL MANUFACTURING METHODS ON BACTERIAL GROWTH DYNAMICS

S Ramirez-Arcos[1], Y Kou[1], M Cayer[2], M De Grandmont[2], M Girard[2] and M Cloutier[2]

[1]Canadian Blood Services, Ottawa [2]Hema-Quebec, Quebec, Canada

Background: In Canada, leukocyte-reduced red blood cell concentrates (RBCC) are manufactured using two methods. In the first method (buffy coat, BC), whole blood (WB) is collected into CPD bags and units are stored ≤ 24 h at 20–24°C prior to the production of RBCC. While Canadian Blood Services (CBS) produces BC RBCC using a semi-automated method, Héma-Québec (HQ) manufactures BC RBCC with the automated Atreus WB processing system. The second method for RBCC production (non-BC) involves WB collection into CP2D (HQ) or CPD (CBS) bags with units stored ≤72 h at 1–6°C prior to RBCC production.

Aims: Compare bacterial growth in RBCC manufactured by the BC and non-BC methods. Influence of additive solutions (AS) and donor gender was also evaluated.

Methods: Three ABO-Rh gender-matched CPD WB units were pooled and then split to manufacture three RBCC, each suspended in different AS: SAGM, PAGGSM or AS-1. The units were prepared using the BC (HQ) or non-BC (CBS) methods. Additionally, CP2D WB units were used to manufacture RBCC suspended in AS-3 using the non-BC method at HQ, which were then distributed to both organizations. Each RBCC was inoculated with one of four bacteria: Klebsiella pneumoniae, Staphylococcus epidermidis, Yersinia enterocolitica or Propionibacterium acnes, targeting 10 colony forming units (CFU/mL) (n = 4). RBCC were sampled weekly to determine bacterial concentration. At the end of storage, viability was determined with BacT/ALERT cultures. Effects of RBCC manufacturing, AS, and donor gender on bacterial growth were statistically analyzed.

Results: S. epidermidis self-sterilized in all RBCC regardless of the manufacturing method or AS. K. pneumoniae viability decreased during RBCC storage with no differences related to gender. While AS did not affect K. pneumoniae viability in units prepared by the non-BC method, a significant interaction between storage days and AS was observed in BC units (P = 0.0432). *P. acnes* concentration declined faster in

male BC units compared to female BC RBCC (P = 0.0113) while higher loads were observed in male units compared to female RBCC prepared by the non-BC method (P < 0.001). Y. enterocolitica grew in all RBCC with differences observed depending on the manufacturing method. This bacterium reached higher concentrations in AS-3 units prepared by the non-BC method compared to BC units suspended in SAGM, PAGGSM and AS-1 (P < 0.05). By contrast, Y. enterocolitica grew to similar levels in most RBCC prepared by the non-BC method, independently of the AS, except for the differential growth observed between AS-3 and PAGGSM units (P = 0.029). BC units had higher Y. enterocolitica concentrations from female donations in all AS compared to male units (P < 0.0001) while no differences were observed related to gender in RBCC prepared by the non-BC method.

Summary/Conclusions: This study demonstrates that RBCC manufactured by the non-BC method supports higher proliferation of Y. enterocolitica compared to BC units. These results might be due to higher iron availability and/or higher residual white blood cells in RBCC prepared by the non-BC method, which merits further investigation. Interestingly, female BC RBCC units, which have been reported to have lower levels of hemolysis than male units, supported higher levels of Y. enterocolitica, a finding that also warrants additional studies.

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Abstract has been withdrawn

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IMPLEMENTING WHOLE BLOOD AUTOMATION AND PLATELET PATHOGEN REDUCTION TECHNOLOGY AT THE RED CROSS LUXEMBURG

N Malvaux[1], A Schuhmacher[2], F Defraigne[2], A Heinricy[3], F Merny[3], M Vanderzwalmen[3], J Leveque[4], L Bagard[4], L Scheer[3], S Bartziali[5], M Cardoso[5] and P Renaudier[6]

[1]Production [2]Quality Control [3]Blood Collection [4]IT, Red Cross Luxemburg, Luxembourg, Luxembourg [5]Medical Affairs, Terumo BCT, Zaventem, Belgium [6]Direction, Red Cross Luxemburg, Luxembourg, Luxembourg

Background: At the end of 2014 the Red Cross Luxembourg (RCL) implemented Mirasol PRT System (Terumo BCT) to treat whole blood derived platelet concentrates (PC). One year later the RCL introduced whole blood automation with the Reveos automated whole blood processing system (Terumo BCT) to optimize component processing, aligning platelet processing and PRT treatment.

Aims: The aim of this study is to describe the impact of the implementation the Reveos technology on the Mirasol PRT process: product quality and logistical aspects.

Methods: Whole blood is collected into Reveos collection bag (target volume 475 ml) and stored on eutectic plates for at least 5 h. Depending on the collection time, the blood is processed either on the same day (d0) or after overnight hold at room temperature (d1). For each whole blood unit, one red cell concentrate, one plasma and one interim platelet unit (IPU) are produced.

After at least four hours of resting and agitation time, IPUs are pooled (4 or 5 units) in T-PAS+ and filtered through a leukoreduction filter. Since August 2016, the pooling process is managed by using T-IPU select tool, which is a software application that sorts and groups IPUs based on the estimated platelet yield by the Reveos system. Currently approximately 26% of the routinely processed PC are treated with the Mirasol PRT system. For this the contents of PC and riboflavin bags are transferred into the illumination bag after connection by using TSCD and the bag is subsequently illuminated. Platelet count and yield are determined with the Beckman Coulter device. Each concentrate is visually checked for the swirling after the completion of the procedure

Results: Since November 2015 through February 2018, the RCL has produced 6895 Reveos-derived PC and 1889 of those concentrates have been treated with the Mirasol PRT system. Average yield of treated PC before Mirasol treatment was 3.11×10^{11} per bag (4 IPUs, n = 425) and 3.51×10^{11} per bag (5 IPUs, n = 1,445). More than 99% of the illuminated products were conform to specifications (platelet content). During this period only 8 products have been discarded mainly owing to technical failures. No aggregates were found in the Mirasol treated platelet concentrates. In 2017, the calculated platelet loss during the process (transfer/illumination) was evaluated to be 4.35%. Implementation of the Reveos system has enabled to spare time for the illumination process, with no increase in full time resources. No delay in the availability of PC was observed.

Finally, there has been no evidence of an increase in notification of transfusion reactions with the Mirasol-treated PC, as recorded in the RCL hemovigilance database.

Summary/Conclusions: The automation of the upstream whole blood separation process with the Reveos system has led to an increase in productivity concomitantly to improved blood component standardisation while staying within the product specifications. This has enabled the RCL to maintain whole blood processing and Mirasol PRT treatment of PC without increasing Full Time Equivalent (FTE) resources involved in the blood component production.

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WHOLE BLOOD PROCESSING USING DINCH® BASED BLOOD CONTAINERS

K Aurich[1], J Wesche[1], P Gebicka[1], A Westphal[1], J Fuhrmann[1], K Selleng[1], A Greinacher[1], F Füssl[2], S Reichenberg[2], G Fagoo[3] and S Chatellier[3]

[1]Transfusion Medicine, University Medicine Greifswald, Greifswald [2]Maco Pharma International GmbH, Langen, Germany [3]Maco Pharma S.A.S., Mouvaux, France

Background: Di(2-ethylhexyl)phthalate (DEHP) is a plasticizer in blood bags that is bound to polyvinylchloride (PVC) polymer and can leach into the blood product. Exposure to DEHP might induce developmental and reproductive toxicity in humans.

Aims: The objective of this study was to evaluate an alternative plasticizer, di(isononyl) cyclohexane-1,2-dicarboxylate (DINCH) for its use in systems for whole blood (WB) processing and the resulting products: plasma, red blood cell concentrates (RBCs) and platelet concentrates (PCs).

Methods: In total WB of 80 healthy volunteers was collected into DEHP and DINCH systems (Maco Pharma, France). Within 4 or 22 h WB was centrifuged (4,000 g, 10 min) and separated in plasma, buffy coat, and RBC. All plasma units per study arm (16) were shock frozen and stored for 14 days. Samples were taken after thawing at day 1 and 7 and analyzed regarding coagulation parameters, triglycerides, protein levels and microparticles. Buffy coats were pooled for 4 PCs in DEHP or DINCH systems by addition of SSP+ additive solution (Maco Pharma, France) in each study arm. PCs were stored for 8 days at room temperature (RT) under agitation. Samples were taken at days 1, 3, 6, and 8 and analyzed regarding metabolism, platelet function and hypotonic shock response (HSR). After addition of additive solution PAGGS-M or SAG-M 16 RBCs in each study arm were leukoreduced and analyzed for in vitro characteristics of metabolism, hemolysis, adenosine triphosphate (ATP), 2,3-diphospho glycerate (2,3-DPG) levels and microparticles during storage at 4 °C at days 1, 14, 35, 42, and 49.

Results: The usage of DINCH based blood bag systems had no influence on whole blood separation and processing. Plasma coagulation factor levels, triglycerides and protein levels were comparable between plasticizers (e.g. factor VIII activity at day 1 after thawing 109.2 ± 17.4% DEHP vs 80.5 ± 6.3% DINCH, P > 0.05). PCs showed equivalent outcomes regarding platelet count, metabolism, HSR, aggregation and activation ability for both plasticizers and different manufacturing times. RBC analysis resulted in comparable results regarding metabolism, RBC count, hematocrit, hemoglobin and microparticles. Hemolysis was increased using DINCH based bags during short time WB separation (0.19 ± 0.06% DEHP vs. 0.37 ± 0.11% DINCH, P < 0.05, day 42), but was below 0.8%. Storage of WB for 22 h showed no difference for hemolysis in DINCH and DEHP bags using PAGGS-M or SAG-M as additive solution (0.46 ± 0.31% DEHP vs 0.45 ± 0.14% DINCH, PAGGS-M, day 42). ATP levels in RBC differed between plasticizers, manufacturing time and additive solution. ATP concentration was highest in bags with DINCH, PAGGS-M manufactured within 4 h (0.250 ± 0.076 μmol/g Hb) and lowest in bags with DINCH, SAG-M manufactured within 22 h (0.009 ± 0.019 μmol/g Hb, day 42).

Summary/Conclusions: Replacing DEHP plasticizer by DINCH does not impair manufacturing processes. Overall, plasma, PCs and RBCs quality parameters are comparable between DEHP and DINCH based bags. Hemolysis in RBCs is increased in DINCH bags processed within 4 h after 42 days of storage, but is far below the threshold of 0.8%. For whole blood separation in plasma, RBCs and PCs, DINCH is an alternative for DEHP.

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DEGLYCEROLIZATION OF MANUALLY GLYCEROLIZED RED BLOOD CELLS USING AN AUTOMATED CELL PROCESSOR

M Cloutier[1], A Laforce-Lavoie[1], J Costanzo-Yanez[2] and M Chevrier[2]

[1]Medical Affairs and Innovation, Héma-Quebec, Québec [2]Héma-Quebec, Montréal, Canada

Background: Our inventory contains rare red blood cell (RBC) that were glycerolized using Meryman's manual method. Currently, those units are deglycerolized using the COBE 2991, which is outdated and will need to be replaced eventually. Although an automated cell processor was integrated into our activities for the glycerolization and deglycerolization of RBC, it has not yet been validated for the deglycerolization of manually glycerolized RBC units.

Aims: This study aims at assessing the possibility of using an automated cell processor system for the deglycerolization of manually glycerolized units. Moreover, since some units are still manually glycerolized in our current operations, the study also aims at assessing post-thaw quality according to the age of the RBC units at the moment of freezing.

Methods: Twenty manually glycerolized RBC units from our inventory that had been frozen for approximately ten years were thawed in a 37°C water bath and deglycerolized using an automated cell processor system (ACP 215, Haemonetics) and resuspended in AS-3. RBC in vitro quality was assessed 24 h after deglycerolization. In a separate experiment, 30 additional RBC units were manually glycerolized 4, 7, 14, 21 or 28 days post-collection (n = 6 per group). Units were frozen at – 80 °C for 14 days. Units were then thawed and deglycerolized with the ACP 215. RBC in vitro quality was assessed 24 h after deglycerolization.

Results: All 20 deglycerolized units from the inventory met the criteria for hematocrit and sterility after 24 h of storage. However, while hemolysis was still lower than what is typically obtained when units are deglycerolized with the COBE 2991, only 85% of the units met the criteria for hemolysis (<0.8%) and hemoglobin (≥ 35 g/unit). Percent recovery could not be assessed for these samples since no data for concentration was obtained upon freezing. The age of the units at the time of glycerolization had an influence on hemolysis upon deglycerolization. Indeed, hemolysis was significantly higher for units that were frozen 25 days after collection. These results justified the need to evaluate the optimal post-collection timing for the units that are still being manually glycerolized at our institution. In this second set of experiments, deglycerolized units respected the standards for hematocrit, hemoglobin, hemolysis and sterility as long as they were glycerolized and frozen no later than seven days post-collection.

Summary/Conclusions: RBC units that were manually glycerolized, deglycerolized with the automatic cell ACP-215, resuspended in AS-3 and stored for 24 h, met in vitro quality standards for sterility and hematocrit. The difficulty in reaching the standards for hemoglobin might be related to centrifuge volume limitations. This aspect warrants further optimization. While standards for hemolysis were not met for every unit, it was vastly improved when compared to what is routinely obtained with the COBE 2991. Thus, the ACP-215 automatic cell processor can be used to deglycerolize RBC units that were manually glycerolized.

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IMPLEMENTING AUTOMATION AND REORGANIZING ALL STEPS OF WHOLE BLOOD COLLECTION AND SEPARATION FOR VICENZA BLOOD DEPARTMENT

A Alghisi, L Pavan, M Colonna, P Dragone and C Sardella

Blood and Transfusion Medicine Department, Vicenza Hospital, Vicenza, Italy

Background: The Vicenza Blood Department processes around 45,000 whole blood units yearly, collected within 11 collection centers and provides blood components to the whole department and plasma for pharmaceutical industry. All blood is processed at Santorso Hospital and, up to February 2017, the transfer of blood collection and processing data on batch basis was done at the end of the day, making statistical quality analysis difficult, and the separation program was assigned manually by the operator for each unit.

Aims: Improve and fully automate the monitoring of all steps concerning blood component production, from donation to processing, and quality controls, in order to ensure high quality standards, traceability and real time data transfer.

Methods: Department reorganization occurred in February 2017 and the Center started using

- In line whole blood collection kit: (Top & Bottom Macopharma bag)
- 57 Macomix DCN7 - blood mixers (Macopharma)
- 5 Macopress Smart Revo automated plasma extractors (Macopharma)

- Emoqualità 3.0 (Macopharma), web-based software for hemocomponents quality control management.

Blood mixers and plasma extractors are bidirectionally connected to the Laboratory Information System (LIS): the mixers receive donor information and transfer data, describing the donation, time and date, kit number, duration and collected volume to the plasma extractors. Three programs are available:

- Program 1: production of Fresh Plasma, Leucodepleted Red Cell Concentrates and Buffy-Coat excluded for platelets production (if processing time exceeds 6 h after collection)
- Program 2: production of Fresh Frozen Plasma, Buffy-Coat and Leucodepleted Red Cell Concentrates
- Program 3: production of Fresh Frozen Plasma, Leucodepleted Red Cell Concentrates and BC excluded for platelets production (donation duration longer than 12', or clinical reasons).

Plasma extractors are also connected to Emoqualità 3.0, which automatically imports volume data of the hemocomponents produced, serial number of separator, to enable a production assessment in addition to the hemocomponents quality control surveillance.

Results: Data exported from Emoqualità 3.0 during the period 04/01/2017–12/31/2017 was analyzed:

- 32.407 blood units were automatically processed as follows: 14.171 using program 1, 17.761 using program 2, and 475 using program 3
- The analysis performed on the devices shows a well-balanced distribution of the workload percentage among the 5 extractors (min 19.3%, max 20.57%), demonstrating an optimized workflow
- 1,329 red cell units out of 32,407 (4.1%) were detected in real time as "out of range volume" (according to international criteria): we were able to check immediately these components in order to verify their compliance in terms of quality and respect of the Italian Regulatory and International Guidelines.

Summary/Conclusions: We demonstrate huge improvements achieved due to a fully automated management system in terms of blood components safety, traceability, workflow and compliance to quality components standards. The bidirectionally connection between LIS, mixer and plasma extractors reduced the work-load for the operators and allowed a better quality of hemocomponents avoiding errors in attribution of separation program: this is particularly important in our Department where blood is collected in multiple centers.

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EFFECT OF SEPARATION TIMES ON THE HEMOLYSIS OF LEUKOCYTE POOR PACKED RED CELLS USING KL-521 AUTOMATED BLOOD SEPARATOR

T Leelarungsun[1], A Klomiamsira[1], S Kitisapkanjana[1], P Witthayawiwat[1], C Prungchaiyaphum[2], N Worachun[2] and P Chiewsilp[3]

[1]Blood Components Production [2]Quality Control [3]Quality Manager, National Blood Centre, Thai Red Cross Society, Bangkok, Thailand

Background: During processing, red blood cells (RBCs) are injured resulting in hemolysis. The separation of whole blood in quadruple top and bottom bag systems mostly takes less than 240 seconds. However, too short separation time may cause higher rate of RBCs hemolysis.

Aims: The aim of this study was to investigate whether hemolysis of Leukocyte Poor Packed Red Cells (LPRCs) is increased when shorter separation time is applied.

Methods: Routine separation time for LPRCs in top and bottom system, 80–120 s (LPRCs-120), as compare to the design separation time within 130–240 s (LPRCs-240) by Kawasumi KL-521 automated separators. The hemolysis of LPRCs-120 and LPRCs-240 was detected on day 3 by visual inspection, then hemolyzed samples were tested for %hemolysis at the end of storage (day 42).

Results: By visual inspection, 16 in 966 units of LPRCs-120 (1.66%) and 12 in 100 units of LPRCs-240 (12.00%) were detected as hemolyzed samples. At the end of storage, it was found that 12 in 16 units of LPRCs-120 and 1 in 12 units of LPRCs-240 were hemolytic (%hemolysis > 0.8%). The average %hemolysis of LPRCs-120 and LPRCs-240 were 1.18% and 0.25% respectively. The average separation time of LPRCs-120 was 102.81 s (maximum 120 s, minimum 80 s), and the average separation time of LPRCs-240 was 166.92 s (maximum 239 s, minimum 131 s).

Summary/Conclusions: LPRCs separated within 80–120 s exhibited a higher mean %hemolysis than 130–240 s of separation (*P < 0.05). Therefore, the commonly use separation time not more than 240 s is suitable as confirmed by this study. Then, the lower limit of separation time should be considered not less than 120 s.

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EVALUATION OF QUALITY CONTROL OF BLOOD COMPONENTS OBTAINED BY REVEOS® SYSTEM: 4 YEARS OF EXPERIENCE

CA Vaz, F Vasconcelos, M Lopes, S Fernandes, J Cruz, I Henriques and M Koch
Imunohemoterapia, Centro Hospitalar de São João, Porto, Portugal

Background: São João Blood Bank is the most active hospital bank in Portugal, being self-sufficient in blood components.

In 2014, we implemented an automated Whole Blood (WB) processing system. The Reveos system processes up to four WB units simultaneously into a red blood cell (RBC) unit, an interim platelet (PLT) unit (IPU), and a plasma unit. A residual leukocyte unit is also obtained as a by-product. Multiple IPUs can be pooled to form a transfusable Platelet Pool.

Aims: Evaluate the quality of components obtained by Reveos System between 2014 and 2017 at our centre.

Methods: WB (450 ± 50 ml) was processed using the Reveos System according to the Terumo BCT protocol (3C protocol, overnight). RBC, IPU and plasma units were obtained by this method.

SAG-M was added to RBC units and then leukoreduced using an integrated filter.

Platelet Pools were prepared by pooling 4 IPUs after 1-hour rest and 2-hours on the platelet shaker.

We analyzed a group of the RBC units and Platelet Pools obtained from March 2014 to 2017.

Quality parameters studied in RBC units were volume, haemoglobin (Hb) content, haematocrit (Hct), and residual leucocytes. In Platelet Pools volume, platelet yield, and residual leucocytes were evaluated.

Results: 194,251 blood components were obtained, 72,662 RBC units, 70,261 plasma units and 51,328 IPUs.

We analyzed 2.6% (N = 3,221) of blood components obtained by the Reveos System, 1,677 (52.1%) of RBC units, and 1,544 (47.9%) of Platelets Pools.

97.5% of the overall units met the portuguese regulation, RBC units achieved the required parameters, in 98.3%, and Platelet Pools in 96.5% of all cases.

In the RBC units, the legal requirements in the parameters were, met in 99.2% for Hct, 99.4% for Hg, and 99.8% for residual leucocytes.

In the Platelets Pools, the percentage of units within the legal requirements was 98.8% for the platelet yield, and 97.7% for residual leucocytes.

Summary/Conclusions: Blood components prepared with Reveos System, using 3C Protocol overnight, met quality criteria established in portuguese regulations in 97.5% of all cases.

The number of units that met the required parameters was higher in the RBC units analyzed (98.3%) than in the Platelets Pools (96.5%).

Since the implantation of this WB automated processing system, at our centre in 2014, this method of blood processing has shown to be efficient and consistent.

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A FIRST AUSTRALIAN STUDY WITH A NATIONAL APPROACH TO SYSTEMATIC TESTING OF DONORS WHEN THEIR WHOLE BLOOD DONATIONS ARE REPEATEDLY DISCARDED DUE TO RED CELL PROCESSING ISSUES

P Pathak[1], R Hirani[2], PJ Mondy[2], P Harper[1], H Ingham[3] and J Lee[1]
[1]Clinical Services and Research, Australian Red Cross Blood Service, Perth [2]Clinical Services and Research, Australian Red Cross Blood Service, Sydney [3]Clinical Services and Research, Australian Red Cross Blood Service, Adelaide, Australia

Background: The Australian Red Cross Blood service (Blood service) operates nationally and has performed leucodepletion of all platelets and red cells since 2008. Filter blockage with leucodepletion failure has been noted in donors with the sickle cell Haemoglobin S (HbS) trait. Failure of leucodepletion increases the risk of CMV transmission and transfusion reaction in the recipients but may also have donor safety implications.

We report the first Australian study to identify and manage donors with recurrent filter blockages. Red cell components which have filtration or clotting issues are discarded. As there was no routine systematic process for contacting donors when red cell processing issues were identified, and reporting functions were not standardised, a donor could have repeated donations discarded.

Aims: To systematically follow-up whole blood donors noted to have issues with leucodepletion during their red cell processing and where the resultant components have been repeatedly discarded.

Methods: The study was approved by the Blood Service ethics committee and initiated in April 2016 and includes data available until the end of January 2018. Discard processes and coding were nationally standardised within the national blood management system. Routine reporting of discard data was aggregated using the IBM Cognos database. Donors with consecutive or a total of 3 whole blood donations discarded were identified. The donors were deferred, records reviewed and a letter sent to the donor's general practitioner suggesting further investigation including a full blood count, reticulocyte count, blood film, ferritin, high performance liquid chromatography (HPLC), lactic acid dehydrogenase (LDH), Serum electrophoresis (EPG) with immunofixation, Direct anti-globulin test and cold agglutinin tests.

Donor consent was sought to analyse the results of the tests. The donor was managed according to the findings.

Routine letters were sent for permanent deferral from blood donation when the HbS trait, cold agglutinins or a paraprotein were identified.

Results: Over the study period, a total of 157 donors were identified as having multiple whole blood donations discarded. Responses were received for 98 (62%) donors. Of these, HbS trait was found in 38 (38.8%); no cause was found for 28 donors (29%), cold agglutinins identified for 21 and a paraprotein found in 3. Chronic lymphocytic Leukaemia was detected in 1 donor.

Summary/Conclusions: Using this standardised report, donors with repeatedly discarded whole blood donations are now systematically reviewed and excluded from blood donation. The whole blood processing failure often arises from the HbS trait, presence of cold antibodies or paraproteins. A large number of implicated donors based on current testing had no known reason for processing failure and could warrant further investigation. As donor safety is of paramount importance, the implicated donors are referred for further management including consideration of genetic counselling for HbS trait, where relevant. This donor review process will be transitioned to become a routine part of donor and component management.

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DURATION OF RED BLOOD CELL STORAGE IS SIGNIFICANTLY ASSOCIATED WITH HEMOGLOBIN INCREASE AFTER BLOOD TRANSFUSION

J Rydén[1,2], M Clements[3], E Hellström-Lindberg[1,2], P Höglund[1,4] and G Edgren[3,5]
[1]Department of Medicine, Karolinska Institutet [2]Department of Hematology, Karolinska University Hospital [3]Department of Medical Epidemiology and Biostatistics [4]Department of Clinical Immunology and Transfusion Medicine, Karolinska Institutet [5]Department of Cardiology, Stockholm South General Hospital, Stockholm, Sweden

Background: Red blood cells are commonly stored for up to 42 days. There has been conflicting evidence on the effect of red blood cell storage duration and clinical outcomes. Previous research has focused on determining the association between duration of storage time and risk for adverse outcomes including mortality, but most data has not supported such association. Surprisingly few studies have addressed the association between red blood cell storage and component efficacy.

Aims: The main aim of this study was to determine the effect of red blood cell storage duration with regard to hemoglobin increment in the transfusion recipient.

Methods: Transfusion data on a well-defined cohort of myelodysplastic syndromes were linked to hemoglobin measurements taken within 2 days before until 28 days following the transfusion. We applied a mixed effect regression model to study the impact of storage duration (categorized as <10, 10–19, 20–29 or ≥30 days) on the hemoglobin yield, per red blood cell unit.

Results: The study population consisted of 243 unique patients who were transfused at 4,419 transfusion occasions. Compared to patients who received units stored 1–9 days receipt of blood units stored 10–19, 20–29, or ≥30 days resulted in a hemoglobin increase that were 0.26 (95% confidence interval [CI], −0.11 to −0.63), 0.75 (95% CI, 0.26–1.23), and 1.12 (95% CI, 0.4–1.85) g/l lower, respectively, per red blood cell unit. Results were consistent in sensitivity analyzes.

Summary/Conclusions: We observed a gradual drop in the mean hemoglobin increase with prolonged red blood cell storage. Although the effect was statistically significant, the effect was modest and if this is clinically relevant in subgroups of patients must be investigated further.

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RED BLOOD CELLS ANAEROBIC STORAGE WITH HEMANEXT® PROCESSING SYSTEM

D Brouard[1], P Landry[1], E Ducas[1], M De Grandmont[1], M Cloutier[1], M Dioguardi[2] and T Yoshida[2]

[1]Medical Affairs and Innovation, Hema-Quebec, Quebec, Canada [2]New Health Sciences Inc., Lexington, Kentucky, United States of America

Background: During storage at 4°C, red blood cells (RBC) are exposed to an increase in oxidative stress, which has been shown to adversely affect their biological properties and their survival when transfused. Hemanext™ has developed a red cell processing system that reduces RBC oxidative stress and enhances metabolic status by reducing the concentration of oxygen and carbon dioxide in the RBCs, before and during refrigerated storage.

Aims: The purpose of this work was to evaluate, in two different studies, the performance of Hemanext product, using leukoreduced red cell concentrate (RCC) stored in SAGM or PAGGSM additive solutions. The first study compared performance in two additive solutions utilizing a pool and split design. In the second study, PAGGSM additive solution was selected to evaluate Hemanext RCC stored up to 49 days.

Methods: For Study 1 (n = 16), four ABORh compatible leukoreduced units were pooled and split four ways, SAGM or PAGSM additive solution with or without Hemanext process, then stored and sampled weekly for 42 days. For the Hemanext process, freshly processed RCCs were sterilely transferred in the Oxygen Reduction Bag (ORB), followed by 3 h agitation at room temperature for O_2/CO_2 reduction, then transferred in Hemanext Storage Bag (HSB) for refrigerated storage for 42 days. RCCs were sampled weekly for CBC, gas panels (tHb, Htc, %SO₂, pO₂, pCO₂, pH, Na⁺, K⁺, glucose, lactate), free hemoglobin, spun hematocrit, ATP and 2,3-DPG. For Study 2 (n = 32), freshly processed RCC in PAGGSM additive underwent Hemanext processing and stored for 49 days while sampled at day 1, 21, 42 and 49 as in Study 1.

Results: The Hemanext® device reduced O_2 levels below 20% SO_2 for the entire storage period for both studies. In Study 1, the SO_2 levels of Hemanext units were reduced from $48 \pm 6\%$ to $7 \pm 3\%$ after treatment and SO_2 was maintained at $6 \pm 2\%$ until day 42, while control units %SO₂ increased to $79 \pm 6\%$ in day 42. In Study 2, the SO_2 levels in PAGGSM units were reduced from $52 \pm 15\%$ to $7 \pm 4\%$ after treatment and was maintained at $4 \pm 1\%$ until day 42 and $2 \pm 1\%$ at day 49. The hemolysis rate at day 42 was the same in both studies in PAGGSM-Hemanext units ($0.3 \pm 0.1\%$). At day 49, hemolysis was $0.4 \pm 0.1\%$ in PAGGSM units. Hemolysis was higher for SAGM-Hemanext with $0.6 \pm 0.1\%$. Storage in O_2/CO_2-reduced conditions significantly improved the 2,3-DPG levels in RBC units with a maximum at day 14 (16.0 ± 0.5 μmol/g Hb in PAGGSM and 11.6 ± 3.2 μmol/g Hb in SAGM vs 1.3 ± 0.4 μmol/g Hb in control).

Summary/Conclusions: The Hemanext device allowed O_2/CO_2-reduced storage of RBC units, which had significant impacts on multiple in vitro metrics of red cell quality. The first study demonstrates that Hemanext-treated RBC units stored in PAGGSM present better overall properties than SAGM at expiration. The second study confirmed results obtained with PAGGSM-RBCs.

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STUDY OF MAGNESIUM ADDITIVE EFFECT ON RBC UNITS IN COMPARISON WITH UNITS ENRICHED WITH GLUTATHIONE

S Zolfaghari[1], R Tanoomand[2], M Keramati[3], M Deyhim[4], V Sharifzadeh Peyvasti[4], M Nekouei[5] and M Ebrahimi[1]

[1]Iranian Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran [2]Department of Hematology and Blood Bank, Faculty of Medical Sciences, Mashhad University of Medical Sciences [3]Department of Hematology and Blood Bank, Mashhad University of Medical Sciences, Mashhad [4]Iranian Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran [5]Medical Students Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Red blood cell (RBC) develops a progressive structural and biochemical alternations during storage which are collectively called RBC storage lesion. According to many studies glutathione as an additive solution can lead to long delay the RBC storage lesions. Magnesium is an essential co-factor for over 300 cellular enzymes involved in glycolytic metabolism that can play a controlling role in cells including RBCs. Erythrocytes with older ages have the lower concentration of magnesium and according to some studies were conducted on mice, significant decrease of magnesium leads to a lower survival as well as some structural defects in the cell membranes.

Aims: To Compare the in vitro quality of RBCs with added magnesium, the RBC units with added glutathione and a control group during RBC storage.

Methods: Whole bloods (WBs) were collected from donors at the Iranian Blood Transfusion Organization (IBTO). WBs were processed into red cell concentrates (RCC) with SAG-M as the additive solution. A total of 22 RCC (11 pairs) were used for this study. Each two units of isogroup RCC were pooled and divided into three equal parts: RCC one and two were considered to be added magnesium chloride (MgCl2) and glutathione respectively and the third one served as a control. RCCs were sampled days 0, 2, 7, 14, 28 and 42. All samples were collected in biosafety cabinets with a sterile sampling device after gentle mixing by inversion for approximately 5 min. Different biochemical parameters were measured including hemoglobin (Hb), hematocrit, hemolysis, mean corpuscular volume (MCV), sodium, potassium, intracellular magnesium, lactate and LDH enzyme activity as well as RBC microvesicles (MVs) and ATP level. RBC microvesicles (MVs) were prepared by low speed centrifugation of RBCs, followed by filtration and ultracentrifugation.

Results: Significant differences in known in vitro measures of RBC storage lesion were seen among three groups of RCC; greater increase in extracellular potassium and higher hemolysis levels were seen in control vs. magnesium and glutathione added RCCs (P < 0.05).

Levels of intracellular magnesium in all three groups have decreased over testing time although this change was not significant between the groups.

ATP levels decreased more rapidly in control group compared to glutathione and magnesium-treated RCCs (P < 0.05). Membrane vesiculation also increased over the storage period in all three groups, however it was significantly lower in glutathione and magnesium-treated RBCs on day 42 (P < 0.05).

Summary/Conclusions: The in vitro data demonstrate attenuation in RBC storage lesion in magnesium and glutathione groups vs the control one. Varying the dose of MgCl2, combining it with applicable RBC antioxidants, applying different models of magnesium and increasing the sample size used for this study are likely to provide more statistically significant observations.

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EVALUATION AND VALIDATION OF TWO BLOOD COLLECTION SYSTEMS WITH IN-LINE FILTERS WITH REFERENCE TO COMPONENT QUALITY AND LEUCODEPLETION PROCESS

RB Sawant[1], P Patankar[2], R Sawant[1], M Rane[2] and V Vadera[1]

[1]Transfusion Medicine, Kokilaben Dhirubhai Ambani Hospital [2]Four Bungalows Andheri West, Kokilaben Dhirubhai Ambani Hospital Mumbai, Mumbai, India

Background: It is very crucial to evaluate and validate the blood collection and processing system for centers practising 100% leucodepletion, especially in the light of complex solid organ transplant and bone marrow transplant patients as intended recipients.

Aims: To evaluate the blood bag's with in-line filters supplied by two different manufacturers and validate the leucodepletion process and outcome using these two different component separation systems.

Methods: N = 118 Compoflow blood bags (Fresenius Kabi) and N = 179 Macopharma bags were used for blood component separation as per the manufacturers instructions. The component volumes, total Hb content of PRBC units, percent recovery of red cells and platelets, platelet yields and component separation time were evaluated. Validation of the leucodepletion process was done by studying the filtration time, percentage loss of red cells from the whole blood collected and residual WBC(rwbc) counts using flow cytometry platform was done.

Results: The volume (259 ml versus 241 ml) and Hb content of PRBC units (53.4 g versus 49.1 g) platelet yield (10.06×10^{10} versus 6.89×10^{10}) and percentage platelet recovery (87.9% versus 63.04%) were higher with the Macopharma bags. The time taken for component separation by the macopress smart system was lesser (Mean=3 min 39 s) than that with the component G5(Mean 4 min 57 s) volume of platelet concentrates was higher (Mean 76.4 ml) with Macopharma bags compared to the campoflow bags (Mean 65.5 ml). The compoflow system resulted in lesser (8.5%) red cell loss during in-line filtration than the Macopharma system(14.7%). Both bag types yielded rWBC counts <10⁵ in 85% of the units. The time taken for filtration was lesser <(19 min 26 s) with Macopharma bags compared to Compoflow bags (24 min 6 s).

Summary/Conclusions: Both blood bags with in-line filters have advantages and limitations associated with their use. However, both the systems ensure achievement of good component quality and leucodepletion of PRBC units which is required to fulfill special transfusion requirements of transplant patients.

P-238

CHALLENGING THE CURRENT 30-MINUTE RULE FOR RED CELL STORAGE IN AUSTRALIA – AUDIT RESULTS FROM AN ACADEMIC MEDICAL CENTRE

D Oh[1,2], K Rushford[1], S Opat[1,3], J Daly[2], A Keegan[2] and E Wood[1,3]

[1]Monash Health [2]Australian Red Cross Blood Service [3]Monash University, Melbourne, Australia

Background: In Australia, red blood cell (RBC) storage is strictly controlled and maintained to preserve product quality, integrity, and safety. Australian national standards (National Pathology Accreditation Advisory Council) and guidelines (Australian & New Zealand Society of Blood Transfusion) state that when removed from controlled storage, RBCs must not exceed 30 min at room temperature at each occasion. However, permissible number or limits of temperature excursions are not defined. Units that have been stored or transported outside of the temperature specifications must not be transfused except at the discretion of the laboratory director, and typically in exceptional circumstances; however no guidance exists to inform decision-making for individual cases. The 30-minute rule is based on historical concerns and a limited evidence base. A number of recent studies have demonstrated no significant difference in RBC quality and/or bacterial contamination rate when exposed to ambient temperatures for 30 or 60 min 5–6 times during storage (Grandmont, Vox Sanguinis, 2014; Ramirez-Arcos, Transfus Med Hemother, 2016).

Aims: Clinical audit of the number of RBCs discarded due to storage and transport outside the temperature-monitored environment for more than 30 but less than or equal to 60 min at the two main campuses (Centre A, 640 beds; Centre B, 573 beds) of Monash Health (MH), a large academic hospital in metropolitan Melbourne, Australia.

Methods: MH RBC wastage data were extracted from the National Blood Authority BloodNet system from January 2014 to December 2017. Paediatric RBCs, units that were discarded for reasons other than temperature control, or where information was missing, were excluded. The issue and return date and time of each unit were individually extracted from the MH hospital laboratory information system.

Results: A total of 1,137 RBCs were discarded over four years, of which 285 units (Centre A = 204, Centre B = 81) were due to 30 min outside controlled storage. In Centre A, 75 units (75/204; 37%) were outside controlled storage for between 30 and 60 min, and in Centre B, 22 units (22/81; 27%). In total, 97 units (97/1,137; 8.5%) discarded RBCs over the 4 years could have been saved if the 30-min rule were extended to 60 min. This translates to AUD $36,237 (~CAD$35,972) wasted with an average of approximately AUD$9,060 (~CAD$8,994) per annum at our health service.

Summary/Conclusions: The "60-minute rule" for RBCs appears safe and is being increasingly widely adopted internationally. Our results suggest that substantial numbers of discarded RBCs may be salvageable if the current 30-minute rule could be extended to 60 min in Australia. Further studies in the Australian setting to investigate the generalisability of our single institution experience and a national consensus on whether to adopt the 60-min rule in Australia, are needed, along with other efforts to improve compliance with storage and handling requirements.

P-239

PLATELET ADHESION AND BLOOD COMPATIBILITY OF ELECTROSTATIC SELF-ASSEMBLY FILM MODIFIED PBT AS LEUKOCYTE FILTER MATERIALS

R Zhong, Z He, J Liu and H Wang

Institute of Blood Transfusion, Chengdu, China

Background: Filtration of leukocytes is a common method of ensuring the safety and effectiveness of clinical transfusion. The current researches on leukocyte filtration materials mostly focus on increasing leukocyte removal and decreasing platelet adhesion, however, there are few reports on the effects of material on platelet function and blood compatibility.

Aims: To immobilize polybutylene terephthalate (PBT) film with chitosan and heparin by electrostatic self-assembly technique, and evaluate its effect on platelet adhesion and blood compatibility. The application prospect of this technique in surface modification of membrane for leukocyte depletion was discussed.

Methods: First, PBT was soaked in polyethyleneimine solution by aminolysis of the material surface with positive electricity, and then alternately adsorbed of negatively charged heparin and positively charged chitosan, while heparin is formed in the outermost layer of the multilayer structure. Platelet adhesion, platelet function, hemolytic rate, erythrocyte deformability, erythrocyte osmotic fragility of the polyelectrolyte multilayers modified PBT were investigated.

Results: The results showed that chitosan/heparin multilayers formed gradually by water contact angle, zeta potential and atomic force microscopy. The hemolytic rate of multilayer films with different layers was less than 5%, and the red cell deformability index increased gradually with the increase of the number of assembled layers. The erythrocyte osmotic fragility of multilayer films with different layers was not statistically different from that of the control group. The results of scanning electron microscopy showed that the number of platelets adhered on original PBT was significantly higher than that on the modified film surface. With the increase of the number of layers, the adhesion of platelets to the surface decreased. Platelet function was influence by the original PBT film, which was shown as the maximum platelet aggregation rate was significantly lower in the control group [(87.22 ± 2.10)%vs (82.36 ± 2.11)%], hypotonic shock relative change rate declined [(79.33 ± 1.27)%vs (77.12 ± 1.09)%], the expression rate of CD62p increased [(9.78 ± 0.58)% vs (17.45 ± 1.25)%). With the increase of the number of assembled layers, the maximum aggregation rate of platelets increased, HSR increased, and the expression rate of CD62p decreased, compared with the unmodified PBT. Among them, the ten layers of the assembly membrane was not statistically significant different from the control group.

Summary/Conclusions: After chitosan/heparin decorated with PBT, the hydrophilicity of PBT were improved, the adhesion of platelets was reduced, and the platelet function and red blood cell was not significantly affected. Electrostatic self-assembled multilayer film is expected to be a new type of biological PBT surface, which shows its application prospect in surface modification of leukocyte filter materials.

P-240

HOW TO STANDARDISE A MANUAL PLATELET PRODUCTION PROCESS AND THE IMPACT OF OPTIMISATION ON PLATELET VOLUME AND QUALITY

L Larsson[1,2] and H Ahlzén[1]

[1]Clinical Immunology and Transfusion Medicine, Karolinska University Hospital
[2]CLINTEC (Clinical Science, Intervention and Technology), Karolinska Institutet, Stockholm, Sweden

Background: In 2015, Karolinska University Hospital converted its production of buffy coat platelets (BCPs) from automated (Orbisac System) to manual, to afford the pathogen inactivation (PI) system Intercept. After implementation of the manual system, the biggest challenge was its higher sensitivity to fluctuation, which was seen as differences in BCP volume and platelet count, compared to the automated system. Aims: The aim was to standardise the manual production procedure by re-evaluating every step of the current process and optimise them.

Methods: We identified weak areas of manual production, removed or optimised them to create a more standardised procedure. Thereafter, we compared BCP count and volume of yearly quality controls (N > 175) before and after optimisation.

Results: The logistical challenge of the Intercept PI system is the 6–16 h window for removal of excess chemical compound (CAD). Before optimisation, four staff members worked daily, under stressful conditions, with BCP production including PI, to meet the 6-hour CAD-time. Prolonging the CAD-time to 16 h allowed the workload to be more evenly spread throughout the workday, thereby allowing reduction to three staff members for the same number of BCPs produced. The more even distribution rendered less stress and clearer "handle-with-care" approach, even with one less person. Longer CAD-time also allowed buffy coats (BC) to rest two additional hours before processing, as well as introduction of a 1-hour pool rest before centrifugation. This likely contributed to higher overall yield.

SOPs were revised to present all necessary processing steps in a more streamlined way. This eliminated a risk of shortcuts to save time.

Shelves were designed, allowing 600 BCs to rest non-overlapping in a confined space. A height-adjustable shelf with optimised hooks for pooling was designed to simplify standardisation of the procedure.

Initially, plasma remained in the top tube of the BC bag after whole blood separation, making sterile connections with long tubes mandatory to achieve correct amount of plasma in the pool. Optimisation of the whole blood separation program left the plasma in the BC bag, allowing tube lengths to be shortened, preventing unnecessary loss of platelets in tubes.

A new way of loading centrifuge liners was invented to prevent BCPs of red colour and low volume, caused by too little or too much space for the pool in the liner.

PLT content was a direct reflection of differences in pool agitation. Therefore, very strict instructions for mixing were implemented.

The number of available centrifuges and separators for production was restricted, forcing the staff to work with smaller batches. Thereby, they had proper conditions to monitor each individual separation.

Platelet count per unit was $2.39 \pm 0.40 \times 10^{11}$/unit in 189 ± 29 ml before optimisation and $2.72 \pm 0.29 \times 10^{11}$/unit in 190 ± 7 ml after.

Summary/Conclusions: After optimisation of our manual process our staff is less stressed, more quality-aware, and working more uniformly. As a result, we see BCPs with higher yield and less fluctuation, regarding both volume and platelet count. It is especially noteworthy that the standard deviation in platelet count per unit is greatly reduced.

We conclude that it is fully possible to standardise a manual production process.

P-241

EVALUATION OF THE VOLUME CONSISTENCY OF BUFFY COATS PRODUCED BY MEANS OF THE ARCHIMEDE AUTOMATED SEPARATOR FOR THE PREPARATION OF BLOOD COMPONENTS

G Kula[1], M Antoon[2], M Woźniak[2] and M Cardoso[2]

[1]Regionalne Centrum Krwiodawstwa i Krwiolecznictwa w Olsztynie, Olsztyn, Poland
[2]Terumo BCT, Zaventem, Belgium

Background: Archimede is an automated extractor (manufactured by Moelca, Italy and distributed by Terumo BCT) used to process blood components. The Archimede device software facilitates the configuration of several customized separation protocols to accommodate the specific needs and processing requirements that are characteristic for the blood center. The separator automatically transfers one or more blood components from the centrifuged container into one or more satellite bags. It can operate with Top and Top or Top and Bottom blood bags. Its high degree of automation allows for additional flexibility and allows for one single operator to manage several machines simultaneously. Archimede was tested at the RCKiK at Olsztyn, Poland.

Aims: The goal was to perform an assessment of the consistency of the separation process on the Archimede device as reflected by the variability.

Methods: Thirty-two (32) whole blood units (target volume 450 ml) were separated by means of the top & bottom separation protocol into a red cell concentrate, a plasma unit and a buffy coat. The volumes of 16 buffy coats were measured. They were stored and centrifuged following the center's standard operating procedures. Volume data were furthermore registered for all other components. Processing time was also recorded.

Results : The average processing time was below 3 min (n = 32). The volume of the red cell concentrates obtained after addition of additive solution was 277 ± 14 ml, while the plasma volumes were 254 ± 14 ml. The main parameter on which the study focused was the BC volume and its consistency. The BC volume averaged 63 ± 2 ml (n = 16), with a minimum and a maximum of 59 and 66 ml. The 95% Confidence Interval for the BC volume was [62–64] mL.

Summary/Conclusions: The Archimede separator performed as planned and was easy to use. The repeatability of the BC separation from pooled BC's was very satisfactory.

P-242

AUTOMATED SEPARATION OF WHOLE BLOOD USING THE ARCHIMEDE AUTOMATIC BLOOD COMPONENT EXTRACTOR

G Jaklin[1], T Bajsić[1], D Tumpić1[1], M Cardoso[2], M Imholz[3] and M Antoon[2]

[1]Transfusion Medicine, General Hospital Varaždin, Varaždin, Croatia [2]Medical Affairs [3]Field Support, Terumo BCT, Zaventem, Belgium

Background: The Archimede Automatic Blood Component Extractor (ABCE) is an automated device (manufactured by Moelca, Italy and distributed by Terumo BCT) used to process blood components. The device provides automated control and management of extraction to help in rationalizing the production of high-quality blood components. ABCE is equipped with saline adenine glucose mannitol (SAG-M) and plasma presses to standardize and optimize the quality of blood components as well as process flow. If desired, an optional omnidirectional barcode reader can capture all barcodes on a blood bag in one, single step. The technology platform furthermore allows for bidirectional communication, as well as remote monitoring and troubleshooting. It can operate with Top and Top (TAT) or Top and Bottom (TAB) blood bags and its high degree of automation allows for additional flexibility and for one single operator to manage several machines simultaneously.

Aims: The goal was to perform an assessment of the effectiveness of the whole blood component separation process by means of the ABCE.

Methods: Twenty-one (21) units of whole blood (target 450 ml) were collected from volunteer donors and transferred to the lab facilities for processing. After collection 15 whole blood bags were stored overnight (O/N) for 24 h and then processed while 6 blood bags were processed fresh. TAB bags were centrifuged (3,931 g–15 min) after which separation was performed with the ABCE (with an applied force of 40 kg). One-hundred milliliter (100 ml) of SAG-M was added to the red cell concentrate (RCC). Each completed process yielded one unit of plasma, a buffy coat (BC) and an RCC. Platelets were pooled by combining 4 BC after centrifugation (1,450 rpm; 5 min).

Results: The volume of the red cell concentrates obtained after addition of additive solution was 258 ± 13 ml, while the plasma volumes were 264 ± 12 ml. The BC volume averaged 53 ± 5 ml (51 ± 3 ml O/N; 58 ± 3 ml Fresh). The average platelet recovery (pool vs. whole blood unit) for the three O/N pools was 91%. The platelet recovery for the one 'fresh' pool was 88%. The hematocrit of the BC was 35 ± 3% and 34 ± 3% (O/N and fresh respectively).

Summary/Conclusions: The repeatability of the BC separation with ABCE was very satisfactory as demonstrated by a narrow standard deviation showing good process consistency. Likewise, platelet recovery was found to be excellent with values above 90% in the overnight pools and just below (88%) in the more challenging fresh pool. The ABCE separator performed as planned and was furthermore easy to use.

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Abstract has been withdrawn

Blood Components

P-244

EFFECT OF PRE–PROCESSING HOLDING TIME ON THE QUALITY OF PLASMA RECOVERED FROM LEUKOREDUCED WHOLE BLOOD DONATIONS

WP Sheffield[1,2], V Bhakta[2] and C Jenkins[3]

[1]Pathology and Molecular Medicine, McMaster University [2]Centre for Innovation, Canadian Blood Services, Hamilton [3]Centre for Innovation, Canadian Blood Services, Ottawa, Canada

Background: In Canada, whole blood donations may be processed either via the buffy coat (BC) method into transfusable plasma and platelet and red cell concentrates, or via whole blood filtration (WBF). Donations manufactured via the BC method must be processed into components within 24 h of phlebotomy. WBF method donations that are stored at 1–6°C may be processed within 72 h of phlebotomy into plasma and red cell concentrates. If the processing takes place between 24–72 h of phlebotomy, the recovered plasma (RP) may be used for fractionation, but not transfusion. While the quality of transfusable plasma made via either manufacturing method has been previously assessed, no such studies of Canadian RP have been undertaken. Here, we considered the possibility that protracted holding time affected the quality of WBF-derived RP.

Aims: To quantify the activity of coagulation factors prothrombin (FII), FV, FVII, FVIII, fibrinogen (Fg), and von Willebrand Factor (VWF), the concentration of IgG and total protein, and the prothrombin time (PT) in WBF-derived RP processed <48 h or >48 h after phlebotomy.

Methods: A total of 26 RP units processed <48 h after phlebotomy and an equal number processed >48 h after phlebotomy were compared. Each group contained 13 type O and 13 type non-O units; male and female donors were also equally represented. All RP units were thawed in a plasma thawer (Helmer) and 1.0 ml aliquots were taken and re-frozen for subsequent testing. An automated coagulation analyzer (STA Compact Max, Diagnostica Stago) was employed to determine FII, FV, FVII, FVIII, Fg activities and PT times, whereas enzyme-linked immunosorbent-type assays were used to measure VWF activity and IgG. Total protein concentration was determined by Bradford assay. Data sets were assessed using unpaired t tests, Welch corrected for unequal variances, with P < 0.05 indicating a statistically significant difference.

Results: Overall holding time did not significantly affect FII, FV, FVII, Fg, or VWF activities, or PT values or total protein concentrations. Values for RP with processing times <48 h vs. >48 h were (mean $\pm$ SD): FII, 0.86 ± 0.11 vs. 0.81 ± 0.10 IU/ml; FV, 0.81 ± 0.16 vs. 0.77 ± 0.13 IU/ml; FVII, 0.95 ± 0.23 vs. 0.95 ± 0.32 IU/ml; Fg, 2.86 ± 0.63 vs. 2.90 ± 0.72 g/l; VWF, 0.84 ± 0.30 vs. 0.73 ± 0.28 IU/ml; PT,

13.1 ± 0.8 vs. 13 ± 1 s; and total protein, 65 ± 5 vs. 63 ± 4 mg/ml. RP units processed <48 h from phlebotomy contained significantly more FVIII activity than longer-held RP units (1.03 ± 0.31 IU/ml vs. 0.72 ± 0.24 IU/ml, P = 0.0002), as well as higher concentrations of IgG (7 ± 2 mg/ml vs. 6 ± 1 mg/ml, P = 0.028).

Summary/Conclusions: Our results show that the majority of assayed plasma protein activities were unaffected by the extension of holding time from <48 h to 48 h to 72 h. While holding times up to 72 h to process whole blood provide operational flexibility to our transfusion service, limiting this time to 48 h would increase yields of FVIII and IgG. This is a relevant concern, as the four plasma protein products currently produced from Canadian RP are FVIII/VWF, intravenous immunoglobulin (IVIg), albumin, and fibrinogen concentrates. Alternatively, the contribution of RP processed >48 h from phlebotomy to plasma pools destined for the manufacture of FVIII/VWF and IVIg could be limited. Loss of FVIII activity in plasma held at 1 - 6°C with storage time has been previously noted, although the bulk of the loss of activity took place in the first 24 h (Sheffield, Transfusion, 2012), in contrast to the temporally later losses in whole blood reported here.

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BREAKAGE POINT OF SEALED TUBE ENDS EXPOSED TO SEVERE MECHANICAL STRESS IS IMPACTED BY CHOICE OF SEALING EQUIPMENT

L Larsson[1,2], J Derving[1] and H Ahlzén[1]

[1]Clinical Immunology and Transfusion Medicine, Karolinska University Hospital
[2]CLINTEC (Clinical Science, Intervention and Technology), Karolinska Institutet, Stockholm, Sweden

Background: Tube sealing is a pivotal part of blood processing. It is important that seals withstand mechanical stress, since they are exposed to large forces and rapid temperature changes within large intervals. We have previously studied the impact of centrifugal force on seals by a single sealer in combination with tubes containing different amounts of plasticizer DEHP (di-2-ethylhexyl phthalate). Now, we want to expand our knowledge to include several sealers from different manufacturers and extended strength testing.

Aims: The aim of the study was to investigate how seals made with multiple types of sealing equipment resist mechanical stress, and a possible link to DEHP content of tube.

Methods: PVC-tubes from blood collection bags containing 35% (Teruflex transfer bag, TerumoBCT) or 32% (NPT6820LE, MacoPharma) DEHP were filled with whole blood containing CPD, from a randomly selected donor.

Seals were created at every 5–10 cm of tube using the following panel of sealers: (i) QSeal-free (Conroy Medical), (ii) CompoSeal Mobilea (Fresenius Kabi), (iii) Sebra model 2,600 (Sebra), and (iv) Möller Medical/Docon Seal handle (Möller Medical). All sealing was performed with tubes and content in room temperature. The seals were inspected to avoid defects. They were then separated, cut in segments (2.5 cm from each sealed end), washed with water and thereafter air-dried.

Two kinds of strength tests were performed:

Test 1: Segments (10 per tube type and sealer) were connected to an air pressure regulator (MINI REG 08A, Atlas Copco). Sealed tube ends were submerged in water to enable detection of small leakages. Air was pressed into each segment, from 0.5 to 10 bar, with measure points at each integer, where pressure was held for 2 s each.

Test 2: Segments (20 per tube type and sealer) were filled with water and stripped with a manual tube stripper (Lmb Technologie) until breakage, thereafter inspected with magnifying glass.

Results: Test 1: All segments resisted 10 bar pressure without breaking for sealer A, B and D. One segment from sealer C, containing 32% DEHP, broke in the seal at 7 bar.

Test 2: All segments made by sealer C broke in the seal. The segments from B broke similarly, except 10% of 32% DEHP tubes where the tube broke (seal intact). For segments from D, 30% of 35% DEHP and 15% of 32% DEHP tubes broke in the seal. None of the segments from A broke in the seal.

Summary/Conclusions: The purpose of a sealer is to create and keep a closed system. Seals are generally very resistant to large forces; however, they can be forced to break by severe mechanical stress. The point of breakage, i.e. seal versus tube, depends on the type of sealer used, meaning there is a quality difference in sealing patterns depending on equipment. Demonstrably, a seal does not have to represent the weakest point in a closed system. Breakage in the seal is avoidable.

Whether the DEHP content of the tube affects the point of breakage is inconclusive, but it may possibly be related to seal mechanics or temperature. This needs to be further investigated.

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RED BLOOD CELLS FOR INTRAUTERINE TRANSFUSION: MEETING THE NEED THROUGH PHENOTYPING AND ANTI-CMV ANTIBODY TESTING

R Romans[1], G Clarke[2], B Gill[3], L Grabner[4], D Neurath[5], C McAuley[6], J McCarthy[7], M Biscocho[8] and G Parke[9]

[1]Utilization, Canadian Blood Services, Toronto [2]Donor and Clinical Service, Canadian Blood Services, Edmonton [3]Testing, Canadian Blood Services, Calgary [4]Diagnostic Services, Canadian Blood Services, Winnipeg [5]Transfusion Service, The Ottawa Hospital, Ottawa [6]Transfusion Service, IWK Health Center, Halifax [7]Transfusion Medicine, Foothills Medical Center, Calgary [8]Transfusion Service, Mount Sinai Hospital, Toronto [9]Transfusion Service, BC Children's Health Center, Vancouver, Canada

Background: In 2017, based on recommendations from the Canadian National Advisory Committee on Blood and Blood Products (NAC), Canadian Blood Services, the blood supplier for Canada (outside of Quebec) prepared to substantially reduce serological CMV testing for donor samples. Only blood components intended for use in intrauterine transfusion would be tested for antibodies to CMV. For all other indications, the NAC guideline recommended that CMV safe (leukoreduced) and CMV IgG seronegative products be considered equivalent. In order to select units of appropriate phenotype for CMV antibody testing, assessment of the number of IUT performed and the usual phenotype requirements for red blood cells (RBC) used in IUT was required.

Aims:
1. To confirm the number and location of hospitals performing IUTs.
2. To determine the phenotype of required RBC units used in IUT.

Methods: Canadian Blood Services conducted a survey. Based on the survey results we would test a limited inventory of donors with RBC phenotype suitable for the most common indications for IUT, and to store these units for up to 5 days in a blood supplier distribution site geographically near the hospitals performing IUT. Testing for anti-CMV would occur twice per week. The RBC units maintained as stock inventory for IUT would be group O Rh D negative, C, E, and K negative, CMV IgG seronegative, five days or less of age. Each Canadian Blood Services operations site that served a hospital that performed IUTs would keep 2 such units on hand. The survey was intended to inform the selected phenotype required for this stock inventory and to determine if additional RBC antigen types may be required.

Results: As of August 2017, we determined that six hospitals served by Canadian Blood Services, in 5 provinces, performed IUTs. The RBC antibodies involved during a 12-month period for the six hospitals are summarized in the chart below. The data are the number of individual procedures performed.

Anti-D; 19
Anti-D, -C; 11
Anti-D, -C, -G; 1
Anti-D, -C, -Jk[b]; 6
Anti-D, -C, -Fy[a]; 1
Anti-D, -C, -S; 5
Anti-D,-C,-G,-E,-Fy[a]; 6
Anti-D, -S; 1
Anti-D, -E; 2
Anti-E; 2
Anti-K; 12
Anti-Jr[a]; 4

Summary/Conclusions: The plan to have a limited inventory of group O Rh negative, C, E, K negative, CMV IgG seronegative RBCs would meet most hospital patient needs (67%). The need for other antigen negative CMV IgG seronegative RBCs would be met by on demand CMV serological testing with a less than 24-h turnaround time. Given that IUTs are a scheduled procedure with advanced transfusion service notice, we were confident that our approach could meet the need for CMV seronegative products in a timely fashion.

To date, for patients with RBC antibodies undergoing an IUT, we have been able to meet hospital patient needs. Recent requirements for c negative RBC units for three patients with anti-c has indicated an additional possible requirement for stock inventory that is c negative as well as CMV IgG seronegative.

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PRODUCTION OF GRANULOCYTE CONCENTRATES FROM POOLED BUFFY-COATS USING THE SPECTRA OPTIA – A NOVEL APPROACH TO BLOOD COMPONENT PREPARATION

H Ahlzén[1], C Bergström[1], S Larsson[1], J Henriksson[1], S Lundquist[1] and E Watz[1,2]

[1]Department of Clinical Immunology/Transfusion Medicine, Karolinska University Hospital [2]Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden

Background: Granulocyte transfusion is a possible treatment of patients with severe granulocytopenia and life-threatening infection when conventional treatment is not successful. Higher granulocyte doses are thought to give better effect on the granulocyte level in the recipient. We currently use granulocyte components (GC) from apheresis. To increase granulocyte yield, the donor is treated with steroids and granulocyte-colony stimulating factor (G-CSF) prior to donation. Both drugs have documented side effects and treating healthy donors with them is debated from an ethical point of view. Drugs can be avoided by using a GC derived from pooled buffy coats (BCs) from whole blood. Publications about GC from BCs have mainly focused on preparation by traditional centrifugation and separation.

Aims: We wanted to investigate whether it is possible to produce GC from BCs using the Spectra Optia Apheresis system (Terumo BCT), which is commonly used for apheresis applications and bone marrow separation. This is a novel approach for GC preparation.

Methods: We pooled 10 BCs in a Spectra Optia BMP Accessory Set (Ref 11300, Terumo BCT) and connected it to a Spectra Optia Apheresis System IDL Set (Ref 12320, Terumo BCT). Granulocytes were extracted using the bone marrow processing program (7 BM-cycles, a flow rate of 80 ml/min, a collection rate of 2 mL/min and a collection preference of 30). Volume, white blood cell (WBC) count, hematocrit and platelet (PLT) count were assessed in the BC-pool as well as the GC and the residual, using scales (Entris, Sartorius Lab Instruments, Germany) and a cell counter (Sysmex XL-300, Sysmex Corporation, Japan). Cell survival (Annexin V/7AAD) in the BC-pool and the GC was analyzed using flow cytometry (Cytomics FC-500 MPL with MPX software, Beckman Coulter, IN, USA).

Results: The GC contained $18 \pm 1.9 \times 10^9$ WBCs and $5.6 \pm 0.6 \times 10^{11}$ PLTs in a total volume of 79 ± 3.3 mL. The hematocrit was $10 \pm 1.3\%$. The original BC-pool contained $18 \pm 1.5 \times 10^9$ WBC and $8.0 \pm 1.8 \times 10^{11}$ PLTs in 470 ± 3 mL with a hematocrit of $37 \pm 1.1\%$. This gives us a recovery of $97 \pm 5.1\%$ for WBC and $66 \pm 1.4\%$ for PLTs. Annexin V and 7AAD analysis showed that there was no significant difference between percentage of living granulocytes in the GC ($76 \pm 5.2\%$) and the BC-pool ($69 \pm 4.3\%$).

Summary/Conclusions: We show a novel method for preparation of GC from BCs using the Spectra Optia Apheresis system. Recovery of granulocytes is high, but a substantial number of platelets is also collected, and the final product contains about two transfusion doses of platelets. Depletion of red blood cells is substantial. The preparation method using Spectra Optia does not seem to affect cell viability. Further investigations are needed, including analysis of the function of the collected granulocytes and comparison of GC from BCs to GC from apheresis.

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Abstract has been withdrawn

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PREDICTING THE FUTURE, UNDERSTANDING THE PAST: IDENTIFICATION OF INNOVATIONS AND MAIN DRIVERS FOR CHANGE IN THE DEMAND OF BLOOD PRODUCTS

P Langi Sasongko[1], M van Kraaij[2], K van den Hurk[3] and M Janssen[4]

[1]Transfusion Technology Assessment, Donor Studies [2]Unit Medical Affairs [3]Donor Studies [4]Transfusion Technology Assessment, Sanquin, Amsterdam, Netherlands

Background: There are various trends that are becoming more apparent in Western blood transfusion practices, such as the persistent decline of red blood cells. Retrospectively, this has also occurred in the Netherlands, along with the decrease of fresh frozen plasma although plasma proteins have increased and platelets have been steady. This could be due to drivers such as patient blood management and new therapeutic options. Furthermore, developing innovations in blood transfusion and related domains have great potential to impact the future transfusion field. These innovations include technological clinical advances, operational blood management,

pharmaceutical, and political (e.g. open borders for international trade). In combination with the aforementioned trends and drivers, these innovations may significantly impact the future demand for blood products. As the first step in a larger project to conduct scenario development of the future demand of blood products in the Netherlands, this topic has been explored using a combination of literature and expert perspectives.

Aims: There is a two-fold aim to explore and identify: (1) the historical development of blood usage in the past twenty years and underlying drivers to these developments and (2) various innovations that would impact the future demand of blood products for the Dutch context.

Methods: Purposive sampling and snowballing were used to recruit experts in blood transfusion in the Netherlands; they were interviewed in a semi-structured manner. Simultaneously, an extensive literature review of Pubmed, Google Scholar and gray literature were performed.

Results: Twenty-one experts with various roles in research, clinic, and management were interviewed. The literature review revealed 300 articles related to historical trends and drivers, and 75 articles related to innovations. Interview respondents reported the decline of blood products are due to drivers such as the rise of evidence-based medicine (EBM) linked to patient blood management (PBM) and changed clinical transfusion policies; safety; costs; and improved or new surgical techniques. However, the increased use of plasma proteins comes from a rising demand for plasma-derived medicinal products, due to increasing research and knowledge of immunoglobulins, for example. Key innovations that may decrease the future blood demand include personalized transfusion treatments, immunotherapy/gene therapy, an improved additive solution for red blood cell storage, and smart prescription drugs. However, innovations that have an uncertain effect on demand (due to diverging opinions) include cultured red blood cells and the socio-political landscape of the EU. Literature findings were compatible with interview findings in terms of trends, drivers, and innovations. However, literature emphasized that in order for these innovations to make a significant impact, it needs to overcome barriers of costs, safety, logistics, and regulations.

Summary/Conclusions: The first step of this ongoing research shows drivers of the past and innovations that may affect the future demand of blood products. The next steps include quantification of historical blood use in the Netherlands using prior data, expert elicitation workshops to construct various medium and long term scenarios, and developing an organizational mathematical model. This approach is expected to contribute towards adaptive policy recommendations to support Sanquin, the Dutch national blood bank.

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TRANS-ENDOTHELIAL ELECTRICAL RESISTANCE ASSAY FOR THE ASSESSMENT OF IMMUNOMODULATORY POTENTIAL OF RED BLOOD CELL PRODUCTS

BJ Kipkeu[1], J Acker[1,2] and J Holovati[1,2]

[1]Laboratory Medicine and Pathology, University of Alberta [2]Canadian Blood Services, Edmonton, Canada

Background: Red blood cell (RBC) transfusion is a widely accepted treatment for anemia. Despite its success, transfusion of RBCs is associated with adverse outcomes in transfused patients, such as the occurrence of transfusion-related immunomodulation (TRIM). The role of RBC storage length and extracellular vesicles (EVs) in RBC concentrates in TRIM is highly controversial. Trans-endothelial electrical resistance (TEER) is often used in pharmaceutical and cancer research and, involves measurement of electrical resistance across a cellular monolayer as a sensitive and reliable method to confirm the integrity and permeability of the endothelium barrier.

Aims: We aim to develop the TEER assay on a real-time cell analyzer (RTCA) as a new approach in evaluating the effect of EVs in stored RBC concentrates on the human vein endothelial cell (HUVECs) permeability.

Methods: HUVECs were purchased as pooled primary cells and grown at 37°C and 5% CO_2 in EGM-2 media (Lonza Group Ltd., Walkersville, MD, USA). Confluent HUVECs monolayers were trypsinized and seeded at concentrations between 2500–3500 cell/well (2–4 passages) on a fibronectin pre-treated 96-well E-plates coated with gold microelectrodes. The E-plate was placed on a xCELLigence RTCA system in the incubator and impedance readings taken as cell index (CI) at an hour interval for 5 to 7 days. Fresh peripheral blood or day 42 (D42) stored RBCs were centrifuged ($2200 \times g$, 10 min.), supernatants collected and diluted in EGM-2 media. HUVECs monolayers were treated with culture media (negative control); 0.1%, 0.5% or 1% v/v Triton X, 0.5%, 2% or 5% v/v disodium-EDTA (positive controls), 1:2, 1:5 or 1:10 dilutions of RBC supernatants. Changes in TEER across the HUVECs monolayers were assessed at 6, 12 and 24 h post-treatment.

Results: The average CI for HUVECs monolayers before treatment was 8.33 ± 0.35. The CI for untreated HUVECs monolayers remained high and stable throughout

experiments; CI = 8.36 ± 0.28, 9.17 ± 0.34 and 7.9 ± 0.46 at 6, 12 and 24 h post-treatment respectively. Treatment with 0.5%, 1% Triton X and 5% disodium-EDTA resulted in immediate drop in the TEER (1 h, CI = 0). Treatment with 0.5% and 2% disodium-EDTA resulted in a statistically significant reduction in TEER in a concentration-dependent manner compared to the negative control (P < 0.05). Treatment with fresh supernatants resulted in a statistically significant reduction in TEER for all the concentrations tested and time points assessed compared to D42 supernatants. For instance, 1:5 dilution fresh vs D42 CI was 2.3 ± 1.02 and 9.46 ± 0.39 at 6 h post-treatment, 0.83 ± 0.14 vs 9.73 ± 0.42 at 12 h post-treatment and, 0.51 ± 0.07 vs 7.42 ± 0.49 at 24 h post-treatment respectively (P < 0.05).

Summary/Conclusions: Impedance-based analysis has the advantage of real-time measurements that allows for sensitive comparison between RBC supernatants. This tool has a unique potential in the study of TRIM, as it would allow in-vitro evaluation of different blood products based on their ability to modulate the integrity of the endothelium.

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PROLONGED BLOOD BANK STORAGE OF RED BLOOD CELLS ACCENTUATES HYPERTHERMIA–INDUCED CATABOLIC ALTERATIONS AND ERYPTOSIS

SM Qadri[1], P Schubert[2], D Devine[2] and W Sheffield[1]

[1]Pathology and Molecular Medicine, McMaster University/Canadian Blood Services, Hamilton [2]Pathology and Laboratory Medicine, University of British Columbia/ Canadian Blood Services, Vancouver, Canada

Background: Prolonged storage of red blood cells (RBC) leads to biochemical and morphologic alterations and enhanced susceptibility to stress-induced eryptosis, an apoptosis-like cell death characterized by Ca^{2+}-dependent cell surface aminophospholipid exposure. Although multiple clinical trials have demonstrated the equivalent safety of fresher and older RBC in recent years, uncertainties remain over the quality of the oldest RBC units in the blood bank. In particular, these concerns apply to those RBC stored for 35–42 days, and have led some countries to limit RBC storage to 35 days. It is also unclear whether patient-specific clinical factors combine with RBC storage age to affect transfusion benefit. Recent evidence points to a substantial reduction in posttransfusion hemoglobin increment in critically ill febrile patients as compared to non-febrile patients. Enhanced eryptosis, documented in a wide range of febrile diseases, is believed to diminish the lifespan of circulating RBCs and cause microcirculatory derangement.

Aims: To examine the impact of the duration of RBC storage under blood bank conditions on cellular metabolism and eryptosis following post-storage exposure to physiologically-relevant increases in temperature.

Methods: RBC units (n = 6), stored at 1–6°C with SAG-M as additive solution for either 4 (Fresh; fRBCs) or 42 days (Old; oRBCs), were incubated in Ringer's solution (0.5 – 10% hematocrit) at 37–41°C for 18 h and multiple variables of the RBC storage lesion, microvesiculation, and eryptotic cell death were analyzed. For comparison, baseline values for indicators of eryptosis were directly determined in RBCs retrieved from refrigerated storage bags.

Results: RBCs subjected to sustained hyperthermia (40°C) displayed an increase in cell membrane phosphatidylserine (PS) externalization from ~5% to ~45% after 4 and 42 days of storage, respectively; the increase in the percentage of PS^+ RBCs under hyperthermic conditions reached statistical significance (P < 0.001) following 28 days of refrigerated storage. In comparison, PS exposure in RBCs incubated at 37°C showed an increase from ~0.3% to ~0.7% after 4 and 42 days of storage, respectively. Exposure to graded increases in temperature (37–41°C) augmented the percentage of PS^+ RBCs, an effect significantly more pronounced in oRBCs as compared to fRBCs at all temperatures examined. Flow cytometry analysis further revealed that hyperthermia (40°C) triggered a significant increase in intracellular Ca^{2+} levels (by Fluo3 fluorescence), generation of reactive oxygen species (by DCF fluorescence), and ceramide abundance (by fluorescent antibody detection), effects which were significantly more accentuated in oRBCs; as judged by forward scatter analysis hyperthermia significantly reduced cell volume in oRBCs, but not fRBCs. The extent of RBC microvesiculation following exposure to hyperthermia was, however, similar in both fRBCs and oRBCs. The variables of RBC storage lesion including hemolysis, cellular pH and lactate production showed subtle age-dependent variations under hyperthermic conditions.

Summary/Conclusions: Prolonged storage of RBCs aggravates the eryptotic phenotype under experimental hyperthermia, potentially contributing to reduced recovery of transfused RBCs in febrile patients by accelerating their phagocyte-mediated clearance in vivo. In future we will seek to replicate these findings in mice in vivo.

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CAN PLATELETS WITH PAS (SSP+) BE CONSIDERED SAFE FOR TRANSFUSION TO RECIPIENT OF ANY BLOOD GROUP?

RB Sawant[1], M Rane[2], V Vadera[1], U Dmello[2] and D Patil[2]

[1]Transfusion Medicine, Kokilaben Dhirubhai Ambani Hospital [2]Four Bungalows Andheri West, Kokilaben Dhirubhai Ambani Hospital Mumbai, Mumbai, India

Background: Platelets with high antibody titers have been reported to cause adverse reactions in recipients. Our PAS-platelets protocol involves removal of 80% of plasma from the platelet unit and its replacement by PAS. We have performed IgM and IgG titers of such platelet units with PAS to ensure the safety of these platelets with reference to antibody titers.

Aims: To evolve a protocol for universal use of PAS added platelets across all blood groups.

Methods: Platelet concentrates (N = 167) comprising (N = 79) pooled platelets and (N = 88) apheresis platelets were studied. The IgM and IgG titers of the platelet units were performed prior to PAS addition and after PAS addition for comparison. The volume of plasma removed and platelet content of the unit was also studied. The results of the above parameters before and after PAS addition were compared. Platelets of blood group A (N = 40). B (N = 75) and O (N = 52) were studied.

Results: The mean volume of platelet units before PAS addition was 379.9 mL and volume of the plasma removal prior to PAS addition was 303.7 mL (79%). The platelet content prior to PAS addition was mean $4.9*10^{11}$ per unit whereas the mean value after PAS addition was $4.8*10^{11}$. The baseline Anti-A titers were 32 for IgM and 128 for IgG and the same were reduced to 4 for IgM and 16 for IgG after plasma depletion and PAS addition. The baseline Anti-B titers were 32 for IgM and 256 for IgG and were reduced to 4 for IgM and 32 for IgG after plasma depletion and PAS addition. An overall 3 tube reduction in antibody filters was achieved by PAS addition. Antibody titers, post – PAS addition greater than permissible levels were found in 2 cases where the baseline titers were above 512.

Summary/Conclusions: Platelets with additive solution can be considered safe for transfusion to recipients of any blood group. However caution should be exercised with platelet units having baseline titers above 512.

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DETERMINATION OF %SO$_2$ IN MORE THAN 1300 FRESH ERYTHROCYTE CONCENTRATES BY RESONANCE RAMAN SPECTROSCOPY

D De Korte[1], T Yoshida[2] and H Korsten[1]

[1]Product & Process Development Blood Bank, Sanquin, Amsterdam, Netherlands
[2]Hemanext, Lexington, United States of America

Background: In support of research on improving erythrocyte storage under low oxygen tension (pO$_2$), haemoglobin oxygen saturation (%SO$_2$) in fresh erythrocyte concentrates (RCCs) was measured non-invasively through the wall of RCC bag using Resonance Raman Spectroscopy (RRS). Surprisingly, a large variation in %SO$_2$ of fresh (0–2 days) RCC was found in a pilot study. For further analysis of this finding, a large number of freshly prepared RCCs at Sanquin Blood Bank were analysed with the RRS device.

Aims: Determine relationships between observed variation in %SO$_2$ and donor/donation variables using external oxygen saturation measurement with RRS of > 1300 fresh RCCs immediately after component preparation.

Methods: For 1337 fresh RCCs, the %SO$_2$ was analysed with RRS device (A3U11 Microvascular Oximeter, Pendar Medical). This device was validated by analysing the %SO$_2$ of 12 RCCs in comparison with %SO$_2$ measurements on a qualified blood gas analyser (Radiometer ABL90 FLEX). Additionally, to investigate whether low or high %SO$_2$ values had an effect on the shelf life, RCCs were sampled on day 1 and 35 for blood gas and CBC (Sysmex XT2000) as well as for haemolysis and ATP content.

Results: The results of the %SO$_2$ measurements with the RRS device corresponded to the %SO$_2$ measurements on the blood gas analyser with a difference of 0.3% ± 1.5%. The %SO$_2$ data from 1337 donors were compared with donor/donation data such as blood pressure, time of donation, donation duration, as well as individual donor characteristics (weight, height, calculated BMI, age, Hb and gender). The %SO$_2$ data from the 1337 RCCs showed a binomial distribution, with two peaks, strongly influenced by gender of the donors; men (56% of subjects; %SO$_2$ = 65.0 ± 16.0) and women (44% of subjects; %SO$_2$ = 52.7 ± 18.6). The other donor parameters showed no clear effects on %SO$_2$. Cell counts, haemolysis (day 1, 0.09% ± 0.02; and day 35, 0.36% ± 0.22) and ATP (day 1, 5.69 μmol/gHb ± 0.43/;

and day 35, 3.19 μmol/gHb ± 0.48) showed normal expected values, regardless of whether the %SO$_2$ value was high or low.

Summary/Conclusions: The %SO$_2$ measured by the RRS laser device correspond to %SO$_2$ measured on a blood gas analyser. The use of the RRS device had no adverse effect on the in vitro quality of erythrocytes during storage in a small test group of 12 RCCs and there was no link between in vitro quality and %SO$_2$ value immediately after collection. The mean %SO$_2$ for female donors was lower than for male donors. This cannot be explained on the basis of other available donor/donation data. Further research is needed to explain this difference.

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QUALITY ASSESSMENT OF STORED PLATELET CONCENTRATES PREPARED BY ACOUSTOPHORESIS

D Francois, N Bertin, X Telot, J Gomez and J Gachelin

Aenitis Technologies, Paris, France

Background: Prophylactic platelets concentrate (PC) transfusion is the first line therapy for patients with hemorrhagic syndrome. Purity and function of transfused PC is the cornerstone of efficient treatment. To obtain PC from whole blood samples, blood banks currently use hard spin centrifugation (5000 g)-based methods, leading to poor resting platelets yield. Prolonged storage is also an issue for blood banks because of platelet storage lesions.

Aims: In order to improve platelet quality and preservation for therapeutic aims, we developed an acoustic-based fractionation device for isolation of human platelets from whole blood bags. We have already shown that acoustic platelet separation is an efficient method to fractionate blood in a low shear stress environment (92.8% ± 12.8 purity, 58.3% ± 19.3 yield), leading to minimal platelet activation and preservation of platelet responsiveness to agonists and function. We now aim to study the impact of acoustic fractionation on platelet storage by comparing the quality of platelet rich plasmas (PRP) produced by acoustophoresis or by soft spin centrifugation (200 g).

Methods: PRP obtained by soft spin centrifugation or acoustic fractionation were stored for 7 days at 20–24°C under constant agitation. Platelets were analyzed under resting conditions and after stimulation with common platelet agonists. We used flow cytometry to monitored the expression of activation markers P-selectin (CD62P), PAC-1 (CD41/CD61) and Annexin V (Phosphatidylserine) and checked morphologic and metabolic characteristics of platelets after 2, 5 and 7 days of storage.

Results: PRP obtained by soft spin or acoustic fractionation showed comparable storage response. Surface expression of P-selectin, PAC-1, and phosphatidylserine increased upon storage in both types of PRP. There was no difference in the surface levels of those platelet activation markers between the two types of PRP. Interestingly, platelets prepared by acoustophoresis retained a slightly increased responsiveness to A23187 and collagen after 7-day storage as compared to platelets prepared by soft spin centrifugation. Metabolite concentration increased during platelet storage for both PRP, while pH simultaneously decreased. Compared to various publications, metabolic change is within the standards for therapeutic transfusion.

Summary/Conclusions: Preliminary results show comparable platelet aging in PRP prepared by soft spin or acoustic fractionation. Our data suggest that there are no side effects on platelet storage after acoustic fractionation. Platelet storage lesions are the result of metabolically active platelets at 20°C and most of them have been shown to be reversible upon transfusion. Quality and function of 7-day platelets obtained by acoustic fractionation appear to match blood bank standards for therapeutic transfusion. We have planned a larger trial in collaboration with the EFS, a French blood bank, to confirm our results and validate the device.

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DONOR AGE IS ASSOCIATED WITH PLATELET STORAGE PROPERTIES

I Bontekoe[1], D Sijbrands[1], P van der Meer[1], J Lagerberg[1], A Verhoeven[2] and D de Korte[1]

[1]Product and Process Development, Sanquin [2]Tytgat Institute, Academic Medical Centre, Amsterdam, Netherlands

Background: Previously it was shown that donors could be classified as having platelets (PLT) with good, average or poor storage properties. In a recent study we demonstrated that PLT storage performance was consistent by donor [Bontekoe, Transfusion 2017]. A main difference between 'good' and 'poor' storage properties

involved metabolic activity, resulting in a faster decline of pH during storage of 'poor' PLT concentrates (PC). This might be caused by mitochondrial defects which have been associated with age and age-related diseases like metabolic syndrome and Type 2 diabetes (T2D).

Aims: To test the hypothesis that PLTs obtained from young whole blood (WB) donors have better storage properties than PLTs from aged donors.

Methods: Fifteen WB donors <30 year, were selected = "selected" and buffy coat (BC) and plasma were shipped to the laboratory. After overnight hold, a single-donor PC (sPC) was prepared. In addition, 11 sPC were prepared from donors >45 year. The sPC were stored for 8 days at 22 ± 2°C in a 600 mL PVC-DEHP container (sub-optimal conditions) on a flatbed shaker and sampled on Day 1, 4 or 5 and 8 for determining the in vitro quality. The diabetic marker HbA1c was determined from red cells and cholesterol and triglyceride levels from plasma. Storage data were analysed using an unpaired one-sided t-test.

Results: Young donors were of age 24 ± 3 year and aged donors were 60 ± 7 year. The aged donors had higher blood pressure before donation, higher HbA1c (38.6 ± 4.9 vs 34.1 ± 3.3 mmol/mol), total cholesterol (4.2 ± 0.7 vs 3.4 ± 0.6) and LDL-cholesterol (2.3 ± 0.6 vs 1.8 ± 0.5) than young donors. All young donors had HbA1c within the normal range of 20–42 mmol/mol but 2/11 aged donors had HbA1c >42 mmol/mol, indicative for T2D. The sPC of both groups had the same volume (71 ± 3 vs 72 ± 2 mL) and PLT content (73 ± 8 vs 74 ± 11 × 10^9). On Day 8, sPC from young donors showed higher pH$_{37°C}$ (6.84 ± 0.15 vs 6.40 ± 0.48, P < 0.01) and lower lactate production. The young group contained only one outlier with pH<6.4, whereas the aged group contained 5 sPC with a pH below the lower limit of 6.3, not being outliers and including two donors with high HbA1c. Also many other variables like swirling effect, CD62P-expression, Annexin A5 binding and hypotonic shock response reflected better in vitro quality of the young group than the aged group. However, no differences in mitochondrial membrane potential, as measured with JC-1, were detected

Summary/Conclusions: PC prepared from BC, obtained from young WB donors showed better storage performance than from aged donors. This might have an impact on donor selection for platelet production, especially for single-donor apheresis products. The higher glycolysis rate in PLTs from aged donors is probably caused by a higher demand for pyruvate by mitochondria or by partial mitochondrial dysfunction due to aging and/or (pre)diabetes

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NATIONWIDE SURVEY ON THE EFFICACY AND SAFETY OF RELEASED WASHED PLATELET CONCENTRATES

Y Ishiyama[1], S Fujiwara[2], N Fujishima[3], M Ito[4], T Sugimoto[5], S Saito[6], T Sakaguchi[7], K Nagai[8], H Masuoka[9], K Nagai[10], A Morita[11], S Kino[12], A Tanaka[13], Y Hasegawa[14], A Yokohama[15], K Fujino[16], M Shigeyoshi[17], M Matsumoto[18], A Takeshita[19] and K Muroi[20]

[1]Department of Hematology, Kanagawa Cancer Center, Yokohama [2]Division of Hematology, Jichi Medical University Hospital, Shimotsuke [3]Division of Blood Transfusion, Akita University Hospital, Akita [4]Department of Laboratory, Japanese Red Cross Narita Hospital, Narita [5]Division of Transfusion Service, Tokai University Hospital, Isehara [6]Department of Clinical Laboratory, St. Marianna University School of Medicine Yokohama City Seibu Hospital, Yokohama [7]Department of Transfusion and Blood Purification Therapy, National Defense Medical College Hospital, Tokorozawa [8]Department of Hematology, Niigata Prefectural Central Hospital, Joetsu [9]Department of Transfusion Medicine, The Jikei University Kashiwa Hospital, Kashiwa [10]Transfusion and Cell Therapy Unit, Nagasaki University Hospital, Nagasaki [11]Transfusion and Cell Therapy Center, Hakodate Municipal Hospital, Hakodate [12]Hokkaido Block Blood Center, Japanese Red Cross, Sapporo [13]Transfusion Medicine, Hachioji Medical Center of Tokyo Medical University, Tokyo [14]Department of Transfusion Medicine, University of Tsukuba Hospital, Tsukuba [15]Division of Blood Transfusion Service, Gunma University Hospital, Maebashi [16]Department of Transfusion Medicine, Osaka City University Hospital, Osaka [17]Department of Transfusion Medicine, Toranomon Hospital, Tokyo [18]Department of Nursing, Shinko Memorial Hospital, Kobe [19]Department of Transfusion and Cell Therapy, Hamamatsu University School of Medicine, Hamamatsu [20]Division of Cell Transplantation and Transfusion, Jichi Medical University Hospital, Shimotsuke, Japan

Background: Management of transfusion reactions remains an important issue in transfusion medicine. Although transfusion reactions caused by platelet concentrates (PCs) are frequent, several clinical studies have confirmed the preventative effects of replaced platelet concentrates and washed platelet concentrates (WPCs). Recently, the Japanese Red Cross Society (JRCS) began suppling WPCs as approved blood

components with identical prices for PCs. Because post-marketing surveillance study on released WPCs (RWPCs) has not been conducted, clinical data associated with the products remain insufficient.

Aims: The aim of this study was to evaluate the clinical efficacy and safety of RWPCs in a national multicenter study.

Methods: We retrospectively evaluated RWPCs supplied by JRCS blood centers from September 2016 to January 2017 in Japan. In the manufacturing of RWPCs, leukoreduced apheresis PCs were washed with bicarbonate Ringer's solution A and automated closed-system cell processor.

Results: Among the 215 institutes that were a part of this study, 50 actually used RWPCs during the study period. This study included 1,210 RWPC bags in 91 patients, which covered 30.2% of RWPCs supplied by JRCS blood center. All patients had hematological disorders and had a median of 48 transfusion histories. The median number of RWPC bags per patient was 8.5 (range, 1–91). RWPCs were transfused to 86 patients (94.5%) with history of transfusion reactions that could not be prevented by premedication with hydrocortisone and antihistamines. Transfusion reactions included serious reactions such as anaphylaxis and respiratory distress in 31% of patients. The median pre-transfusion platelet count was 18 (range, 0–130) $\times\ 10^9$/L, and the premedication prior to RWPCs was implemented in 702 RWPC bags (59%). On clinical response to transfusion reactions before RWPC, complete response, partial response, no change, and progression were observed in 91.6% (n = 1,105), 8.2% (n = 99), 0.2% (n = 2), and 0% (n = 0) bags, respectively. By subgroup analysis, overall response rate was not affected by disease, RWPC transfusion history, and type and severity of transfusion reactions. The median corrected count increment (CCI) at 1 and 24 h after transfusion were 13.5 (range, 1.9–35.4) $\times\ 10^9$/L and 3.5 (range, −13–53.6) $\times\ 10^9$/L, respectively. In patients without risk factors associated with platelet transfusion refractoriness such as bleeding or infections, the median CCI at 24 h was 5.5 (range, −13–53.6) $\times\ 10^9$/L. Transfusion reactions were associated with RWPC infusions in 9 RWPC bags (0.7%), such as pruritus (n = 5), urticaria (n = 2), chills/rigor (n = 1), and chest discomfort (n = 1).

Summary/Conclusions: This retrospective multicenter study was the first to evaluate the clinical effects of RWPC transfusion. The effectiveness of RWPCs to refractory transfusion reactions were recognized in almost all transfusions. The transfusion reactions associated with RWPC infusions were mild and occurred at a low frequency. Further studies are needed to evaluate the transfusion efficacy and healthcare cost of RWPCs, and preparation of guidelines for RWPC indications is desirable.

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DOSE–RESPONSE EFFECTS OF IBUPROFEN ON PLATELET AGGREGATION DURING STORAGE

I Bontekoe, S Groot, D Sijbrands, P van der Meer, J Lagerberg and D de Korte
Product and Process Development, Sanquin, Amsterdam, Netherlands

Background: Buffy coats (BC) from donors who used pain medication like aspirin, diclofenac, ibuprofen and naproxen up to 4 days prior to the donation are discarded in our centre, because a known side effect of these non-steroidal anti-inflammatory drugs is inhibition of platelet aggregation. These drugs inhibit the enzyme cyclooxygenase-1 in a reversible or irreversible manner, thereby blocking synthesis of thromboxane A_2 from arachidonic acid (AA). Previously, we observed little or no deviations in single platelet concentrates (PC), prepared from BC and plasma obtained from donors who used ibuprofen, including aggregation properties with ADP or collagen. This was explained by the known fast (<24 h) disappearance of ibuprofen from the blood circulation and the reversible binding to PLT. Levels of ibuprofen in PC were <10 mg/L.

Aims: To investigate the effects of different ibuprofen doses on in vitro quality of PC in PAS-E during storage, in particular on aggregation properties

Methods: On Day 1, leukoreduced PC (n = 3) were prepared from 5 BC and 300 mL PAS-E and aliquoted into 4 units of 70 mL. To 3 of these units 1 mL of ibuprofen (Sandoz, granular) solution was added, adjusted to reach final concentrations of 5, 10 or 20 mg/L. To 1 control unit 1 mL of NaCl 0.9% was added. The PC were stored on a flatbed shaker at 22 ± 2°C in a 600 mL container and sampled on Day 2, 5 and 8 for in vitro quality. Light transmission aggregometry was performed by stimulation with AA, also on Day 1 15, 60 and 240 min after addition of ibuprofen. A repeated measures ANOVA with Dunnett's post-test was applied for statistical analysis.

Results: During storage, no differences in pH, lactate production, CD62P expression, Annexin A5 binding, swirling effect or MPV between the groups were observed (data not shown). Aggregation with AA was reversibly inhibited by lower concentrations of ibuprofen: with 5 mg/L aggregation was fully recovered after 60 min, with 10 mg/L aggregation was almost fully recovered after 24 h (>80%, P < 0.05). In PC with 20 mg/L, no recovery of aggregation was observed throughout storage (<5%).

Summary/Conclusions: Storage properties of PC in PAS-E with added ibuprofen were comparable with PC from controls, confirming former results. Aggregation with AA showed clear dose-response effects ranging from almost immediate and full recovery with 5 mg/L ibuprofen to full impairment until Day 8 with 20 mg/L. Because expected levels in BC from donors who used ibuprofen are <10 mg/L, use of BCs obtained from a donor who used ibuprofen is considered still feasible for pooled BC, due to dilution with PAS-E. In vitro quality of PC in PAS-E will be further investigated in a 'best case' scenario with 1/5 BC obtained from such a donor.

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THE EVALUATION OF SOME OXIDATIVE STRESS MARKERS DURING STORAGE OF PLATELET CONCENTRATE

F Khoshnaghsh[1] and M Deyhim[2]
[1]Shariat Razavi Hospital, Social Security Organization [2]Clinical Chemistry, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: During storage, platelets undergo numerous morphological, biochemical and functional changes. These changes in platelet during storage are collectively termed platelet storage lesion (PSL) that effect on platelet in vivo survival and platelet quality. Oxidative stress is one of the main factors that cause improves PSL in platelet concentrate during storage

Aims: To evaluate the oxidative stress markers in platelet during storage of platelet concentrate.

Methods: In this experimental study, we selected ten platelet concentrated (PC) from healthy donors prepared from Iranian Blood Transfusion Organization (IBTO) and stored at 22°C with gentle agitation up to 5 days. Platelet units were sampled on the day of collection (day 0), 3th and 5th day. We measured the total antioxidant capacity (TAC), the levels of Malondialdehyde (MDA) and nitrate/nitrite metabolites in the platelet concentrates during storage. Also we measured some biochemical parameters such as glucose, lactate concentration and lactate dehydrogenase (LDH) enzyme activity and pH. Platelet count and mean platelet volume (MPV) were measured by automated cell counter.

Results: According to results, we have observed that MDA was increased during platelet storage ($MDA_{day0} = 1.64 \pm 0.98$, $MDA_{day3} = 3.63 \pm 1.18$, $MDA_{day5} = 5.83 \pm 2.61$ nmol/PLT). Also our results showed that TAC was decreased during storage ($TAC_{day0} = 0.347 \pm 0.038$, $TAC_{day3} = 0.334 \pm 0.04$, $TAC_{day5} = 0.266 \pm 0.056$ mM/PLT).Nitrite/nitrate metabolites was so decreased during platelet storage (nitrate/nitrite$_{day0}$ = 15.86 ± 5.3, nitrate/nitrite$_{day3}$ = 13.66 ± 4.31, nitrate/nitrite$_{day5}$ = 11.58 ± 5.53 mmol).Lactate concentration and LDH enzyme activity, both were increased during platelet storage (lactate$_{day0}$ = 20.93 ± 8.8, lactate$_{day3}$ = 58.5 ± 14.1, lactate$_{day5}$ = 92.4 ± 47.5 mg/dl; LDH$_{day0}$ = 294 ± 33, LDH$_{day3}$ = 2478 ± 631, LDH $_{day5}$ = 3107 ± 732 IU/L). Moreover, the concentration of glucose was decreased during storage (glucose$_{day0}$ = 463 ± 31, glucose$_{day3}$ = 404 ± 32, glucose$_{day5}$ = 394 ± 36 mg/dl). PLT count was decreased from 557 ± 137 at day 0 of storage up to 338 ± 84 PLT $\times\ 10^3$/μl at day 5 of platelet storage.

Summary/Conclusions: According to our results, oxidative stress was increased during platelet storage. On the other hand, the results showed that platelet metabolism was impaired during this period. It seems that changes in platelet oxidative stress and platelet metabolism both can play important role to improve platelet storage lesion.

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THE DEVELOPMENT OF RANDOM PLATELET CONCENTRATES (PC) IN PLATELET ADDITIVE SOLUTION (PAS)

J Akahat[1], T Jaroonsirmaneekul[1], N Mungkhunkhamchaw[1], P Darunikorn[1], K Jenwitheesuk[2] and K Phunikhom[3]
[1]Blood Transfusion Centre [2]Department of Surgery [3]Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Background: Platelet additive solutions (PAS) are crystalloid nutrient media used in place of plasma for platelet storage. They replace 60–70% of plasma in platelet components. So the amount of storage plasma can be decreased. Platelet stored in PAS have been demonstrated to have a lower risk for allergic transfusion reactions and appeared to have equivalent clinical efficacy for controlling bleeding, compared to platelets stored in 100% plasma and increase storage time to 7 days with bacterial detection test and due to decrease in the titer of ABO agglutinins, platelets in PAS

do not require ABO compatibility between donor plasma and recipient cells or use as universal platelet. The separation of random platelet concentrates (PC) from whole blood is base on the differential densities of various cellular components when blood is subjected to variable centrifugation forces. The problem in our routine work is 3.8% of PC showed no swirling features before 5 days.

Aims: To prepare PC in PAS in our routine work, instead of the traditional PC.

Methods: Whole blood (WB) was high-speed centrifuged before separation by automated system. Platelet concentrate (PC) was prepared by an alternative approach involved PC preparation from a single BC unit by adding approximately 50–70 ml of plasma/PAS before centrifugation, followed by transfer of the PC to a 300 ml transfer bag and stored in a flat agitator at 20–24°C for up to 5 days after collection and observed the swirling every days. The PC were measured volumes, residual leukocyte and platelet content. The pH was determined on day 6 at 20–24°C.

Results: Random platelet concentrates (PC) in traditional method (n = 31) had the mean of volume 51.3 ml and platelet yields 9.4×10^{10} cells/unit. Compared to the PC in PAS (n = 43) had the mean of volume 62 ml and platelet yields 7.2×10^{10} cells/unit. 100% of PC in PAS increased storage time to 7 days and the mean of pH 6.72 while the traditional PC had storage time only 4 days and the mean of pH 5.69.

Summary/Conclusions: PC in PAS increased storage time to 7 days 100% and provides reached the recommended quality of Council of Europe (EU), American Association of Blood Banks (AABB) and National Blood Centre, Thai Red Cross Society (TRC);random platelet concentrates (PC) had content more than 5.5×10^{10} cells/unit, volume 50–70 ml, pH>6.4.

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ROLE OF PLATELET ADDITIVE SOLUTION (PAS) IN ABO-INCOMPATIBLE SINGLE DONOR PLATELETS TRANSFUSION – A RETROSPECTIVE ANALYSIS OF 126 CASES

A Verma[1], P Negi[1], J Singh[1], S Singh[1] and M Khan[1]
[1]Transfusion Medicine, Max Super Speciality Hospital Vaishali, Ghaziabad, India

Background: Platelet apheresis is used to obtain platelets from volunteer donors, patients' family members, or donors with HLA or platelet-antigen-compatible phenotypes. By design, apheresis procedures are intended to collect large numbers of platelets from an individual, thereby providing a more potent product with fewer donor exposures for the patient. Although platelets are often transfused without regard to ABO compatibility, the use of mismatched platelets frequently results in lower post-transfusion recovery rates. In some cases, high-titer immunoglobulin G (IgG) A,B antibodies in blood group O recipients are reactive with transfused platelets carrying large amounts of A or B antigens, resulting in platelet transfusion refractoriness. Recovery of transfused platelets can also be influenced by the transfusion of group O platelets to group A recipients. Anti-A and/or anti-B in the donor plasma might be reactive with soluble A or B in the recipient plasma to form immune complexes that bind to transfused platelets decreasing the survival of the transfused platelets. Clinical trials comparing ABO-identical to unmatched platelets in patients with cancer who require multiple platelet transfusions have suggested that rates of refractoriness are significantly higher when unmatched components are used

Aims: The main aim of this case study is to highlight the importance of Platelet Additive Solution (PAS) in ABO incompatible Single Donor Platelets (SDP) Transfusions

Methods: The study was carried out at Department of Transfusion Medicine over a period of 1 year from January 2017 to December 2017. A total number of 419 SDP Procedures were done during this period. Out of 419, 126 ABO incompatible SDP Procedures were done with PAS SSP+. A ratio of 80% SSP+/20% plasma was used.

Results: No transfusion reactions mediated by 80% SSP+/20% plasma including allergic, febrile nonhemolytic transfusion reactions [FNHTRs], ABO isoagglutinin-mediated hemolysis or antibody-mediated transfusion-related acute lung injury [TRALI] were observed in any of the 126 cases.

Summary/Conclusions: A high titer of isoagglutinins in a platelet unit can cause hemolysis of recipient red cells that may be clinically significant and even fatal. This outcome may be more likely in situations when apheresis units are used as all the plasma comes from the same donor and is not "diluted" by plasma of lower isoagglutinin titers from other units in the pool or neutralized by the presence of soluble ABO antigens in the other units. Transfusion of only ABO-compatible Single Donor Platelets is not always possible due to limited availability of group-specific donors and maintaining the daily SDP stock due to the short life of platelets. In our study, we found that replacing the plasma with PAS is the best approach not only to overcome adverse effects due to ABO-incompatible SDP transfusions but also in maintaining the stock by having a product that can be issued across all group patients especially during dengue season.

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THE (NON-)COMMUTATIVE PROPERTY OF ADDITION TO RED BLOOD CELL STORAGE FORMULATIONS: EFFECTS OF ALKALINE ADDITIVES AND GUANOSINE/GLUCONATE

A D'Alessandro[1], R van Bruggen[2], J Reisz[1], R Culp-Hill[1], H Korsten[3] and D De Korte[2,3]
[1]Biochemistry and Molecular Genetics, University of Colorado Denver – Anschutz Medical Campus, Aurora, United States of America [2]Blood Cell Research [3]Product & Process Development Blood Bank, Sanquin, Amsterdam, Netherlands

Background: After the introduction of component therapy in the 1950s, for a long time SAGM (Europe) and AS-1 (North America) were the main additive solutions (AS) used for red blood cell concentrates (RBCs). Main improvements in the quality of RBCs in the last part of 20th century came from introduction of leukodepletion and PAGGSM and AS-3/5 as generation two AS. Still, storage in the blood bank results in the progressive accumulation of a so-called storage lesion, characterized by a large number of in vitro changes in parameters like hemolysis, morphology, 2,3-diphosphoglycerate (2,3-DPG) and adenosine triphosphate (ATP) content, membrane stability etc. The storage lesion can be, at least partial, mitigated by storage in novel storage additives, such as alkaline additive solutions. While several novel alkaline additive formulations have been proposed, no metabolomics characterization has been performed to date.

Aims: To perform metabolomics characterization for several novel alkaline additive formulations in comparison to SAGM and PAGGSM.

Methods: We performed UHPLC-MS metabolomics analyses of red blood cells stored in SAGM (standard additive in Europe), PAGGSM or alkaline additives SOLX, ESOL-5 and PAG3M for either 1, 21, 35 (end of shelf-life in The Netherlands) and 56 days.

Results: Metabolic linkage analysis provides at a glance an overview of metabolic rewiring across additives, indicating a strong effect on redox homeostasis, carboxylic acid, fatty acid and purine metabolism in alkaline additives when compared to SAGM. Results indicate that alkaline additives (especially PAG3M) better preserve 2,3-DPG and ATP. Correlations between ATP and DPG were poor for all additives except for PAG3M, suggesting a rewiring of the Rapoport-Luebering shunt specific to this additive. In addition, deaminated purines such as hypoxanthine were predictive of hemolysis and morphological alterations. Guanosine supplementation in PAGGSM and PAG3M fueled ATP generation by feeding into non-oxidative pentose phosphate pathway via phosphoribolysis. Decreased urate to hypoxanthine ratios were observed in alkaline additives, suggestive of decreased generation of urate from purine degradation, and as a consequence less formation of hydrogen peroxide by xanthine oxidase activity. Despite the many benefits observed in purine and redox metabolism, alkaline additives did not prevent accumulation of free fatty acids and oxidized byproducts, opening a window for future alkaline formulations including (lipophilic) antioxidants.

Summary/Conclusions: Alkalinization via different strategies (replacement of chloride anions with either high bicarbonate, high citrate/phosphate or membrane impermeant gluconate) results in different metabolic outcomes, in all cases superior to current canonical additives. The results from our metabolic analyses indicate superior preserving of RBC in PAG3M over the other alkaline additives and, in general, of alkaline additives over non-alkaline SAGM and PAGGSM. In particular, DPG and ATP generation and maintenance, as well as purine metabolism and redox homeostasis (especially the PPP and its non-oxidative phase byproducts) were favorable in PAG3M and other alkaline additives in comparison to SAGM and PAGGSM. However, the observed metabolic benefits do not extend to the prevention of storage-induced fatty acid release and lipid oxidation. Results from the present study provide additional insights in the metabolic benefits of alkaline storage additives and will likely guide the formulation of novel additives in the near future.

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SELECTED RED CELL ANOMALIES IN BLOOD DONATED AT THE REGIONAL BLOOD TRANSFUSION CENTRE – MOMBASA, KENYA

RN Wigina[1], M Kahato[2], S Mzee[1] and S Kaggia[3]
[1]Medical Sciences Department, Technical University of Mombasa, Mombasa [2]Medical Sciences Department [3]Human Pathology, Jomo Kenyatta University of Agriculture, Science and Technology, Nairobi, Kenya

Background: Blood transfusion is an important clinical intervention during surgery and in the treatment of severe tissue hypoxia. During transfusion, components of blood including RBC, Platelets or plasma are directly administered into the recipient to alleviate conditions such as anaemia and haemostatic deficiencies. Effective blood

transfusions will positively affect prognosis. The efficacy of a red blood cell unit depends on the amount of blood delivered, the quality of cells and the life span of a given unit.

Aims: This study was aimed at establishing the point prevalence of red blood cell abnormalities in donated blood. Specifically we screened for the presence of unstable haemoglobins, determined the haemoglobin concentration, red cell indices, osmotic fragility, G6PD enzyme deficiency and haemoglobin AA, AS and AC chain variants that may be present in donor blood at the Regional Blood Transfusion Centre, Mombasa-Kenya. We were also able to determine the ABO and RhD types of the donors.

Methods: This cross-sectional study was based at the Regional Blood Transfusion Centre, Mombasa. Consecutive blood samples were analyzed for red blood cell parameters and haemoglobin (Hgb) concentration by haematology analyzer (MS4S™ Melet Schloesing Laboratories haematology analyzer), haemoglobin electrophoresis, red cell lysis using the osmotic fragility test, and the isopropanol methaemoglobin reduction test.

Results: We found the percentage of donor ABO and RhD types at "A" (27.07%) "B" (22.78%), "AB" (4.14%), "O" (46.01%) RhD positive (97.63%) and RhD Negative (2.37%). The overall proportion of donors showing one or more anomalies was 31.07%. Specific anomalies were found in the following areas; 2.96% of donors had low haematocrit (34–50%), 14.05% had their Mean Corpuscular Volume outside the normal range (80–100 fl), 10.21% of donors showed reduced Hgb content (12–18 g/dl), Glucose 6 Phosphate dehydrogenase screening test showed that 9.62% had deficient activity 13.17% while and borderline activity. The Pearson's chi-squared test did not return a significant association between ABO type and G6PD deficiency however, an "AB" person is marginally more likely to be normal than a blood type "A" individual (coef = 1.09, s.e = 0.63. P-value = 0.08). At a P-value of 0.0426, An ANOVA model reveals that the G6PD status (normal, intermediate or deficient) maybe related to a certain haemoglobin level, however, when fit to an ordinal logit model the relationship is not reflected in the pairwise comparisons. We did not find any unstable haemoglobins during the study.

Summary/Conclusions: Donor red cells exhibit anomalies which could be potential causes of adverse events during both donation and transfusion. The percentage anomalies in this study were higher than those in a previous study in Western Kenya where 16.5% of donors did not meet the normal range values (Rajab, East African medical, 2015). We recommend that (1) blood banks employ stricter red cell assays procedures to enhance blood quality. (2) G6PD assays be considered for inclusion in the minimum assay protocols for blood banks. (3) The use of copper sulphate as a screening method be re-evaluated and if found necessary be replaced by more accurate methods such as Hemocue™.

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A NOVEL PROTOCOL FOR CRYOPRESERVATION OF PAEDIATRIC RED BLOOD CELL UNITS ALLOWS OPTIMISED AVAILABILITY OF RARE BLOOD

L Larsson[1,2], S Larsson[1], J Derving[1], E Watz[1,2] and M Uhlin[1,2]

[1]Clinical Immunology and Transfusion Medicine, Karolinska University Hospital
[2]CLINTEC (Clinical Science, Intervention and Technology), Karolinska Institutet, Stockholm, Sweden

Background: Increasing migration of people in the world is generating a growing mismatch between donor and patient population, causing a more frequent demand for availability of red blood cells (RBCs) of rare blood group antigens. Even though such RCCs (RBC concentrates) are frequently cryopreserved for prolonged storage, locating matching RCCs when an acute demand arises is often problematic. Paediatric patients often only need a fraction of a whole RCC at each transfusion. The remaining volume is generally wasted, even though new matching RCCs are difficult to find.

Aims: Develop a new method to cryopreserve paediatric RCCs with a closed-system automated cell processor.

Methods: Eight leukoreduced RCCs, pre-pooled to eliminate donor variability, were glycerolised in ACP215 (Haemonetics Corp.) on day 1 (d1) after donation. Unit 1–4 were kept as references (whole units, WU). Unit 5–8 were divided into three splits each (split units, SU) before freezing. After >1 month in <−65°C, all units were thawed and deglycerolised in ACP215 with SAG-M as additive solution. WU were stored (2–6°C) in 600 ml bags directly after finished procedure. To reduce excess supernatant, SU rested 1 h in RT and were thereafter centrifuged (1255 × g, 10 min). After manual extraction, SAG-M was re-added to adjust haematocrit to 60%. The final product was transferred into 150 ml paediatric storage bags before 2–6°C storage. Sampling was executed on d1–4; extended to d10 for haemolysis and extracellular potassium (K+). Haemoglobin (Hb), haematocrit, haemolysis, K+, pH,

ATP, glucose, lactate, 2,3-DPG, MCV (mean corpuscular volume) and microvesicles were measured. Medians were calculated and compared.

Results: All SU had haematocrit of 60 ± 1% and Hb of 169 ± 2 g/L after production, showing a robustness of the production method. WU, with no reduction of supernatant, had markedly lower haematocrit (45 ± 1%) and Hb (133 ± 2 g/L). Haemolysis and K+ increase rate was lower for SU, with significant difference between SU and WU from d3 (P < 0.01, P < 0.05 from d4). At d10, haemolysis reached 0.59% (SU) and 0.71% (WU), both below EDQM guidelines (0.80%). K+ reached 41.2 (SU) and 43.8 (WU) mmol/mg Hb. Glucose and pH were significantly lower (P < 0.01) in SU (explainable by different supernatant composition/concentration), generating significantly lower ATP and lactate (P < 0.01) than WU. ATP and pH decrease rates were however slower in SU. 2,3-DPG decreased evenly in both SU and WU. Levels were undetectable on d3. MCV was significantly higher (P < 0.01) in SU, not reflecting microvesicle count. Microvesicles increased throughout the storage period with non-significant difference between SU and WU.

Summary/Conclusions: Split units of cryopreserved RBCs can be successfully produced. Haemolysis and K+ content is lower, making them more suitable for paediatric transfusions, along with higher haematocrit that reduces risk of hyperhydration. This suggests they may resist storage lesion better than traditional whole units and can be stored longer time post-thawing. Post-deglycerolisation replacement of supernatant appears to be favourable for storage of RBCs and outweighs the detrimental effects of additional mechanical stress.

Production of split units can contribute to increase of stock supply and reduce unnecessary waste of RBCs of rare blood groups.

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REFORMULATING THE RED CELL STORAGE SOLUTION: THE EFFECTS OF BICARBONATE AND GUANOSINE

P Van Der Meer, H Korsten, J Lagerberg and D de Korte
Sanquin Blood Bank, Amsterdam, Netherlands

Background: Red cells show a decline in ATP and 2,3-diphosphoglycerate (2,3-DPG) when stored under blood bank conditions. As a result, red cells have a higher oxygen affinity, resulting in poorer oxygen delivery to the tissues. While this defect is corrected within 24 h after transfusion, for immediate oxygen delivery and overall red cell quality, ATP and 2,3-DPG levels should be close to values found in fresh whole blood. The development of the experimental red cell additive solution (RAS) Sol-X (containing phosphate, adenine, bicarbonate, glucose and mannitol, in the absence of sodium chloride; pH = 8.5) has led to further optimization of the quality of red cells during storage. The key to optimal red cell storage is maintaining the internal pH>7.2, as above this level the enzyme phosphoglycerate mutase remains active, and is able to synthesize 2,3-DPG without decreasing ATP. This can be achieved by a high external pH, and also by the absence of chloride in the storage solution. Addition of the RAS leads to chloride moving out of the red cell, and to maintain the electrolytic balance, hydrogen enters the cell, thus increasing the internal pH. This phenomenon is known as the chloride shift. Extra bicarbonate in the RAS can serve as additional buffer, preventing the drop in the internal pH. Further, guanosine is known to shift red cell metabolism towards the pentose phosphate pathway, resulting in synthesis of NADHP, which can be used to synthesize 2,3-DPG and ATP.

Aims: To study the effect of addition of extra bicarbonate and guanosine to Sol-X RAS on the in vitro quality of stored red cell concentrates.

Methods: One leukoreduced packed red cell concentrate was split in 4 equal parts. To each part, 24 ml of Sol-X was added; to the first part A standard composition (contains 26 mM bicarbonate); to the second part B with extra 26 mM bicarbonate (52 mM total), to the third part C with 1.4 mM guanosine, and to the fourth part D, with extra 26 mM bicarbonate (52 mM total) and 1.4 mM guanosine. The concentrates were stored for 56 days with weekly sampling to determine various in vitro quality parameters. Three replicate experiments were performed.

Results: The addition of extra bicarbonate led to an increased external and internal pH (day 35: pH$_{external}$ A, 6.47 ± 0.04, B, 6.57 ± 0.02*, C, 6.40 ± 0.03*, D, 6.44 ± 0.06; pH$_{internal}$ A, 6.52 ± 0.05, B, 6.63 ± 0.04*, C, 6.36 ± 0.03*, D, 6.41 ± 0.04*; *P < 0.05 versus A). However, this did not have an effect on 2,3-DPG levels (day 35: A, 1.0 ± 0.5, B, 1.5 ± 0.7* mmol/g hemoglobin (Hb)), and had a minor effect on ATP content (day 35, A, 4.3 ± 0.6, B, 5.0 ± 0.6* mmol/g Hb). The presence of guanosine in addition to adenine led to a significant increase in ATP (day 35, C, 6.1 ± 1.1*, D, 5.4 ± 1.5* mmol/g Hb) and 2,3-DPG (day 35, C, 20.1 ± 8.6*, D, 18.7 ± 8.8* mmol/g Hb) during storage, to which the addition of bicarbonate had no beneficial, and even a slightly deleterious, effect.

Summary/Conclusions: The addition of extra bicarbonate to this RAS increased pH, but ultimately had no effect on ATP or 2,3-DPG content during storage. The

addition of guanosine increased ATP and 2,3-DPG to levels that even on Day 56 conformed to acceptance criteria for stored red cell concentrates.

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2,3 DIPHOSPHOGLYCERATE CONTENT AND OXYGEN AFFINITY OF HEMANEXT RED BLOOD CELLS STORED UNDER OXYGEN REDUCED CONDITIONS

P Whitley[1], M Wellington[1], S Sawyer[1], S Hanley[1], F West[1], M Dioguardi[2], W Iselin[2], T Yoshida[2], A Dunham[2] and S Sowemimo-Coker[2]

[1]Blood Bank, American Red Cross, Norfolk [2]Research and Development, Hemanext, Lexington, United States of America

Background: Red blood cells (RBCs) are transfused into patients to correct anemia and to treat or prevent inadequate tissue oxygenation. During refrigerated storage of RBCs, the 2, 3 diphosphoglycerate (2,3DPG) concentration decreases to less than 0.5 μmol/gHb or undetectable level at 21 days of storage with corresponding increase in oxygen affinity (decrease in p50). These storage -induced changes in the 2,3DPG and p50 suggest that these RBCs may be less efficacious in oxygen delivery especially in medical conditions where there is an immediate need for adequate tissue oxygenation.

Aims: The main objective of the present study was to compare the concentrations of 2,3DPG and p50 of conventionally (aerobic) stored RBCs and Hemanext RBCs which were stored in Hemanext Storage Bags (HSB) after an initial processing with Hemanext Processing System.

Methods: Ten units of whole blood (500 ± 50 ml) were collected into CP2D anticoagulant. Each unit was processed into plasma and a leukocyte-reduced red cell concentrate (LR-RCC) in AS3 storage solution about 2 h from collection but stored at room temperature for about 7 h before Hemanext treatment. Prior to Hemanext processing, 40–60 ml of LR-RCC was removed from each unit and transferred into a sterile mini sample PVC RBC storage bag labeled as control. Each mini storage bag was configured to have the same surface area to volume ratio as a standard full unit of LR-RCC in regular RBC storage bag. The control bags were stored at 1–6°C within 8 h of blood collection. The remaining LR-RCCs (about 270–300 ml) were processed with Hemanext oxygen managed processing system with room-temperature agitation for 3 h before being transferred into HSBs for storage at 1–6°C within 12 h of whole blood collection. Samples were taken for measurement of complete blood counts (CBC), gas panels, hemolysis, morphology, adenosine 5′ triphosphate (ATP), 2,3DPG and p50 before and during storage.

Results: Salient results showed a significant decrease in 2,3DPG of control RBCs from 12.2 ± 1.8 μmol/gHb on day 1 to 2.2 ± 5.2 μmol/gHb on day 21 of storage, with corresponding decrease in the p50 from 25.5 ± 1.1 mmHg to 19.6 ± 1.1, P < 0.01. In contrast to the control, the concentration of 2,3DPG and the p50 in Hemanext RBCs were maintained at 13.0 ± 5.2 μmol/gHb and 30.3 ± 4.0 mmHg respectively on day 21. Although the concentration of ATP was slightly higher and less variable in Hemanext RBCs (5.3 ± 0.8 μmol/gHb) than the control (5.2 ± 2.2 μmol/gHb) on day 21 of storage, this difference was not statistically significant, P > 0.05.

Summary/Conclusions: These results show that the levels of 2,3DPG, p50 and ATP are well maintained in Hemanext when compared to conventionally stored RBCs. Since these parameters are very important in normal functions of the RBCs and in oxygen delivery, these data suggest that Hemanext RBCs may be more efficacious in oxygen delivery than conventionally stored RBCs especially in medical conditions where there is an immediate requirement for adequate oxygen delivery to the tissues and vital organs.

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THE EFFECT OF CRYOPRESERVATION ON A RARE MCLEOD DONOR RED CELL CONCENTRATE

TR Turner[1], R Skeate[2], G Clarke[3] and J Acker[1,4]

[1]Centre for Innovation, Canadian Blood Services, Edmonton [2]Medical Services, Canadian Blood Services, Toronto [3]Donor and Clinical Services, Canadian Blood Services [4]Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

Background: Canadian Blood Services' frozen blood program aims to provide red cell concentrates (RCCs) to patients with rare blood types. Many of the units in frozen inventory have rare phenotypes involving protein structural variations that may

interact with the red blood cell (RBC) membrane. Several blood groups are epitopes of multipass proteins which may be absent from rare RBCs and could impact the stability of the cell membrane. Collectively these phenotypic changes could affect the cryobiology of the cells. The McLeod phenotype is a result of the absence of the Kx protein in the Kell blood group system which leads to acanthocytosis of the RBCs. As cryopreservation methods continue to be modernized with the adoption of new anticoagulants, additive solutions and blood component manufacturing methods, the compatibility of processing cryopreserved units stored for extend periods should be routinely evaluated.

Aims: This study was performed to determine if units processed using a different production and freezing method could be deglycerolized using modern methods and meet regulatory standards. In addition, the specific evaluation of a McLeod donor unit will determine whether cryopreservation and subsequent deglycerolization can be successfully performed while preserving the integrity of the RBCs.

Methods: A control group (n = 3) was selected from units frozen using the same production and freezing methods as a McLeod donor unit cryopreserved in 1993. All four units were frozen in Charter Medical containers from non-leukocyte reduced whole blood collections. The units were previously glycerolized using the high glycerol method and were stored in a −80°C freezer for 24 years. Deglycerolization was performed using an automated cell processor (Haemonetics ACP-215) after the units were centrifuged to remove the supernatant glycerol. The standard deglycerolization protocol was then performed resulting in AS-3 RCCs. All units were tested immediately post thaw and post deglycerolization for hemolysis, glycerol concentration, and recovery. Additional testing at 24 h, 7 and 14 days included hemolysis, hemoglobin, potassium, mean cell volume, RBC deformability, osmotic fragility and ATP.

Results: Immediately post thaw, the control group and the McLeod unit had a glycerol concentration of 37.4 ± 0.4% and 37.5% respectively. Immediately post deglycerolization, all units had a residual glycerol of < 1%. Hemolysis of the control group at immediate, 24 h, 7 and 14 days post deglycerolization was 0.15 ± 0.02%, 0.19 ± 0.02%, 0.31 ± 0.02%, and 0.52 ± 0.10%. The McLeod unit had increased hemolysis at all time points (0.21%, 0.23%, 0.48%, 0.55%) when compared to the control group. The McLeod unit also had a decreased MCV (85.1 fl vs 104.1 ± 9.3 fl), increased mean corpuscular fragility, and increased RBC rigidity (4.308 vs 1.690 ± 0.103) at 24 h when compared to the control group.

Summary/Conclusions: RCCs processed and frozen using different methods tested in this study can be successfully deglycerolized using current automated cell processing methods and meet Canadian Standard Association (CSA) standards for cryopreserved RBCs. The McLeod unit met CSA standards at 24 h post deglycerolization however this unit has increased fragility and hemolysis potentially due to the unique RBC phenotype which may affect decisions on the appropriateness of extended post-thaw storage.

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ICE RECRYSTALLIZATION DUE TO TRANSIENT WARMING OF RED CELL CONCENTRATES CAN BE MITIGATED BY NOVEL SMALL MOLECULE INHIBITORS

TR Turner[1], R Ben[2] and J Acker[1,3]

[1]Centre for Innovation, Canadian Blood Services, Edmonton [2]Department of Chemistry and Biomolecular Sciences, University of Ottawa, Ottawa [3]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

Background: Cryopreservation of red cell concentrates (RCCs) is used for long term storage of blood products to support patients with rare blood types or requiring antigen negative blood. These units are often cryopreserved using a high glycerol method and stored for up to 30 years at temperatures below −65°C. However, throughout the RCC lifespan there are many types of operational events that may cause the RCC to warm above −65°C. Transient warming events (TWEs) can induce cellular damage due to ice recrystallization. The addition of novel ice recrystallization inhibitors (IRIs) has been previously demonstrated to mitigate this damage in 15% glycerolized red blood cells (RBCs).

Aims: The purpose of this study was to determine the characteristics of TWEs on RCCs cryopreserved with 40% glycerol and to evaluate the effect of TWEs with or without IRIs.

Methods: To characterize warming profiles of RCCs exposed to room temperature (RT), a RCC was glycerolized using an automated cell processor (Haemonetics ACP-215). Briefly, the RCC was SAGM and glycerol-reduced to an approximate hematocrit of 50%. Prior to freezing in a −80°C freezer, a thermocouple was inserted into the unit. TWE profiles from −75°C to −60°C, −40°C, and −20°C were recorded in triplicate. A small scale method was used to collect hemolysis data by the Drabkin's

method under single and multiple TWEs. Samples were cryopreserved in cryovials using a similar method to the RCC. For TWE exposures, samples in a Styrofoam rack were placed at RT and returned to frozen storage when the desired temperature was reached. Glycerolized RBCs were exposed to various single TWEs and tested weekly and samples with and without an IRI were exposed to 10 cycles to either −20°C or 20°C.

Results: When the cryopreserved RCC was exposed to RT the average time for the core temperature to rise from −75°C to −60°C was 4 min, to −40°C was 12 min, and to −20°C was 31 min. After the RCC was returned to frozen storage it took 22, 41, and 61 min respectively to return to −65°C. Exposure of 2 ml volumes to a single TWE (−60°C, −40°C, −20°C, 5°C) demonstrated an increase in post-thaw hemolysis (2.4 ± 0.1%, 3.0 ± 0.3%, 4.2 ± 1.5%, 4.5 ± 0.3%) when compared to a non-TWE control (2.0 ± 0.4%) after 28 days of frozen storage. When samples were exposed to 10 cycles of TWEs to −20°C or 20°C an increase in hemolysis was seen. Glycerol samples after 3, 6 and 10 cycles to −20°C had hemolysis of 9.8 ± 1.7%, 12.4 ± 0.2%, and 19.5 ± 2.2% and samples with an IRI had hemolysis of 3.8 ± 0.0%, 5.8 ± 0.4%, and 8.6 ± 1.0% (P = 0.04, 0.06, 0.02). Glycerol samples after 3, 6 and 10 cycles to 20°C had hemolysis of 7.9 ± 2.3%, 14.7 ± 0.3%, and 17.8 ± 0.9% and samples with an IRI had hemolysis of 4.4 ± 0.7%, 7.9 ± 0.4%, and 11.7 ± 1.0% (P = 0.18, 0.00, 0.03).

Summary/Conclusions: Single TWEs do not significantly impact post-thaw hemolysis with 40% glycerol. Multiple TWE cycles increase hemolysis suggesting reduction of post-thaw RCC quality after extensive storage where TWEs occur. However, the addition of an IRI appears to reduce the effect of TWEs on RBC integrity.

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QUALITY PARAMETERS OF FROZEN RED CELLS THAWED AFTER 10 YEARS

M Bohonek[1], E Sladkova[1], E Staskova[1], L Landova[1], M Blahutova[1], T Hradek[2] and J Lovecky[3]

[1]Hematology and Blood Transfusion, Military University Hospital Prague [2]Synlab CZ [3]Hospital Pod Petrinem, Prague, Czech Republic

Background: The shelf life of frozen RBCs is 10–30 year in frozen state and storage times vary from country to country without clear evidence. Cryopreservation is a costly process and the long shelf life of frozen RBC, especially rare units, is the most desirable.

Aims: We present study in vitro laboratory parameters of freezing red cells thawed after 10 years and reconstituted in two additive solution – SAG-M and Nutricel with aim to verify their quality.

Methods: Leucodepleted RBCs from double apheresis or whole blood were frozen in 40% glycerol a stored more than 10 years (121 – 132 month) at −80°C. Thawed RBCs were deglycerolisated, using device Haemonetics ACP-215 and reconstituted in additive solution: 20 units in SAG-M, 20 units in AS-3 (Nutricel). Thawed units were tested in days 0, 7, 14 and 21 for hemoglobin loss, hematocrit, leucocytes, haemolysis, osmolality, pH, K, P, NH$_3$, ATP and 2,3 DPG.

Results: Thawed RBCs, reconstituted in both solutions (SAG-M and Nutricel) had the comparable values in the timeline in total HGB, HCT, K, ATP and 2,3 DPG. RBCs in SAG-M had higher osmolality in all days and displayed significantly higher hemolysis, which was in limit <0.8% only in day 7 with corresponding increase in free HGB. On the other hand, in RBCs in Nutricel hemolysis were in all day <0.8%.

Summary/Conclusions: Thawed RBC reconstituted in both solutions have the best vitality and energy potential in the first days after reconstitution, but RBC reconstituted in AS-3 show improved quality and vitality during storage, than RBC in SAG-M. It can generally be stated, that the collected data correspond with previously published data on the quality of frozen RBC and storage and storage for more than 10 years has no effect on their quality.

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Abstract has been withdrawn

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BAND 3 PHOSPHORYLATION INDUCES IRREVERSIBLE ALTERATIONS OF STORED RED BLOOD CELLS

C Le Van Kim[1], S Azouzi[2], M Romana[3,4], N Arashiki[5], Y Takakuwa[6], W El Nemer[2], T Peyrard[7], Y Colin[2] and P Amirault[8]

[1]UMR_S1134/University Paris Diderot/Institut national de la Transfusion Sanguine [2]UMR_S1134/University Paris Diderot/Institut national de la Transfusion Sanguine, Paris, France [3]University Antilles [4]UMR_S1134, Pointe à Pitre, Guadeloupe [5]School of Medicine, Tokyo Women's Medical University [6]Tokyo Women's Medical University, Tokyo, Japan [7]Institut natinal de la transfusion Sanguine/UMR_S1134/University Paris Diderot [8]Institut naitonal de la Transfusion Sanguine/UMR_S1134/University Paris Diderot, Paris, France

Background: Hypothermic storage of therapeutic red blood cells (RBCs) concentrates is accompanied by cellular changes referred to as the storage lesions. These storage lesions are likely to affect RBC post-transfusion survival/efficacy and increase risks of adverse reactions in the recipients, especially in an inflammatory context. The underlying mechanisms leading to RBC membrane changes during storage are poorly known, but putative actors are lipid peroxidation, phospholipid asymmetry, accumulation of oxidative damage, and Band 3 oligomeric state. Cellular senescence or oxidative damages induce a cascade of biochemical events leading to detachment of Band 3 from the cytoskeleton and clustering. Band 3 also plays a key role in the clearance of altered and old RBCs by forming senescence antigens capable of binding to naturally-occurring autoantibodies (Nabs). Besides, Band 3 is a prominent substrate for tyrosine kinases and Band 3 phosphorylation was largely documented in severe hematologic disorders.

Aims: We aim to elucidate the mechanisms leading to irreversible erythrocyte alterations during storage and to identify a relevant marker for transfusion yield. Elucidation of the molecular mechanism leading to Band 3 modifications during storage should ultimately lead to new approaches towards improving RBC storage and/or survival, and efficacy and safety of transfusion. For this purpose, leuko-depleted RBC units were prepared from 6 whole blood donations drawn from healthy volunteer donors and stored for up to 42 days under standard conditions in SAGM solution at 4°C.

Methods: RBCs samples were taken at day 3, 14, 21, 28, 35 and 42 of storage and used for all biochemical, molecular and cellular analyses. Eosin-5-maleimide (EMA) were used for RBCs labelling and flow cytometry analysis. RBC membranes were prepared and western blots were performed using an anti-phosphotyrosine antibody, a mouse monoclonal anti-Band 3 and the specific anti-clustered Band 3 antibody previously described (Arashiki, et al 2013). Microparticles were prepared from RBC supernatants and analyzed by flow cytometry using PE-labeled Band 3 antibody. Band 3 activity was measured by HCO3$^-$/Cl$^-$ exchange in RBC ghosts using a stopped-flow spectrophotometer

Results: Using EMA test we observed a progressive decrease of EMA labeling during storage and a change in Band 3 oligomeric state

Using specific antiphosphoTyr antibody, we showed that this oligomeric state is correlated with higher tyrosine phosphorylation of Band 3

Using a unique antibody that specifically recognizes the Band 3 clustered form (Arashiki, et al 2013), we showed that the increased Band 3 phosphorylation is associated with its clustering

Using flow cytometry, we found an important increase in the level of erythroid Band3-positive microparticles during storage.

Using stopped-flow, we observed a partial loss of Band 3 exchange function during storage

Summary/Conclusions: In conclusion, we postulate that blood bag storage induces profound molecular changes in Band 3 leading to the formation of clusters that very probably generate the presentation of neoantigens. Transfused red blood cells could then be subjected to the binding of autologous Nabs directed to those neoantigens and may lead to their quick and important sequestration from the blood stream. Furthermore, we demonstrated that the antibody specific of the clustered form of Band 3 represents a simple and relevant new tool for the monitoring of the RBC storage lesion.

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TRANSFUSION OF FRESH AND DATE OF EXPIRY RED BLOOD CELLS IN A SHEEP MODEL – AGE DOES NOT MATTER

G Simonova[1,2,3], S Diab[2], K Dunster[2], M Passmore[2,3], J Fraser[2,3] and J Tung[1,2,3]

[1]Research and Development, Australian Red Cross Blood Service [2]Critical Care Research Group, The Prince Charles Hospital [3]School of Clinical Medicine, The University of Queensland, Brisbane, Australia

Background: The possible association between duration of red blood cells (RBC) storage and poor clinical outcomes has been intensively researched, recent randomised clinical trials (RCTs) appear to have resolved the uncertainty, suggesting no significant differences between freshest available and standard practice issued (oldest in inventory) RBCs. However, ethical considerations precluded these RCTs from investigating RBCs at the end of their shelf-life. Animal models can play a crucial role in complementing RCTs by addressing this limitation. Sheep transfusion models provide an excellent screening tool to elucidate the underlying mechanisms of stored blood transfusion-related complications.

Aims: To investigate cytokine/chemokine release after transfusion with either fresh or date of expiry RBCs using a sheep model.

Methods: Anesthetized and mechanically ventilated sheep (n = 13) received lipopolysaccharide (LPS; to mimic a bacterial infection) followed by transfusion of pooled heat-treated supernatant (SN) from leucodepleted human RBC units stored for either 2-days (n = 6) or 42-days (n = 7). Blood was collected pre- and post-LPS infusion, post-transfusion and pre-mortem and plasma aliquots were stored at −80°C. Sheep specific in-house ELISAs were used to quantify the concentrations of IL-6, IL-1β and IL-8 in plasma. Lung tissues were collected post-mortem and stored in RNAlater. Total RNA was isolated using the RNeasy Mini Kit and real time Quantitative PCR was performed using a Taqman Viia7 Real Time PCR system with SYBR Green PCR Master Mix for primers IL-6, IL-1β and IL-8. Reactions were performed in triplicate and data was normalized to a geomean of PGK1 and ACTB housekeeping genes. Data were analysed by repeated measures one-way ANOVA with Bonferroni multiple comparison to assess the effects of transfusion. Unpaired t test was applied to detect differences between groups (P < 0.05).

Results: In the group of sheep exposed to LPS and day 2 RBC transfusion, plasma levels of IL-1β (P = 0.0408) and IL-6 (P < 0.0001) increased throughout the experiment. Post-tests showed that compared to baseline plasma IL-1β increased at pre-mortem (P < 0.05) and IL-6 increased at post-transfusion (P < 0.01) and pre-mortem (P < 0.0001). These post-tests also showed that plasma IL-6 increased throughout the experiment. In the group of sheep exposed to LPS and day 42 RBC transfusion, plasma levels of IL-6 (P = <0.0001) and IL-8 (P = 0.0186) increased throughout the experiment. Post-tests indicated that plasma IL-6 was increased at post-transfusion (P < 0.05) and pre-mortem (P < 0.001) and plasma IL-8 was increased at post-LPS (P < 0.05) and post-transfusion (P < 0.05) compared to baseline levels. However, no differences in cytokine levels between transfusion of day 2 and day 42 RBC SNs were observed. Increased lung IL-1β gene expression was observed post-mortem in sheep transfused with RBC SN stored for 2 days compared to 42 days (P = 0.048), but no differences in IL-6 or IL-8 expression were observed.

Summary/Conclusions: In this model transfusion of RBC SN into LPS-treated sheep was associated with increased plasma cytokine levels; however, increased RBC storage duration was not associated with a further increase in these levels. These results complement findings of recent RCTs and do not provide evidence that transfusion of date of expiry RBC is harmful.

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THE EFFECT OF N-ACETYL CYSTEINE (NAC) ON RBC METABOLISM AND RBC OXIDATIVE STATUS DURING RBC STORAGE IN BLOOD BANK

MR Deyhim[1] and N Mehrdadi[2]

[1]Clinical Chemistry, High Institute for Research and Education in Transfusion Medicine [2]Biology, Science Branch, Azad University, Tehran, Iran

Background: Oxidative stress is one of the main causes of Red Blood Cell (RBC) storage lesion during RBC storage in blood bank condition. In this study, we evaluate the effect of N-acetylcysteine (NAC) as an additive solution on RBC oxidative stress during RBC storage.

Aims: To evaluate the oxidative stress markers in RBC during storage of packed RBC.

Methods: In this experimental study, 10 bag of packed RBC were randomly assigned to the Iranian Blood Transfusion Organization's (IBTO) Innovation Center. We evaluate the effect of NAC (1.5 mmol) on RBC's metabolic parameters including; glucose and lactate concentration, lactate dehydrogenase enzyme activity, pH and oxidative stress biomarkers such as malondialdehyde (MDA) concentration and total antioxidant capacity (TAC). Also, hematological parameters including; RBC count, Hb, HCT, MCV, MCH and MCHC concentration and percentage of hemolysis were measured during RBC storage up to 42 days of storage. The results were compared between two groups of NAC treated RBC and untreated RBC as a control group. All of the data were analyzed with SPSS statistical program version 18.

Results: In this study, the concentration of lactate and LDH enzyme activity in the NAC treated RBC were significantly lower than the control group (without NAC).Also MDA concentration was decreased in the NAC treated RBC compared to the control group. Total antioxidant capacity was so significantly higher in the NAC – RBC than in the control group, especially in the 28th day of storage (P_{day28} <0.05).

Summary/Conclusions: The results of this study indicated that the use of NAC as an additive solution could decrease oxidative damage via maintaining of the RBC antioxidant capacity during RBC storage. In the future NAC may be use as an additive for maintaining of the RBC survival and RBC quality during storage in blood bank condition.

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VALIDATION OF GLYCEROLIZATION AND DEGLYCEROLIZATION OF RED CELLS IN A CLOSED SYSTEM USING HEMONETICS ACP215

CG Kohombange[1], C Wijesinghe[2] and K Kuruppu[1]

[1]Quality Management [2]National Blood Center, Colombo, Sri Lanka

Background: In 1950, it was first demonstrated that human red blood cells (RBC) could be cryo-preserved, thawed and washed free of glycerol and transfused with normal in vivo survival of 85–90% of recovered cells. Cryoprotecting agent is essential to prevent the dehydration and mechanical trauma to RBC during freezing. Glycerol is a penetrating group of cryoprotecting agent, which is used in the National Blood Center. The high concentration of glycerol in RBC prevents formation of ice crystals and consequent membrane damages. In cryopreservation of RBC, NBRL (Naval Blood Research Laboratory, Boston University School of Medicine) method which is based on HGC using HemoneticACP 215 is adopted by the National Blood Center and the Standard Operating Procedures for this system is adopted for the validation.

Aims:
1. Validate the procedure of glycerolization and deglycerolization of red cells.
2. To assess the quality of deglycerolized RCC units which are glycerolized within 7 days of collection.
3. To assess the quality of deglycerolized RCC units which are glycerolized after 20 days of collection.

Methods: Prospective validation was conducted following system specific standard operating procedure for High Glycerol Concentration glycerolization method and 40% W/V glycerol was used for cryopreservation. SAGM was used as the preservative solution. 20 RCC units within 7 days of collection date and 20 RCC units after 20 days from the date of collection were selected for validation. Both series were tested for the recommended QC parameters. Products were assessed in relation to the required specifications as per the EDQM guideline and AABB standards. Results of the comparative study analyzed using independent sample t-test. Correlation assessed by Pearson Correlation Regression.

Results: There is no significant difference (P > 0.05) between the two series in relation to total Hb content of starting RBC units. The Hb level before freezing is statistically significantly low in the older RCC units (P < 0.05).Volume of the end product is significantly high (P < 0.05) in the older RCC units. Similarly the Hb (g/dl) of the end product is significantly low in older units (P < 0.05). Further, the Hct% of the end products prepared from older RCC units are significantly low (P < 0.05), in comparative to the freshly frozen RCC. There is no significant difference between the freeze-thaw-wash recovery percentages of the two series. pH of the end products are significantly low in older RCC units (P < 0.05), in comparison to the freshly frozen RCC units. There are no significant differences between the two series in relation to osmolality and K+ levels on day 0. There is a moderate positive correlation between decreasing of pH and rising of supernatant Hb level (r = +0.5). In freshly frozen RCC, both reduction of pH and rising of supernatant Hb are evident in average of 12 days. In older RCC units, both reduction of pH and rising of supernatant Hb are evident in average of 4 days and 6 days respectively.

Summary/Conclusions: QC parameters of both series are acceptable on the date of deglycerolization. However the post deglycerolization shelf life of RCC frozen nearing to expiry date is significantly shorter and the clinical outcome has to be assessed to determine the efficacy of the product. RCC units frozen after 20 days of collection, also show a rapid lowering of pH levels in comparison to the freshly frozen

units. This may indirectly reflect the reduction of ATP and 2,3-DPG levels and the reduction of oxygen carrying capacity of red cells.

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EVALUATION OF OPTIMUM CONCENTRATION OF N-ACETYL CYSTEINE (NAC) ON RBC METABOLISM DURING RBC STORAGE IN BLOOD BANK CONDITION

MR Deyhim[1] and N Mehrdadi[2]

[1]Clinical Chemistry, High Institute for Research and Education in Transfusion Medicine [2]Biology, Science Branch, Azad University, Tehran, Iran

Background: Red blood cell (RBC) metabolism impairment is one of the main causes of RBC storage lesion during RBC storage in blood bank condition. In this study, we evaluate the effect of different concentrations of N-acetyl cysteine (NAC) on RBC metabolism and quality during RBC storage.

Aims: To optimize concentration of NAC for better maintaining packed RBC metabolism during storage.

Methods: In this experimental study, 5 bag of packed RBC were randomly assigned to the Iranian Blood Transfusion Organization's (IBTO) Innovation Center. Each blood bag split into 4 equal blood bags. Three of them for injection of different concentration of NAC (0.5, 1 and 1.5 mmol) and one of them have kept as a control bag (untreated NAC). The effect of different concentrations of NAC on metabolism parameters; including glucose and lactate concentration, lactate dehydrogenase enzyme activity and pH were investigated. Also, hematological parameters including; RBC count, Hb, HCT, MCV, MCH, MCHC concentration were measured during RBC storage up to 42 day. The results of this study were compared between 3 groups of NAC treated RBC and untreated RBC. All of the data were analyzed with SPSS statistical program version 18.

Results: In this study, the concentration 1.5 mmol of NAC compared to 0.5 and 1 was more effective to maintain concentration of lactate and Glucose (P < 0.05). Also this concentration was more effective than other concentration of NAC on RBC count, Hb, HCT and MCH concentration in treated-RBC compare with untreated RBC during storage.

Summary/Conclusions: The results of this study indicated that the use of concentration of 1.5 mmol of NAC as an additive solution could better maintain RBC metabolism and RBC quality during storage. In the future NAC in concentration of 1.5 mmol may be used as an additive for maintaining of the RBC survival and RBC quality during storage in blood bank condition.

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OXYGEN IN RED BLOOD CELL CONCENTRATES: INFLUENCE OF DONOR'S CHARACTERISTICS, LOCATION AND BLOOD PROCESSING

M Prudent[1,2], A Martin[2], M Abonnenc[2], N Dögnitz[3], A Dunham[4] and T Yoshida[4]

[1]Faculté de Biologie et de Médecine, Université de Lausanne, Lausanne [2]R&D Products, Transfusion Interrégionale CRS, Epalinges [3]Approvisionnement Produits Sanguins, Transfusion Interrégionale CRS, Bern, Switzerland [4]Hemanext, Lexington, United States of America

Background: Donors' variability influences the storage of red blood cells (RBCs). One of the variables is the oxygen saturation (SO_2) that was recently and unexpectedly reported to vary widely from <5 to >95%. The reasons of such distribution are not totally explained whereas the role of oxygen and oxidative lesions during the storage of RBC concentrates (RCCs) are known.

Aims: The objectives are to characterize the SO_2 distribution in RCCs produced in a regional blood center in Switzerland and to investigate the origin of the wide distribution.

Methods: On November 2017, the level of $\%SO_2$ was measured in 1701 leukoreduced RCCs derived from whole blood donations in both top-bottom (TB, CQ32250, Fresenius-Kabi, Germany, component filtered, n = 1366) and top-top (TT, FQE 6240LU, Macopharma, France, whole blood filtration, n = 335) kits. In addition, 112 TB bags were analyzed before and after processing. SO_2 was measured noninvasively through the PVC bag prior to storage by resonance Raman spectroscopy (Pendar Microvascular Oximeter A3U11, Pendar Technologies, Cambridge, USA). Gender, age, blood type, hemoglobin level and location of donors, and process method and time-to-process were recorded.

Results: Overall, the $\%SO_2$ exhibited a wide non-Gaussian distribution with a mean of 51.3%+/- 18.6, median 50.0%, IQR 35 – 67. TT processing showed a higher $\%SO_2$ than TB processing with a mean of 58.9%+/-18.3 vs 49.4%+/-18.1, a median of 55.0% vs 48.0% and an IQR 32.0 vs 31.0, respectively (P < 0.0001). Time-to-process did not

show any significant difference however the processing itself (n = 112) reduced the $\%SO_2$ from 57.3%+/-18.7 to 50.6%+/-18.1 (P < 0.0001). SO_2 was also affected by the donors' characteristics. RCCs from male (n = 1008) exhibited higher $\%SO_2$ than from female (n = 693) of 57.0%+/-17.7 vs 42.8%+/-16.3 (P < 0.0001) whereas no correlations were observed in function of age or hemoglobin level. Finally, the donors' location clearly influences the SO_2. Despite the absence of correlation in female, there was a positive correlation between the $\%SO_2$ and the minimal location elevation [m] (Elevation_min = $0.8409*\%SO_2 + 436.5$, $r^2 = 0.015$, P < 0.0001) in male donors. In addition, the comparison of grouped municipalities (equivalent gender, age, hemoglobin level and processing distributions) in country side of a mean elevation of 1180 m and cities of 470 m exhibited 57.5%+/-16.9 vs 43.2%+/-15.2, respectively. These data indicate that the living altitude might influence the $\%SO_2$ in RCCs but other factors such as the pollution or life style cannot be excluded here.

Summary/Conclusions: These data confirm wide $\%SO_2$ distribution in RCCs reported recently. Independently of the level of hemoglobin, the $\%SO_2$ was influenced by the processing and particularly by the donors' characteristics such as the gender and the location. At this stage it is not possible to clearly identify the origin of these differences and confounding variables should be considered. Nevertheless, it provides new hints on the influence of donors. Since the RBCs lesions are known to increase during storage and are related to O_2 content in RCCs, it is important to characterize the donors' population in order to better process and to better store RBCs for transfusion.

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DO TRIGLYCERIDE LEVELS MEDIATE THE ASSOCIATION OF LIFESTYLE BEHAVIOURS OF DONORS AND HAEMOLYSIS?

R de Groot[1], J Lakerveld[2], J Brug[3], J Lagerberg[4], D de Korte[4], T Hoekstra[5], W de Kort[1] and K van den Hurk[1]

[1]Donor Studies, Sanquin Blood Supply Foundation [2]Epidemiology and Biostatistics, Amsterdam Public Health, VU University Medical Center [3]Amsterdam School of Communication Research, University of Amsterdam [4]Product and Process Development, Sanquin Blood Supply Foundation [5]Health Sciences, Vrije Universiteit Amsterdam, Amsterdam, Netherlands

Background: Lifestyle behaviors such as physical activity, sedentary behavior and dietary habits have been shown to influence blood lipid levels, and both lifestyle and blood lipids may be associated with hemolysis during storage of blood products.

Aims: To investigate whether a relatively unhealthy lifestyle, i.e. low levels of moderate to vigorous physical activity, high levels of sedentary behaviour, and high intake of unhealthy foods, are associated with higher levels of haemolysis during storage of miniature red cell concentrates from Dutch blood donors. Furthermore, we explored whether the associations between lifestyle behaviours and haemolysis in red cell concentrates were mediated by triglyceride levels.

Methods: A cross-sectional analysis was performed on data of 2552 Dutch blood donors participating in Donor InSight (DIS)-III. The average number of minutes spent per day on moderate to vigorous physical activity and sedentary behaviour were measured using the IPAQ questionnaire. In a subset of 760 donors this was also objectively measured using a GT3X Actigraph accelerometer for seven consecutive days during waking hours. Intake frequency and amount of fish, nuts, eggs and meat was assessed using a food frequency questionnaire. Blood samples were taken from the diversion pouch, processed to and stored as mini red cell concentrates in SAGM at 2–6°C for 28 days. Total haemoglobin was measured by haematology analyser and free haemoglobin was determined by a spectrophotometer. To increase readability, regression coefficients with haemolysis were expressed as a hundredths of a percent of free haemoglobin of the total haemoglobin present in the red blood cells after correction for haematocrit (i.e. a hundredths percentage of red blood cells in blood). Mediation analyses were performed to study triglyceride level as a potential mediator in the association of lifestyle behaviours and haemolysis level. Sensitivity analyses were conducted on the subset of 760 donors with objectively measured physical activity and sedentary behaviour.

Results: The median and interquartile range (IQR) of haemolysis in red cell concentrates was 1.42 (1.00–1.66). Median (IQR) mmol/l triglycerides was 1.29 (0.93–1.81). The median (IQR) number of minutes per day were 51 (21–112), 480 (300–660) for moderate to vigorous physical activity and sedentary behaviour, respectively. Sedentary behaviour was significantly associated with haemolysis levels in red cell concentrates ($\beta = -0.04$, 95%CI = −0.08; −0.01) which remained after adding triglycerides to the model, however no significant association was found for sedentary behaviour and triglycerides. Thus, no evidence for mediation was found. Regardless of the lifestyle behaviour under study, triglyceride levels were significantly associated with haemolysis in red cell concentrates (sedentary behaviour model $\beta = 14.50$, 95%CI = 10.63; 18.36). These latter findings were confirmed by

sensitivity analysis (β = 17.82, 95%CI = 12.50; 23.14). The sensitivity analyses did not show a significant association of sedentary behaviour and haemolysis.

Summary/Conclusions: In this large cohort of blood donors, lipid levels were strongly and consistently associated with haemolysis in red cell concentrates. Sedentary behaviour was associated with haemolysis in red cell concentrates but no evidence was found that triglycerides mediated this association.

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PROTHROMBIN KNOCKDOWN ABROGATES ANTI–HEMORRHAGIC PROPERTIES OF TRANSFUSABLE PLASMA IN A MOUSE MODEL OF COAGULOPATHY

L Eltringham-Smith[1], R Yu[2], S Qadri[1,3], V Bhakta[1], Y Wang[2], E Pryzdial[4,5], J Crosby[6], H Ni[2,7] and WP Sheffield[1,8]

[1]Centre for Innovation, Canadian Blood Services, Hamilton [2]Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Toronto [3]Pathology and Molecular Medicine, McMaster University, Hamilton [4]Centre for Innovation, Canadian Blood Services [5]Centre for Blood Research, University of British Columbia, Vancouver, Canada [6]Drug Discovery and Corporate Development, Ionis Pharmaceuticals, Carlsbad, United States of America [7]Centre for Innovation, Canadian Blood Services, Toronto [8]Pathology and Molecular Medicine, McMaster University, Hamilton, Canada

Background: The typical goal of plasma transfusion is to treat coagulopathy and restore hemostasis in bleeding patients. Some national regulators use FVIII activity to monitor transfusable plasma quality but the linkage between this marker and hemostatic control is unclear. Previously, we established a normovolemic coagulopathic mouse model (BECA) and demonstrated that plasma from mice deficient in FVIII, but not fibrinogen, reduced blood loses in transfused BECA mice subjected to standardized injuries (Eltringham-Smith, Transfusion, 2015). Assessing the ability of plasma from other knockout mice to restore hemostasis is limited by embryonic lethality of several coagulation protein genes in mice, including prothrombin (FII).

Aims: To obtain murine plasma with minimally expressed FII, and assess its ability to restore hemostasis and limit hemorrhage in BECA mice after induced injury.

Methods: Donor CD1 mice were injected subcutaneously with 10 mg/kg control antisense oligonucleotides (ASO) or ASO directed against FII mRNA, twice weekly for four weeks to produce ASO-control (CON) or ASO-FII plasma pools. Recipient BECA CD1 mice were subjected to sequential blood exchange to reduce all plasma protein levels 5-fold while maintaining normal blood volume, and received 12 ml/kg body weight ASO-CON or ASO-FII plasma prior to injury. Shed blood was measured directly following tail transection (TT) and liver laceration (LL), while platelet deposition over time was measured using intravital microscopy after intravascular laser injury (ILI).

Results: ASO-FII plasma contained 19.5 – 20.7% of the prothrombin concentration of ASO-CON plasma by FII immunoassay. In the TT model, ASO-CON-transfused mice lost 3.3-fold less blood than ASO-FII-transfused mice (62 ± 40 μl versus 210 ± 110 μl, n = 15, P < 0.0001) (all data herein are given as mean $\pm$ SEM). In the LL model, ASO-CON-transfused mice lost 1.7-fold less blood than ASO-FII-transfused mice (370 ± 40 μl versus 610 ± 60 μl, n = 7, P = 0.0034). In the ILI model, the product of the platelet mean fluorescence intensity (MFI) $\times$ time, measured as the area under the curve, was 6.3-fold greater for ASO-CON-transfused mice than for ASO-FII-transfused mice ($19 \pm 5 \times 10^6$ versus $3 \pm 2 \times 10^6$ MFI-sec, respectively, n = 6, P < 0.05).

Summary/Conclusions: ASO-FII plasma, containing <21% normal FII concentration, was less effective than ASO-CON plasma in treating induced murine coagulopathy, as evidenced by significantly greater blood losses following either tail or liver injuries. In addition, ASO-FII-transfused mice were significantly less able to form a durable arteriolar hemostatic plug in response to laser injury than their ASO-CON-treated counterparts. These findings suggest that FII is a critical component of transfusable plasma, and must be a constituent of minimal component plasma alternatives. Assuming analogous mechanisms in humans, our results suggest that FII would be an improved quality marker for transfusable plasma compared to FVIII.

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USE OF SOLVENT–DETERGENT PLASMA AT CANADIAN BLOOD SERVICES

HM Aljedani[1], T Butler-Foster[2,3], N Rickards[1], B Eurich[4], S Alkhan[5], D Young[6], T Petraszko[5], R Skeate[7] and E Kahwash[1]

[1]Canadian Blood Services, Halifax, Nova Scotia [2]Canadian Blood Services [3]Western University, London, Ontario [4]Canadian Blood Services, Regina, Saskatchewan [5]Centre for Blood Research, University of British Columbia, Vancouver, Canada [6]Canadian Blood Services, Calgary, Alberta [7]Canadian Blood Services, Toronto, Ontario, Canada

Background: The Canadian National Advisory Committee (NAC) on Blood and Blood Products recommends Solvent Detergent Plasma (SDP) be used for the following defined indications: patients with Thrombotic Thrombocytopenic Purpura (TTP), Hemolytic Uremic Syndrome (HUS) with factor H deficiency, or clotting factor deficiency for which there is no specific licensed concentrate. Also, patients should have a history of allergic transfusion reaction, pre-existing lung disorder, or that blood group compatible frozen plasma is not readily available.

Aims: The aim of this study is to retrospectively examine indications of SDP requests submitted to Canadian Blood Services (CBS) and any associated transfusion reactions.

Methods: All electronically available data on SDP requests was collected and analyzed for the period of January 1st, 2015 to July 31st, 2017. Data for transfusion reactions associated with SDP was collected from the hemovigilance website for the same study period.

Results: There were 326 SDP requests from 34 hospitals, with a total of 65,570 SDP units issued. Of all SDP requests, 297 (91.1%) were approved by CBS physicians, 27 (8.3%) were missing data on approval status, and 2 (0.6%) were rejected. Among the 297 approved requests, 59.6% met the NAC criteria, 38.4% had missing data and 2% did not meet the NAC criteria. Among NAC-indicated requests (117), 75.1% were for TTP, 20.9% for HUS, and 4% for factor deficiency. 85.9% had allergic transfusion reactions, 5.6% pre-existing lung disorders, 1.7% no available ABO compatible plasma and 6.8% had combinations of the secondary qualifiers. Of all issued SDP units, 94.5% were for approved requests, 4.5% for requests missing data and 0.05% for rejected requests. For SDP units issued for approved requests, 54.7% were for NAC-indicated requests, 44.7% for requests missing data and 0.6% for requests not meeting NAC criteria. The incidence of the transfusion reactions was estimated to be 0.016% per transfused SDP unit compared to published incidence of 0.05–0.27% per transfused frozen plasma (FP) unit. Out of 9 reported transfusion reactions from SDP, 3 (0.004%) were severe allergic reactions compared to the reported incidence of 0.045–0.17% per unit of FP. Five thrombotic events (0.007%) were documented, all in TTP patients. Thrombotic events were reported to be up to 6.45% in TTP cases from FP. There were no reported transfusion-related acute lung injury (TRALI) reactions with SDP transfusions in our study. Data from the American Red Cross and the Serious Hazard of Transfusion report demonstrated a TRALI incidence of 1:250,000 to 317,000 after implementation of a male-only plasma strategy. The estimated cost of all issued SDP units was $11,462,011, $874 per liter (average $174 per unit). The estimated cost for FP transfused in the same study period was $441 per liter (average $153 per unit).

Summary/Conclusions: The majority of requests for SDP were approved, and the majority of SDP units issued were for approved requests. A small number of approved were classified as not meeting NAC criteria, but data were missing for approximately one third of the requests. Most of SDP associated reactions were allergic or possible thrombotic events but no reported cases of TRALI.

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TRENDS IN IVIG USE AT A TERTIARY CARE CANADIAN CENTRE AND IMPACT OF PROVINCIAL USE MITIGATION STRATEGIES: 10–YEAR RETROSPECTIVE STUDY WITH INTERRUPTED TIME SERIES ANALYSIS

M Murphy[1], A Tinmouth[1], M Goldman[2], M Chassé[3], E Saidenberg[1], J Colas[1], N Shehata[4], D Fergusson[1], A Forster[1] and K Wilson[1]

[1]Ottawa Hospital Research Institute [2]Canadian Blood Services, Ottawa [3]Centre Hospitalier de l'Université de Montréal, Montreal [4]University of Toronto, Toronto, Canada

Background: Intravenous Immune globulin (IVIG) is a fractionated plasma product used to treat a range of autoimmune or inflammatory conditions, as well as immunodeficiency. Demand for this high-cost product are increasing despite limited evidence for efficacy. Characterizing the use of IVIG over time and the impact of

provincial strategies to mitigate its use would provide information to guide future policies.

Aims: To describe trends in IVIG use at a tertiary care centre and determine the impact of the implementation of policies to optimize its use.

Methods: This was a 10-year retrospective cohort study of a large tertiary care hospital in Ontario, Canada. The Ottawa Hospital Data Warehouse was queried for all inpatient and outpatient encounters involving an IVIG transfusion between January 2006 and December 2016. IVIG use over the study period was reported, including number of hospital encounters, amounts of IVIG prescribed, and clinicians responsible for IVIG ordering. An interrupted time series analysis was performed to evaluate the impact of provincial initiatives to optimize IVIG use: (1) the Ontario IVIG Utilization Management Guidelines, released in November 2009 (2) the IVIG toolkit released September 2010 that included a Standard IVIG Request Form; IVIG Dose Calculator; Standard Infusion Guidelines; and Adverse Events Chart.

Results: 2,785 patients of The Ottawa Hospital received 1,732,290 g of IVIG from 2006–2016. There were 32,170 patient encounters, 92% of which occurred in outpatient clinics. Attending physicians in the divisions of Hematology and Neurology were responsible for 60% of all IVIG hospital encounters. Although IVIG use increased 820 g/quarter (P < 0.0001) from 2013–2016, total volume used was 21% lower than what would have been expected had the provincial policies not been implemented. IVIG use decreased after implementation of new policies, −2,032 g/quarter (P = 0.0004) from 2011–2012, although increased +820 g/quarter (P < 0.0001) from 2013–2016. Changes in utilization varied considerably by specialty. In hematology, the total use of IVIG decreased (−1608 g/quarter, P = 0.0004) during the intervention period and then remained stable. In neurology, there was no change in total utilization during the intervention period, although the use of IVIG increased (+110 g/quarter, P = 0.0032) from 2013–2016. Similar post-intervention increases were also seen in rheumatology (+260 g/quarter, P = 0.0003).

Summary/Conclusions: Provincial initiatives had significant short-term impacts on IVIG administration. Continued increases in IVIG use may reflect changing demographics and lack of access to alternative therapies for neurologic and rheumatologic conditions. Future work should assess temporal changes in subcutaneous Ig use and the diagnoses underlying Ig administration.

Plasma Products

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INHIBITION OF PHAGOCYTOSIS BY IVIG IS INDEPENDENT OF IGG SIALYLATION IN HUMAN THP-1 MONOCYTE–DERIVED MACROPHAGES

M Hou, S Ye, F Liu, D Li, P Jiang, L Ma and C Li

Research Center of Blood Biochemistry and Molecular Biology, Institute of Blood Transfusion, Chinese Academy of Medical Sciences & Peking Union Medical College, Chengdu, China

Background: Intravenous immunoglobulin (IVIG) preparations, the main component of which is polyclonal immunoglobulin G (IgG), are plasma protein products prepared from ~3000–60000 healthy human blood donors. Several autoimmune diseases, such as warm autoimmune hemolytic anemia (wAIHA) and immune thrombocytopenia (ITP), are mediated by erythrocytes and thrombocytes opsonized with IgG autoantibody, respectively. The IgG-opsonized blood cells are mainly recognized and bound by Fcγ receptors (FcγRs) on innate immune cells, and are further phagocytosed by macrophages in the spleen and liver. Researches have shown that high doses of 1–2 g/kg of IVIG infusion directly blocks activating FcγRs, and upregulates the expression of the inhibitory receptor FcγRIIB, which leads to reduced erythrocytes and thrombocytes phagocytosis to achieve an efficient therapeutic effect. Interestingly, recent evidences suggest that sialylation of IgG plays an important role in the immunomodulatory of IVIG. Furthermore, sialic acid-rich IVIG shows a stronger immunosuppression activity for ameliorating autoantibody-induced inflammation, is currently debated.

Aims: To investigate whether the inhibitory effect of macrophages phagocytosis by IVIG is related to the sialylation of IVIG in a fully human in vitro system.

Methods: Firstly, IVIG preparations were loaded on a lectin affinity chromatographic column with sialic acid-specific Sambucus nigra agglutinin (SNA) and then three fractions were obtained: flow through fraction (FT), elution fraction 1 (E1) and elution fraction 2 (E2). Of note, E1 and E2 were both highly sialylated IVIG fractions, while the level of sialylation of FT was less than that of untreated IVIG. In addition, IVIG treated with neuraminidase was sialic acid-free IVIG (NAase IVIG) that used as a non-sialylated control preparation. Secondly, a co-culture system of macrophages that

derived from human monocytic cell line THP-1 induced by phorbol 12-myristate 13-acetate (PMA) and human erythrocytes opsonized with anti-RhD antibody serum was established in vitro. Finally, five IVIG fractions with different levels of sialylation (including untreated IVIG, FT, E1, E2 and NAase IVIG) were separately added to macrophages, which subsequently incubated with IgG-opsonized erythrocytes. The rate of IgG-mediated phagocytosis was measured using flow cytometry assay.

Results: IVIG preparations could be able to effectively inhibit the phagocytosis of macrophages. With the increased of IVIG concentration, the stronger inhibition of macrophage phagocytosis and the lower IgG-mediated phagocytosis rate. However, when five different sialylated IVIG fractions in same concentration were separately added in the human co-culture system, there were no differences among the rates of different sialylation levels of IVIG-mediated phagocytosis.

Summary/Conclusions: Our data indicate that five different levels of sialylation of IVIG preparations show the same capacity of inhibition of macrophage phagocytosis. Together, the inhibition of IgG-mediated phagocytosis in human THP-1 monocyte-derived macrophages by IVIG is independent of IgG sialylation.

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TRANSFUSION AUDIT AND TARGETED EDUCATION AS TOOLS TO IMPROVE PRACTICE OF FRESH FROZEN PLASMA TRANSFUSION – AN INTERVENTIONAL STUDY

N Navin[1] and K Usha[2]

[1]Transfusion Medicine, Government Medical College, Alappuzha, Alappuzha
[2]Transfusion Medicine, Mookambika Institute of Medical Sciences, Kanyakumari, India

Background: The use of FFP has significantly increased in the past 10 years and it is the most common inappropriately used product despite the existence of guidelines. The appropriate use of FFP requires an understanding of its properties, inadequacies, as well as an appreciation of its complications. This study tries to analyze the effect of transfusion audit and educational interventions on reducing inappropriate FFP transfusions and modifying FFP transfusion practices in Government Medical College, Trivandrum, Kerala, India

Aims: 1. To know the current indications, usage pattern and appropriateness of FFP transfusion in various departments 2. To administer an educational intervention in the form of half-day workshops and distribution of guidelines. 3. To find out the difference in awareness about and practice of FFP transfusion after the intervention

Methods: This is a prospective interventional study done on all medical professionals who requested for FFP for various reasons for a period of one year. The first phase was a 4-month baseline phase in which prospective monitoring of request forms for FFP was done to identify the indications for FFP transfusion, to assess the appropriateness and the usage pattern in various specialties. The second phase was a two-month educational interventional phase during which various educational strategies were adopted to increase awareness among clinicians. The next and last phase was a six-month post education phase in which prospective monitoring of request forms was done to assess the effectiveness of educational interventions given in the previous phase.

Results: During the initial four-month audit, out of the 1258 patients studied, we received a total of 1449 requests, in which 42.2% (626) were inappropriate and 56.7% (823) were appropriate. The maximum number of inappropriate requests were from the Department of General Surgery (89%) followed by Other Surgical Specialities (52%) and Obstetrics & Gynaecology (35%). Leading cause of inappropriate use in our study was found to be for hypoproteinemic states, which accounted for about 31%. After the educational intervention for a period of 2 months, a re-audit was conducted to assess its effectiveness. We identified 1742 FFP requests for 1585 patients over six months. We found a definite reduction in the inappropriate FFP requests from 42.2% to 26%. When a department wise comparison was done, a reduction was seen in all specialties but it was statistically significant in General Surgery (89%-52%, p

Summary/Conclusions: Education as to the appropriate blood and blood products utilization and concurrent quality assurance audit techniques can safely reduce blood and blood product usage in the operating room as well as in the entire hospital thus providing maximum benefit to the patient with minimal risk. For sustained improvement in practice of FFP transfusion, prospective monitoring of requests forms and educational interventions must be a never ending process as residents are changing every year in our Institute.

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COMPARISON OF IVIG WITH REDUCED ANTI-A/ANTI-B ISOAGGLUTININS TO IVIG WITHOUT REDUCTION OF ISOAGGLUTININS USING SEROLOGY AND MONOCYTE MONOLAYER ASSAY

S Cen[1] and D Branch[1,2]

[1]Canadian Blood Services [2]University of Toronto, Toronto, Canada

Background: Intravenous immunoglobulin (IVIg) has been used to treat a number of autoimmune/inflammatory diseases with few side effects. However, high doses of IVIG (1–2 g/kg) have been recognized as a cause of hemolytic anemia in non-O blood group patients. Approximately 30% of high-dose IVIg recipients are documented to suffer from hemolytic anemia of Grades 1–4 by various reports with group A1B at higher risk of hemolysis than heterozygous A1O or BO. Hemolysis when observed has been due to anti-A and anti-B isoagglutinins contained in the IVIg preparations. These isoagglutinins reacting with patients' red blood cells (RBCs) can result in hemolytic anemia through destruction of the patients' isoagglutinin-coated RBCs via the mononuclear phagocyte system through phagocytosis. Recently, one manufacturer has produced an IVIg whereby the anti-A and anti-B titers have been greatly reduced by an immunoaffinity chromatographic approach.

Aims: We aimed to investigate whether IVIg depleted of isoagglutinins, used to opsonize group A1, B or A1B RBCs, induces significantly lower phagocytosis compared to non-depleted IVIg and whether, when used in vitro in the MMA at an equivalent in vivo dosage of 2 g/kg, would result in a potential for clinically significant hemolysis.

Methods: A1, B, and A1B RBCs were opsonized with isoagglutinin-reduced or non-reduced IVIg using the same total IgG levels. An indirect antiglobulin test (IAT) was performed to evaluate reactivity of anti-A and anti-B isoagglutinins in the two IVIg preparations using titration. A monocyte monolayer assay (MMA) was performed to examine the erythrophagocytosis of IVIg-opsonized A1, B, and A1B RBCs.

Results: Isoagglutinin-reduced IVIg had significantly lower anti-A and anti-B titers compared to non-reduced IVIg. IAT was maximal (4 +) at 30 mg/ml input with IVIg having non-reduced isoagglutinins, and titrated to a low IAT (1 +) at 2 mg/ml. In contrast, isoagglutinin-reduced IVIg opsonized A1, B and A1B RBCs showed a significant reduction in IAT titration, with a 2 + IAT at 30 mg/ml and negative IAT at 2 mg/ml. Using 33 mg/ml of IVIg (to give the approximate high-dose IVIg that would be administered to a patient of 80 kg; equivalent to 2 g/kg), phagocytosis of non-reduced IVIg opsonized A1, B, and A1B RBCs was determined to be clinically significant using MMA, with a phagocytic index (PI) of 42, 18, and 31 respectively. However, phagocytosis was largely absent when isoagglutinin-reduced IVIg was used at the same concentration to opsonize A1, B, and A1B RBCs with PI of 3, 1, and 2 respectively. A PI of >5 is considered potentially clinically significant.

Summary/Conclusions: We have shown that the titers of anti-A and anti-B were significantly lower for isoagglutinin-reduced IVIg. Phagocytosis observed using an MMA with isoagglutinin-reduced IVIg at an equivalent in vivo dose of 2 g/kg to opsonize RBCs predicted a non-hemolytic event if infused into a patient of group A1, B, or A1B. In contrast, non-isoagglutinin-reduced IVIg using a 3-fold dose of total IgG was predicted to cause a hemolytic event. We conclude that isoagglutinin-reduced IVIg would provide fewer hemolytic events in patients requiring high-dose IVIg therapy.

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CAN THE THAWED CRYOPRECIPITATE BE STORED BEYOND SIX HOURS?

M Hareuveni[1], G Fingold[1], M Cipok[2], T Badalbaev[2], V Deutsch[2] and I Kirgner[1]

[1]Blood Bank [2]Hematology, TASMC, Tel Aviv, Israel

Background: The cryoprecipitate concentrate is mainly used for replacement of fibrinogen in hypofibrinogenic patients. It is also important part of therapy in massive transfusion protocols. Beside fibrinogen it contains Factor (F) VIII, FXIII, von Willebrand factor (VWF) and small amounts of other plasma proteins. The American and European guidelines recommend that after thawing, cryoprecipitate must be held at room temperature and used within 4–6 h. Storage of cryoprecipitate for longer period will reduce wastage and increase availability of this product.

Aims: We investigated the stability of coagulation factors in cryoprecipitate, thawed and held at 4°C up to 48 h or refrozen and thawed again.

Methods: Individual units of cryoprecipitate (n = 66) were thawed at 37°C for 15 min, passed through an infusion set and sampled over time. The samples were held either at room temperature (RT) (20–24°C) or at 4°C. Samples were tested for

FVIII, FXIII, VWF and fibrinogen activity at 0, 6 (RT and 4°C), 24, 48 (4°C) h after first thawing, and at 0 and 4 h kept at RT for thawed twice defrosted samples.

Results: The median volume of the individual cryoprecipitate units tested, after thawing was 18 (12–20) ml. Clotting factors content FVIII 76 IU (27–175), FXIII 76 IU (34–126), VWF Ag 147 IU (54–351) and Fibrinogen 171 mg (93–477) Content of FVIII dropped to a minimum amount of 70 IU (15–164) when kept at 4°C up to 6 h or in thawed twice defrosted samples. Amount of VWF decreased to the lowest point of 132 IU (31–360) when kept for 48 h at 4°C. Fibrinogen amount was even higher than at time 0 at all-time points measured: the highest contents was 200 mg (77–503) in defrosted samples. All these changes were not statistically significant over all time and storage conditions as compared to the baseline. However, there was a significant decrease (P < 0.001) in FXIII, dropping to 62 IU (12–130) in units kept at 4°C for 48 h, but never decreased below guidelines specifications (60 U/unit).

Summary/Conclusions: The stability of fibrinogen and other factors in thawed cryoprecipitate stored at 4°C up to 48 h, refrozen and thawed again suggests that the shelf life of this product may be safely extended if sterility maintained.

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EPIDEMIOLOGY OF IVIG USE IN CRITICALLY ILL ADULTS WHO RECEIVED A RED CELL TRANSFUSION

C Jutras[1], P Hébert[2], D Fergusson[3], R Zarychanski[4], A Turgeon[5], T Ducruet[1], J Lacroix[1] and M Tucci[1]

[1]Department of Pediatrics, CHU Sainte-Justine [2]Department of Internal Medicine, CHUM, Montreal [3]Departments of Medicine, Surgery, & of Epidemiology and Community Medicine, University of Ottawa, Ottawa [4]Department of Internal Medicine, University of Manitoba, Winnipeg [5]Department of Anesthesiology, Hôpital Enfant-Jésus, Quebec, Canada

Background: The use of intravenous immunoglobulins (IVIG) in clinical medicine increased considerably over the past 10 years. Current use now threatens the capacity of blood products suppliers to fill the demand. More importantly, the use of IVIG in adults admitted to the intensive care units (ICU) is not well known.

Aims: To describe the participants of the "Age of Blood Evaluation" (ABLE) study (N Engl J Med 2015;372:1410–8) who received IVIG in the ICU and determine if some adverse events were more common in these patients compared to patients who did not receive IVIG while in ICU.

Methods: We reviewed the data on patients enrolled in the ABLE study and who received at least one dose of IVIG while in the ICU. The ABLE study was a large international randomized controlled trial that compared the outcomes of adults who received red blood cell (RBC) units stored ≤ 7 days versus RBC units delivered according to the standard policy, which was to deliver the oldest available unit (first-in first-out policy). The use of IVIG, as well as other clinical data, were prospectively collected.

Results: From March 2009 through May 2014, 2411 patients enrolled in the ABLE study. IVIG was administered to 77 (3.2%) patients. The mean age of patients receiving IVIG was 58.2 ± 18 years; 55.8% were male. Medical and surgical non-trauma admissions were more common in the IVIG group compared to controls (98.7% vs 84.1%). The most common causes of ICU admission in the IVIG group were: bacterial/viral pneumonia (10.4% vs. 10.9%), sepsis (40.3% vs. 14.1%), neuromuscular diseases (7.8% vs. 0.2%) and other neurologic diseases (5.2% vs. 1.2%). The severity of illness, measured by the APACHE II score, was not different in patients who did or did not receive IVIG. With respect to pre-existing significant co-morbidities, patients who received IVIG had less previous myocardial infarction (2.6% vs. 10.7%) but more of them were receiving immuno-suppressive therapy (23.4% vs. 9.7%). IVIG patients received more plasma and/or platelets than controls. With respect to outcomes, patients receiving IVIG had more acute lung injury (10.4 vs. 2.5%), cardiovascular failure (11.7% vs. 4.4%) and cardiac ischemia or infarction (9.1% vs. 3.9%). Treatments with vasopressors (87.0% vs. 78.1%) and continuous renal replacement therapy (29.9 vs. 20.5%) were also more frequent in IVIG recipients. Patients in the IVIG group had also a greater positive fluid balance (almost 1 liter) while in the ICU when compared to controls (4754 vs. 3724 ml). There was no difference in mortality at any point between the two groups.

Summary/Conclusions: IVIG were given to 3.2% of ABLE participants. IVIG therapy was potentially associated with significant morbidity (fluid overload, heart failure, acute lung injury, acute renal failure). More attention should be paid to the cost/benefit ratio of IVIG therapy in critically ill adults.

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DYE-LIGANDS AFFINITY CHROMATOGRAPHY IN PROCESS OF FACTOR VIII PURIFICATION: ADVANTAGES AND PERSPECTIVES

N Shurko, T Danysh and V Novak

State Institution "Institute of Blood Pathology and Transfusion Medicine NAMS of Ukraine", Lviv, Ukraine

Background: The important alternatives to natural ligands for specific affinity chromatography are textile dyes, offer clear advantages over biological ligands, in terms of economy (inexpensive), ease of immobilization, safety, stability and adsorbent capacity. Dyes are synthetic hydrophilic molecules bearing a reactive, usually a chlorotriazine, moiety by which they can easily be attached to various polymeric supports. The biomimetic monocholoro or dicholoro triazinyl dyes are able to bind most type of proteins, especially enzymes. Industrial chromatographic fractionations have been used increasingly in the last few years for plasma fractionation. This has led to the emergence of a new generation of products derived of blood, especially factor coagulation. The commercial concentrates of factor VIII (FVIII) are used for the treatment of Haemophilia A. The main method of obtaining of plasma concentrates of FVIII remains the method of ion-exchange chromatography. We have developed a method for obtaining of FVIII by using dye-ligand affinity chromatography.

Aims: Investigation the advantages of the dye-ligand affinity chromatography in the technology of FVIII purification.

Methods: Precipitation of proteins, ion-exchange on DEAE-Sepharose and dye-ligands affinity chromatography on Diasorb-aminopropyl matrix with Procion Blue MXR as ligand.

Results: The Cryoprecipitate was initial raw material for the work (working activity 0.087 IU/mg protein). It was resuspended and purified with 3.0% Al $(OH)_3$ and 3.5 % PEG-4000. The mixture was processed by ion-exchange chromatography on DEAE-Sepharose. The working buffer: 50 mM Tris-HCl, 1 mM $CaCl_2$, 100 mM NaCl and 10 mM sodium citrate, pH 7.4. They collected eluate FVIII (as a buffer for elution using the same buffer, but increased the ionic strength to 300 mM NaCl) and spent the next phase affinity chromatography. Dye affinity chromatography is a protein purification procedure based on the high affinity of immobilized dyes for the binding sites on many proteins. There are three types of dye affinity chromatography: negative, positive and tandem chromatography. The principle of negative chromatography: the undesired proteins are retained by the immobilized dye while the desired proteins flow through the column. Studies have found that purification of FVIII occurs on the principle of negative sorption of non-target proteins (albumin, thrombin, fibrinogen, FVII, FIX et al.). Because, the purification of FVIII was due to the phenomenon of negative sorption, there was practically no loss of activity of the initial activity of factor (yield was 96.4%). The concentrate of FVIII with specific activity 72.44 ± 4.26 IU/mg protein is received. We researched that factor on Will-abrand (vWF) isn't absorbed with dye-Diasorb sorbents too. At the stage of dye-ligand affinity chromatography, changes in the ratio almost were not. The ratio of FVIII/vWF complex in the eluate Diasorb-Procion Blue MXR was 1.96 ± 0.12.

Summary/Conclusions: It was established that at the stage of dye-ligand chromatography, the loss from the initial activity of FVIII is practically absent and the original ratio of FVIII/vWF is saved.

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EFFICACY OF QUARANTINE PLASMA PRODUCTION IN AN IMMUNOHEMOTHERAPY SERVICE IN PORTUGAL – A TEN-YEAR STUDY

S Lopes, L Vieira, I Alonso, J Marques, D Ferreira and M Figueiredo

Immunohemotherapy, Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

Background: The demand for plasma transfusion is still significant in high-income countries. Although the substantial progress in blood safety, the hypothetical risk of transfusion-associated infections still exists. In order to guarantee the security of plasma for direct therapeutic use, besides the standard screening tests, there are essentially three methods: quarantine, pathogen reducing technology and solvent-detergent treatment. Quarantine plasma is substantially less expensive than the other processes, which may be decisive to some countries and institutions. As another advantage, comes the greater preservation of the therapeutic contents of the plasma, assessed by measuring the VIII factor. In this method, the unit is only released when the donor returns to the blood center and tests repeatedly negative for the transfusion-relevant viruses, which assures the security of the plasma. In Portugal, there

are 32 blood banks and transfusion medicine services; only two use quarantine plasma and our service is one of them.

Aims: Determine the efficacy of the method of separation and storage of quarantine plasma in our hospital when compared with European guidelines of quality assurance.

Methods: Based on the internal quality control since 2007 until 2017, it was constructed a retrospective data base regarding the quarantine plasma used for therapeutic purposes in our hospital. In each sample it was registered the storage time and determined the level of VIII factor. The quality of these products was controlled and validated by intern procedures and extern entities (NEQAS®). All the data was analyzed using IBM® SPSS® Statistics 23.

Results: In a total of 975 samples it was observed a variation of storage time from 6 to 1061 days (M = 120; SD = 159.07) and ranging in level of VIII factor from 11 up to 218 IU/100 ml (M = 84.4; SD = 31.01). It was detected that 11% of all samples had VIII factor levels below 50 IU/100 ml (n = 112). There was a poor, positive correlation between storage time and level of VIII factor ($r_s = 0.1$, $r_s^2 = 0.01$, P = 0.002), demonstrating that there is no association between these two variables. Maintenance of the adequate temperature all along the process was verified and guaranteed by controlled methods. When comparing samples with the highest VIII factor level with samples below the acceptable level, no statistically significant differences were found in the time elapsed from collection to processing (z = −0.13, r = −0.01, P = 0.99). From 2010 till 2017, there was a steady and progressive decrease of the number of samples below 50 IU/100 ml.

Summary/Conclusions: The levels of therapeutic content of quarantine plasma separated and stored in our hospital are satisfactory, which demonstrates the effectiveness and efficiency of our method. We must also emphasize that the proportion of units with VIII factor below the acceptable has consistently reduced between 2010 and 2016, which supports the improvement of our method. Maintenance of the adequate temperature, time elapsed from collection to processing and storage time, which are factors controllable only by operator/technique, demonstrated that they were not related to inadequate VIII factor levels.

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EVALUATION OF RATIONAL USE OF FRESH FROZEN PLASMA: RESULTS OF AN AUDIT

A Wazeer[1], A Riaz[2] and Z qasim[3]

[1]Department of Pathology/Blood Transfusion Service, Div. Headquarters Teaching Hospital [2]Department of Pathology/Transfusion Service, Div. Headquarters Teaching Hospital [3]Department of Pathology/Transfusion Service, Div. Headquarters Teaching Hospital, Mirpur, Ajk, Pakistan

Background: There is severe shortage of blood and blood components in most of the developing countries including Pakistan. The resources are inadequate in terms of meeting the ever growing demand of blood components. The blood and its components carry a potential risk of adverse reactions if use inappropriately. Fresh frozen plasma (FFP) is a major source of coagulation factor replacement therapy for patients with clotting factor deficiency. Although FFP is readily available for use in clinical practice, yet its administration isn't without risk. Studies on the use of FFP reveal that it is often overused or inappropriately used. Until recently, the FFP usage was negligible; however, consistent with the national trend, FFP usage has been growing in our hospital for the last few years, hence inappropriate usage also. The current study was planned to audit FFP transfusion practice based on pre- and post-transfusion coagulation testing and if further FFP was transfused as a follow-up of the post-transfusion coagulopathy.

Aims: To evaluate the usage of fresh frozen plasma (FFP) according to indications and to assess its audit for transfusion.

Methods: The study was conducted at the Divisional Headquarters Teaching Hospital, Mirpur, AJK, Pakistan. Ethical approval was obtained from the hospital ethical committee. All the patients (age > 18 years) who were transfused with FFP between June 1, 2017 to December 31, 2017, were reviewed for indications and appropriateness of use. Patients who were transfused FFP for massive transfusion protocol and plasma exchange was excluded from the study. Patient's basic demographic data, blood CP and coagulation parameters (PT, INR and APTT) before and after the transfusion, and transfusion indications were reviewed retrospectively. Patient's with incomplete data were excluded. The appropriateness of FFP transfusion was analysed on the basis of Guideline on the Administration of Blood Components – British Committee for Standards in Haematology 2012. The SPSS 20.0 (SPSS Inc., Chicago, IL) was employed for the statistical analyses.

Results: We evaluated 423 units of FFP transfusion in 103 patients. The common indications for FFP usage were acute DIC with high INR (27 patients, 110 units),

followed by excessive bleeding with high INR (19 patients, 51 units) and volume depletion (14 patients, 59 units). If FFP was transfused in an inadequate dosage or for un-indicated reason as per the guidelines, it was recorded as inappropriate. Inappropriate FFP usage was seen in 48 patients with 141 transfusions (33.3%). The inappropriate use was high in patients transfused with the aim of bleeding prophylaxis. Post-transfusion reactions were also recorded. Allergic reactions were reported in five patients and volume overload in three patients. For seven patients, the values of INR could not be established as these values were too high to be measured.

Summary/Conclusions: FFP is a scarce resource, hence it is recommended to adopt a preferential use of FFP for those patients who fulfil the guidelines and have a high pre-transfusion INR. Further audits on these lines and with a larger sample size are required in order to improve the utilization of this resource.

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OVERVIEW OF THE PRODUCTION OF CRYOPRECIPITATE IN THE PAST 5 YEARS AT THE OUR REGIONAL CENTER FOR BLOOD TRANSFUSION

J Vitlarova[1], M Shorova[1], N Ivanova[1], E Velkova[2], T Timova[3] and D Stambilieva[3]

[1]Regional Center for Transfusion Medicine, Clinical Hospital Shtip, Institute for Transfusion Medicine, Clinical Center "Mother Teresa", Skopje, Shtip [2]ITM Skopje, ITM Skopje, Skopje [3]Regional Center for Transfusion Medicine, Clinical Hospital Shtip, Institute for Transfusion Medicine, Clinical Center "Mother Teresa", Skopje, Strumica, The Former Yugoslav Republic of Macedonia

Background: In contrast with plasma from which it is derived, cryoprecipitate (CRYO) is highly concentrated with coagulation factors such as factor VIII, factor XIII, von Willebrand factor, fibrinogen and fibronectin. Although it was originally developed as an antihaemophilic treatment strategy today CRYO presents crucial chain in the treatment process of coagulopathy in patients with liver failure, polytrauma, as well as in the obstetric and cardiovascular surgery we don't use cryo to treat patients with hemophilic disease in the last 10 years. Since 1999 the production of Fresh Frozen Plasma (FFP) and CRYO is a daily routine at our Regional Center (RC) in Shtip.

Aims: To show the number of produced CRYO units and the potential factors that influenced the production process in the past 5 years.

Methods: The whole blood units were collected from voluntary un-paid blood donors in Terumo triple bags and then CRYO was prepared according to the Standard Operation Protocol. We reviewed our data records in order to extract the number of CRYO units produced at our RC as well as the additional delivery of them into diverse hospital departments/centers.

Results: In 2012 from the total 710 produced CRYO bags 18.3% were provided to Department of Internal medicine (DIM), 26.7% were sent to Department of Surgery (DS) and 46.5% were sent to the Institute for transfusion medicine (ITM) in Skopje. Moreover in 2016 our production increased in 2320 CRYO bags, from which 12.6% were sent to DS and only 7.69% were supplied to DIM. However, more than a half (78.0%) of the produced CRYOs in 2016 were provided to central ITM. Our data has shown that in the 5 year period the Department of Gynecology (DG) has always received the minimum number of produced CRYOs i.e. 8.4% in 2012, 11.4% in 2014, and 2.6% in 2016.

Summary/Conclusions: The production of CRYO at our RC has undoubtedly increased in the past 5 Years, from 710 (2012) to 2320 (2016). Since 2011 our transfusion department was integrated as RC into the main Institute of Transfusion Medicine and additionally new machine was implemented. Consequently the number of CRYOs suppled into ITM has increased from 46.5% in 2012 to 78.0% in 2016. On the other hand the percentage of CRYO suppled to the clinical departments in the regional clinical hospital in Shtip has decreased in the past 5 years due to the falling number of treated patients with difficult and complex diseases at the regional Hospital. Concerning to the underlying risks of transmission of blood borne pathogens and transfusion related acute lung injury (TRALY) CRYO has been withdrawn from usage in many European countries and has been replaced with alternative fibrinogen preparations. However, in our country CRYO is routinely used in the treatment of acquired coagulopathy mostly due to liver failure and emerging of adverse events due to CRYO transfusion were not analyzed in our study. Further research is needed in order to determine the clinical efficacy of the CRYO Transfusion in our country.

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STUDY ON IN VITRO PYROGEN TEST FOR BLOOD PRODUCTS USING MONOCYTE

J Kim, J Lee, J Jeong and K Jung

Blood Products Division, National Institute of Food and Drug Safety Evaluation, Ministry of Food and Drug Safety, Cheongju-si, Chungcheongbuk-do, Korea

Background: Blood product such as human plasma protein fraction is a therapeutic biologic drug prepared from large pools of human plasma obtained from human whole blood. For example, human serum albumin, immunoglobulin, coagulation factor and fibrinogen are plasma-derived preparations. Since most of these drugs are administered intravenously, it should be confirmed that there are no pyrogenic substances that can cause fever when administered to humans. Currently, In national lot release of finished blood products, the absence of pyrogen is confirmed by the rabbit pyrogen test to ensure the safety of these blood derived products. However, it costs many lives of rabbits and it does not line with the international efforts for minimization of animal use in the life sciences, also represented as 3R. There also has been a need of replacement due to its impossibility in quantification of pyrogen, and also to its sensitivity to condition of animals and technique of examinant.

Aims: The aim of our study is to develop an alternative in vitro pyrogen test for national lot release of final blood derived products using monocyte activation test. And also it is to avoid unnecessary animal sacrifice, and to secure more reliable, scientific, and advanced pyrogen detection in blood products thereby contributing to improvement of quality control and public health.

Methods: In this research, we have studied on monocyte activation test as an alternative method for the rabbit pyrogen test. We used cryopreserved rabbit peripheral blood mononuclear cell as a source of monocyte and employed enzyme-linked immunosorbent assay (ELISA) to measure the release of fever inducing cytokines. And we conducted both rabbit pyrogen test and monocyte activation test for endotoxin and non-endotoxin pyrogens from gram positive bacteria or fungi.

Results: As a result, we established an assay protocol of in vitro alternative pyrogen test using monocyte. And we compared the results from rabbit pyrogen test and monocyte activation test for some pyrogens, and investigated the possibility of replacement by correlation analysis between two methods. The temperature rise of rabbit increased in proportion to the pyrogens in rabbit pyrogen test. And the release of fever inducing cytokines proportionally increased according to increasing concentration of the pyrogens in monocyte activation test. And the secretion of pyrogenic cytokines in monocyte activation test and the temperature rise in rabbit pyrogen test showed a similar tendency.

Summary/Conclusions: By this study of alternative pyrogen test, especially monocyte activation test for national lot release of finished blood products, we reduced significantly the use of animals and also predicted substitutability of the rabbit pyrogen test. The results of this research will be used as baseline data for introduction of in vitro pyrogen test which is mainly inspected for safety of blood product, and will also contribute to improvement of quality control for blood products. Further study will be conducted to confirm that this alternative method can be applied to the final blood products and also it can be used as an official quality control test.

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EXPERIENCE OF THE IMPLEMENTATION OF INTERCEPT AMOTOSALEN TREATMENT FOR PLATELETS

T Bocquet[1], R Djoudi[2] and M Asso Bonnet[2]

[1]EFS Île-de-France, Rungis [2]EFS Île-de-France, Ivry, France

Background: The French national blood agency (EFS) delivered about 71,000 platelets in the Parisian region in 2017 (100% in additive solution). Intercept for platelets (amotosalen + UVA, Cerus, Netherlands) has been implemented nationwide, since November 2017, to decrease the risks of contamination with bacteria and emerging pathogens (CHICK, DENGUE, WNV, etc.).

Aims: We describe here our regional experience in the implementation of platelet treatment with amotosalen (INTERCEPT Blood System -IBS). Our organization, operational aspects, and compliance with product standards are reported. We also discuss post-implementation feedback.

Methods: Pooled platelet concentrates (PPCs) are obtained by the buffy coat method with a TACSI device (TERUMO BCT, USA). Apheresis platelets (APC) are collected from MCS+ (Haemonetics, USA) and TRIMA separators (TERUMO BCT, USA). Platelets are labeled and individually treated with the Intercept device. The entire product is transferred into an illumination bag and amotosalen solution is added. The product is then exposed to UVA (6 J/cm²) for about 6 min before storage for 6 to 16 h, with agitation on a Compound Adsorption Device integrated into a storage

container. The product is then transferred to a storage bag, quality control tests are performed, and the product is labeled and sent out to distribution sites.

Results: Before the implementation period, adjustments were made to ensure that the products complied with the requirements of Intercept IFU. We modified our logistic organization and made a number of modifications at our blood production sites. The Cerus Deployment Team provided three days of training per production site. IBS treatment reached 160 units/day/site, with 3 illuminators and 2 or 3 technicians. The treatment satisfied requirements, with losses due to the process during the trial period of $8.4\% \pm 3.3$ (n = 18) for APC and $10.6\% \pm 2.4$ (n = 14) for PPC. As expected, platelet content decreased after two months of implementation: from 4.05×10^{11} to 3.75×10^{11} for PPC (n = 5954), and from 4.7×10^{11} to 3.95×10^{11} for APC (n = 5232). We adjusted our logistic organization to meet new release time requirements. We anticipated a routine complication of the use of the kit for pediatric preparations: an inability to separate the platelets immediately into two units. However, a number of unexpected adverse effects were also observed:

A large volume of waste (packaging, etc.)

Time lost for rehabilitation, for the saving of final products (not compliant with IFU) and loss of swirling scores for APC in 1.5% of cases (8/507 during the first seven days). We limited to the volume to 410 ml for MCS+ and, as swirling score loss was correlated with platelet concentration, we limited the collection target to 5.5×10^{11} platelets for TRIMA, to overcome these problems.

Product losses due to final bag breaches (7/10,000). These losses seem to be linked to the mode of storage in the cart and the use of platelet agitators.

Summary/Conclusions: The IBS treatment for platelets has had a major impact on the entire blood transfusion chain, but its implementation can be considered a success. This technique satisfies French quality requirements. Given the significant difference in platelet content and the costs associated with this technique (devices, technicians, non- compliant products etc.), the use of IBS for platelets has had a major economic impact. The use of a dual storage (DS) device, combined with a revision of IFU, can reduce the cost per unit obtained. Other pooling methods for buffy coats combined with the DS device might also increase the cost-effectiveness.

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EFFECT OF A 24 H AND 40 H CAD TIME IN QUALITY OF PLATELET CONCENTRATE TREATED BY AMOTOSALEN AND ULTRAVIOLET LIGHT A

H Isola[1], A Dupuis[2], A Eckly[3], B Belcour[2] and C Gachet[4]

[1]Production [2]Quality Control [3]Research [4]Direction, EFS Grand EST, Strasbourg, France

Background: Since 2006, EFS Grand Est produces and delivers pathogen reduced Platelet Concentrates (PC) using a photochemical treatment (PCT) combining Amotosalen and ultraviolet light A (UVA) (INTERCEPT™ Blood System, Cerus). Residual amotosalen is adsorbed by a compound adsorption device (CAD). Incubation time of 4 h to 16 h (Small Volume sets, SV) or 6 h to 16 h (Large Volume sets, LV) is required. Residual amotosalen has to be less than 2 μM which is the limit specified by the French regulatory authority.

Aims: To evaluate the quality of pathogen reduced-PC (PR-PC) processed with an incubation time in the CAD (CAD time) of 24 h and 40 h in comparison with a CAD time of 16 h.

Methods: Two buffy coat platelet concentrates (BCPC) from 5 donors were pooled and split to obtain two identical BCPCs: BCPC1 was treated for PR with a 16 h CAD time (Control, n = 6), BCPC2 was treated for PR with a 24 h or 40 h CAD time (CAD24, n = 3; CAD40, n = 3). Biological parameters (swirling, platelet content, residual leukocytes, pH, pO_2, pCO_2, lactate, glucose, LDH, soluble p-selectine) and residual amotosalen concentration were assessed at the end of each CAD time, at day 5 and day 7. The Kunicki score, which requires electron microscopy, was measured for BCPCs control and BCPC40 only (n = 2).

Results: The mean platelet contents were $4.0 \pm 0.5 \times 10^{11}$ (Control) and $4.0 \pm 0.4 \times 10^{11}$ (CAD24 and CAD40) respectively. All the units presented maximum swirling and compliant pH. Residual amotosalen concentration was <2 μM for each unit. At day 5, mean glucose concentration was 1.7 ± 0.1 mM for Control, 1.9 ± 0.2 mM for CAD24, and 1.7 ± 0.2 mM for CAD40. Mean soluble p-Selectin concentration was 68.5 ± 2.9 ng/ml for Control, 78.0 ± 3.9 ng/ml for CAD24, and 72.5 ± 1.9 ng/ml for CAD 40. The Kunicki score was not different between the Control and the CAD40 group (292.5 ± 9.5 for both group after illumination; 276.5 ± 15.5 for Control and 281.5 ± 16.5 for CAD40 at day 3; 235.5 ± 33.5 for Control and 222.5 ± 23.5 for CAD 40 at day 7).

Summary/Conclusions: The quality control of PR-BCPCs treated by amotosalen + UVA showed no difference when the CAD time was 24 h or 40 h as compared to a

CAD time of 16 h. These results may help to make a decision if the CAD time would exceed the specified maximum 16 h CAD time.

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HOW THE KFSHRC BLOOD TRANSFUSION SERVICE INTRODUCED AUTOMATED PROCESSING OF WHOLE BLOOD AND RIBOFLAVIN–BASED PRT

H AlHumaidan[1], F AlZaher[2], B McGee[3] and M Cardoso[4]

[1]Department of Pathology and Laboratory Medicine [2]Department of Surgery, 1 King Faisal Specialist Hospital & Research Center, Riyad, Saudi Arabia [3]Product Support, Terumo BCT, Lakewood, United States of America [4]Medical Affairs, Terumo BCT, Zaventem, Belgium

Background: In 2015 the Blood Bank and Transfusion Service of the King Faisal Specialist Hospital & Research Center (KFSHRC) processed 26,496 whole blood units and 3,996 apheresis collections. In 2016 it decided to improve efficiency of blood processing by introducing the Reveos automated whole blood processing system (Terumo BCT) and maintaining a high level of safety by treating platelet concentrates (PC) with the Mirasol PRT System (Terumo BCT) while increasing by 10% the number of blood products processed with the newly added stem cell and organ transplant site.

Aims: To report the experience of KFSHRC with the introduction of whole blood automation with Reveos and Mirasol PRT in its blood banking routine.

Methods: Whole blood units of 450 ml are collected and processed daily from 7.30 am to 12am by 6 technicians distributed into two working shifts. All blood is processed with the Reveos into 3 components: a red blood cell concentrates (RBCC), a plasma unit and one interim platelet unit (IPU). With the help of the T-IPU select 4 IPUs are selected and pooled to generate a PC with an average platelet yield of 3.0×10^{11}. The T-IPU select tool is a software application that sorts and groups IPUs based on the estimated platelet yield by the Reveos system. In addition to whole blood derived platelets, KFSHRC also collect platelet by apheresis with the Trima Accel device (Terumo BCT). Apheresis allows for collection of single and double platelet concentrates. Characteristics of both whole blood- and apheresis-derived PC in 35%: 65% (plasma: TPAS+) coincide with the Mirasol product specification. PRT treatment is performed per manufacturer's instructions and takes 4 to 5 min, warranting the release of very fresh PRT-treated PC.

Results: Since the start of implementation of automated whole blood processing, 33,250 whole blood units have been processed into three components. In total 10,631 PC derived from apheresis and whole blood have been treated with Mirasol PRT. The processing of whole blood with the Reveos system results in an RBCC with an average hematocrit of 65 to 70%, a final PC with an average platelet yield of 3.0×10^{11} PLTs/unit and a unit of plasma with an average volume of 250 ml. Residual WBC values in RBCC and PC were far below 0.01×10^6. Sixty-five percent of apheresis donors are repeat donors who have been selected over the years to donate on this platform. There is an average split rate of 85% of total apheresis platelet collections based on yield count with target of 6.75×10^{11}.

Summary/Conclusions: The introduction of two new technologies, the Reveos automated whole blood processing system and the Mirasol PRT systems has been performed simultaneously at the KFSHRC. Training and implementation has been seamless due to their ease of use and compatibility. Moreover, KFSHRC Blood Transfusion Service was able to improve production efficiency and component safety without addition of resources or increased product release time allowing for an escalation of 10% in collections.

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WHY USE THE SAME STORAGE PROTOCOL FOR ALL RED BLOOD CELLS (RBCS)? THE EFFECT OF BLOOD DONOR'S AGE AND BLOOD DONATION TIME ON STORAGE RBC LESION IN BLOOD BANK CONDITION

M Rafiee[1], S Jahanshahi Ghajar[2] and M Deyhim[1]

[1]Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine [2]Biochemistry, Science and Research Branch, Islamic Azad University, Tehran, Islamic Republic of Iran

Background: The antioxidant capacity decreases during the RBCs storage and the side effects of blood transfusion are the challenges that are resulted from the RBC

storage lesion due to oxidative stress. Given that previous studies have shown that the antioxidant capacity has a diurnal variation in blood plasma with a decreasing trend with aging in the elderly. So, it is possible that donated blood, based on donor's age and donation time, has a different antioxidant capacity and following a different response during storage.

Aims: This study attempts to uncover the effect of blood donor's age and blood donation time on biochemical and hematological parameters during the storage RBC lesion.

Methods: Twenty packed RBCs taken from the volunteer, male donors and analyzed according to the variables: (i) donation time: morning (8–11 am; n = 10) and evening (5–8 pm; n = 10); (ii) donor age: 20–30 y (n = 5), 30–40 y (n = 8) and 40–60 y (n = 7). All RBC bags studied during the storage of RBCs under blood banking regulations at Iranian blood transfusion organization (as days 3, 7, 14, 21, 28, 35, and 42). Biochemical parameters including sodium, potassium, glucose, lactate concentration, lactate dehydrogenase (LDH) enzyme activity, pH, oxidative stress biomarkers such as malondialdehyde (MDA) concentration, and total antioxidant capacity (TAC) was performed using commercially available kit. Nitrate/nitrite metabolites and RBC Hemolysis index were measured by drabkin and Griess method, respectively. Hematologic parameters were measured by automated cell counter.

Results: All groups were shown as expected a decreasing trend in TAC, glucose, sodium, and pH and an increasing trend in potassium release, lactate, LDH, MDA, and Hemolysis index during the storage with a time-specific manner ($P < 0.05$). But in the evening group compared to the morning, nitrate/nitrite, MDA, LDH, and some hematologic parameters (MCV, Hb, HCT) increased significantly ($P < 0.05$). In the age groups of 30–40 y and 40–60 y, nitrate/nitrite, MDA and some hematologic parameters (MCV, MCH) exhibited a significantly increase in comparison with group of 20–30 y of blood donors ($P < 0.05$).

Summary/Conclusions: This study indicated that donated blood in the evening and or donated from elderly donors has the potential for more peroxidation and nitric oxide depletion (due to oxidize to its metabolites) during the storage. The results of donor's age effect are consistent with the "donor-variation effect" presented by "Tzounakas, Proteomics Clin Appl, 2016"; it may lead to the production of highly unequal blood labile products in a similar storage strategy. However, genetic, undiagnosed/subclinical medical conditions and lifestyle factors that affect RBC characteristics at baseline, cannot be ignored. In addition, it seems that the donation time has an effect on RBC lifespan, energy metabolism, and sensitivity to oxidative stress. Although for the confirmation of this important finding, the results of two main parameters TAC and Hemolysis index were disappointing, we believe that the small sample size was a possible reason to produce not meaningful results. In regard to using the same protocol for storage of all donated RBCs (for up to 42 days), a deeper insight with a more sample size need into the donation time and the apparently complex donor age effect on the RBC storage lesion.

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THE COMPARISON OF THE QUALITY OF CRYOPRECIPITATE OBTAINED FROM QUARANTINED FRESH FROZEN PLASMA AND THE CRYOPRECIPITATE OBTAINED FROM INACTIVATED FRESH FROZEN PLASMA

B Janowska-Stuchlak and K Olbromski
Blood Center in Poznan, Poznan, Poland

Background: Cryoprecipitate is a fraction of cryoglobulins derived from a single unit of fresh frozen plasma (FFP) that is concentrated to the volume of about 30 ml. As it contains the major amounts of the factor VIII, von Willebrand factor, fibrinogen, factor XIII and fibronectin it is a perfect source of these factors in the cases of their insufficiency. In order to increase the safety of the recipients the cryoprecipitate is produced from FFP that has been quarantined or inactivated of pathogens. The quarantine means storing the plasma for at least 16 weeks and subsequently testing it for the presence of the markers of infectious diseases (obligatory tests in Poland involve: HBsAg, anti-HCV, anti-HIV1/2, DNA HBV, RNA HCV, RNA HIV and markers of the Treponema pallidum infection). In Poland there are 2 commonly used methods of inactivation of pathogens: with methylene blue (Theraflex BM Plasma system) and with riboflavin (Mirasol system).

Aims: The aim is to evaluate and compare the content of fibrinogen and activity of factor VIII in the cryoprecipitate obtained from quarantined FFP and from inactivated FFP.

Methods: For the analysis 80 units of cryoprecipitate obtained from recovered plasma were used: 40 units of plasma that was quarantined for 16 weeks and 40 units of plasma that was inactivated of pathogens using the Theraflex BM Plasma. For the production of cryoprecipitate the method of centrifugation was used. The

test of the concentration of fibrinogen and activity of factor VIII was performed on samples collected directly after the production using the Sysmex CA-600 analyser (clotting method for factor VIII and Caluss method for fibrinogen). In Poland the quality requirements for the cryoprecipitate are as follows: content of fibrinogen ≥14 mg/unit; activity of factor VIII: >70 IU/quarantined unit; >50 IU/inactivated unit.

Results: Cryoprecipitate obtained from quarantined plasma: activity of factor VIII 103 ± 47 IU/unit; content of fibrinogen: 265 ± 105 mg/unit. Cryoprecipitate obtained from inactivated plasma: activity of factor VIII 8 ± 26 IU/unit; content of fibrinogen: 233 ± 84 mg/unit. For the analysis 80 units of cryoprecipitate obtained from recovered plasma were used: 40 units of plasma that was quarantined for 16 weeks after its production and 40 units of plasma that was inactivated of pathogens using the Theraflex BM Plasma. For the production of cryoprecipitate the method of centrifugation was used. The test of the concentration of fibrinogen and activity of factor VIII was performed on samples collected directly after the production using the Sysmex CA-600 analyser (clotting method for factor VIII and Caluss method for fibrinogen). In Poland the quality requirements for the cryoprecipitate are as follows: content of fibrinogen ≥14 mg/unit; activity of factor VIII: >70 IU/ quarantined unit; >50 IU/inactivated unit.

Summary/Conclusions: The analysis proved high content of factor VIII and fibrinogen in cryoprecipitate obtained from quarantined plasma as well as in cryoprecipitate obtained from inactivated plasma. The comparison of the content of the clotting factors in the cryoprecipitate obtained from quarantined and inactivated plasma shows that the process of reduction of the biological pathogens in the plasma for the production of the cryoprecipitate does not cause substantial decrease in activity of factor VIII and fibrinogen. It can be concluded that because of the wide spectrum of activity of the inactivation methods of various pathogens, cryoprecipitate obtained from inactivated plasma is safer for its recipients and hence it should be in common use in haemotherapy.

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Abstract has been withdrawn

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COMPARISON OF LABORATORY PARAMETERS OF PATHOGEN REDUCED AND IRRADIATED RBC SUSPENSION

I Kumukova[1], P Trakhtman[1], N Starostin[1], D Borsakova[1], A Ignatova[1] and M Cardoso[2]

[1]*Department of Transfusion Medicine, National Medical Research Center for Pediatric Hematology, Oncology and Immunology, Moscow, Russia* [2]*Medical Affairs, Terumo BCT, Zaventem, Belgium*

Background: Accumulated data describe effective pathogen and WBC inactivation and a safe toxicological profile of whole blood (WB) treated with riboflavin and ultraviolet (RF+UV)-based pathogen reduction technology. Trials on animals and healthy volunteers demonstrated no neoantigen formation or other serious safety problems in such blood product. We conducted an open, parallel, nonrandomized in vitro study of RBC concentrates (RBCC) obtained from leukoreduced RF+UV-treated WB compared to standard X-ray irradiated leukoreduced RBCC.

Aims: Compare the quality of RBCC prepared from RF+UV-treated WB (PRT) to RBCC irradiated with X-rays (Irradiated) and determine the shelf-life of the RBCC prepared from RF+UV-treated WB.

Methods: Units of WB (450 ml) were obtained from healthy donors (n = 50). On the day of donation, 25 WB units were leukoreduced (IMUFLEX-WB-RP, Terumo BCT), treated with RF+UV (Mirasol, Terumo BCT) following manufacturer's instructions and separated into PRT RBCC. Irradiated control RBCC (n = 25) originating from leukoreduced WB were irradiated by X-rays at a dose of 25 Gy on day 0. All RBCC were stored at $6 \pm 2°$ C in SAGM solution for 4 weeks. The following parameters were studied: hematocrit, pH, total and free hemoglobin, extracellular potassium, glucose, lactate, ATP, reduced glutathione (GSH), phosphatidylserine expression on RBC membranes, hemolysis, and osmotic resistance of the cells. The measurements were carried out in WB prior to PRT or Irradiated treatment on day 0, as well as in PRT and Irradiated RBCC on day 0, 7, 14 and 21. On day 0 and 28 of storage, the sterility of the stored RBCC was tested.

Results: There were no statistically significant differences between groups at any storage times for pH, concentrations of total hemoglobin, extracellular potassium, phosphatidylserine expression, ATP and GSH. The concentrations of glucose and

lactate were significantly lower in the PRT group than in the Irradiated groups, at all times of storage, except for the day 0 in the case of lactate (P < 0.01). Osmotic resistance in the PRT group was statistically significantly lower from day 7 on of storage (P < 0.01). On day 14 of storage higher free hemoglobin concentration, and hemolysis were detected in the PRT group relative to the Irradiated group, but no sample in either group had a hemolysis value greater than 0.8%. On day 21 of storage 9 samples (36%) of the PRT group exceeded 0.8% hemolysis. All samples of the Irradiated group had a hemolysis value of less than 0.8% during storage. All samples in both groups were negative for bacterial culture on days 0 and 28.

Summary/Conclusions: The laboratory parameters for RBCC prepared from WB treated with RF+UV are similar to RBCC irradiated by X-ray and meet the quality criteria through day 14 of storage. The PRT group exhibited higher hemolysis seen by lower osmotic resistance and hemolysis levels. Due to this fact, the clinical use of these components after 14 days of storage in SAGM is not recommended, but may be prolonged with newer generation additive solutions

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MAINTAINING A SAFE AND SUSTAINABLE BLOOD SUPPLY IN THE DUTCH CARIBBEAN ISLANDS WITH RIBOFLAVIN-BASED PRT

A Duits[1], L Sille[2] and M Cardoso[3]

[1]Medical Affairs [2]Quality Management, Red Cross Blood Bank Foundation, Willemstad, Curaçao [3]Medical Affairs, Terumo BCT, Zaventem, Belgium

Background: The Red Cross Blood Bank Foundation (RCBF) serves a population of 320,000, including inhabitants of the Dutch Caribbean islands of Curaçao (C), Aruba (A), Bonaire (B) and Sint Maarten (S). Maintaining a safe, sustainable and completely self-sufficient blood supply is challenging due to the geographical and epidemiological situation. Nearly 10,000 whole blood units are processed into three components per year. All blood donations are on voluntary non-remunerated basis and donors donate in average 2.2 times yearly. In case of emergent threats there is an intense collaboration with PAHO and Sanquin.

Aims: To describe the system established by the RCBF that ensures a sustainable, safe and stable blood supply in the region that can deal with emerging infectious threats and natural catastrophes.

Methods: Newly recruited donors undergo a first physical and blood screening before they are admitted as regular donors to the blood program. First whole blood donation is collected after 3 months of the initial testing. Whole blood is collected at two collection sites (C and A) and processed into components following GMP standards. Components are quarantined until results of the screening tests are known. Donations are screened for: HIV (Ab/Ag), HCV, HBsAg, HTLV and Treponema (all 4th generation ELISA) and NAT (HIV, HCV, HBV). Five percent of components undergo quality control per EU, AABB and Sanquin standards. Red Blood cells are stored up to 35 days. Platelet concentrates (PC) result from pooling of 4 buffy coats (BC) with single donor plasma. Since January 2016 100% of PCs are treated with the riboflavin-based method (Mirasol PRT System, Terumo BCT) per manufacturer's recommendations and stored up to 7 days at 22°C. Required standard PC testing for bacterial contamination before blood product release was terminated after PRT introduction. Fresh frozen plasma (FFP) is stored for up to 2 years at −30°C.

Results: In the past 5 years, 1 HIV-1 positive, 2 HCV and 1 HBV and 1 HTLV positive donor applicants were eliminated from the blood program after initial screening and 2 HTLV positive after routine donation screening. All blood components were compliant with international standards. Implementation of the Mirasol- PRT technology had no real impact on the logistics of the RCBF due to its simplicity, ease of use and proper training. After more than 1,000 Mirasol-PC transfusions there has been no increase in rates of transfusion reactions and no case of severe adverse reactions in recipients, including recipients in the Neonatal Intensive Care department.

Summary/Conclusions: The RCBF has been very successful in covering the blood demand of a very challenging geographical area composed of islands where logistics, inventory management and communication with stakeholders are extremely important. A direct involvement with patient care in very different clinics, e.g. trauma care, neonatology, oncology and hemodialysis through active consultation with clinicians and daily inventory checks is required. Periodically the region is hit with outbreaks of emerging pathogens like Dengue, Chikungunya and ZiKA virus. Hence, the implementation of the Mirasol PRT system has proven feasible and valuable to develop preparedness for any emergent infectious threat.

Pathogen Inactivation

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SWIRLING SCORE LOSS IN APHERESIS PLATELETS FOLLOWING THE IMPLEMENTATION OF INTERCEPT PATHOGEN INACTIVATION

T Bocquet[1], A Errami[1], M Asso-Bonnet[2] and A François[2]

[1]EFS Île-de-France, Rungis [2]EFS Île-de-France, Ivry Sur Seine, France

Background: The French national blood agency (EFS) delivered about 71,000 platelets in the Parisian region in 2017 (100% in additive solution). Intercept for platelets (amotosalen + UVA, Cerus, Netherlands) has been implemented nationwide, since November 2017, to decrease the risks of contamination with bacteria and emerging pathogens (CHICK, DENGUE, WNV, etc.). Since the introduction of Intercept, we have observed an increase in the rate of premature swirling score loss in platelets from apheresis

Aims: We report here our regional experience with the premature loss of swirling score following the implementation of platelet treatment with amotosalen (INTERCEPT Blood System -IBS).

Methods: Single-donor platelet concentrates were collected by apheresis (APC) with the Trima Accel System (Terumo BCT, Lakewood, CO, USA) or MCS+ (Haemonetics, Braintree, MA, USA). Platelet additive solution (SSP+, Macopharma, Tourcoing, France) was added, with the aim of achieving a fixed plasma carryover of 37% for Trima and 40% for MCS+ (v/v). Before Intercept introduction, we adjusted target concentration and volume for APC to comply with 'Large Volume' bag sets use for IBS. Collection targets were limited to 420 ml and 7×10^{11} platelets. Platelets are labeled and treated with the Intercept device. The entire product is transferred to an illumination bag, and amotosalen solution is added. The product is then exposed to UVA (6 J/cm²) for about 6 min and stored for 6 to 16 h, with agitation on a Compound Adsorption Device integrated into a storage container (mean time: 13 h). The product is then transferred to a storage bag, quality control tests are performed, and the product is labeled and sent out to distribution sites.

Results: In accordance with French regulations, platelet concentrates routinely undergo swirling tests before their distribution. During the seven first days after the introduction of Intercept, no swirling score was reported for 8 of the 507 APC collected (1.5%), three or four days after collection. Mean platelet concentration was $1496(\pm167) \times 10^3/\mu l$, significantly higher than the mean concentration of APC delivered $1246(\pm288) \times 10^3/\mu l$. Mean pH was 6.4(±0.2), significantly lower than the mean pH obtained in routine practice (pH 6.8 ± 0.2 on day 5). As previously reported, loss of swirling score was correlated with platelet concentration and platelet content. We limited the collection target to 5.5×10^{11} platelets, to limit platelet concentrations in the final bag. This immediately restricted swirling loss, to 12 of the 5203 (0.23%) APC collected up to the end of 2017. Glucose (Glc) concentration and residual plasma determinations were systematically performed (n = 21). Mean Glc concentration was 0.62(±1.24) mmol/l: significantly lower than normally observed on day 5 (between 3 and 5 mmol/l). Mean residual plasma level was 36 (±3)%.

Summary/Conclusions: Premature losses of swirling score continues to occur (9/2858; 0.31% in January 2018) and appears to have several causes: platelet concentration during treatment, storage time for adsorption, limited volume of the treatment and adsorption bags (1 liter), plasma carryover close to the lower limit (32%) and platelet content in the final bag. Cerus has tried to improve storage conditions by increasing the volume of the treatment bag and the CAD storage container to 1.3 liters. These changes, and the use of dual storage (DS) device, may decrease the rate of swirling score loss.

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IN VITRO CHARACTERIZATION OF AMOTOSALEN-UVA PLATELET COMPONENTS STORED FOR 7 DAYS

S Yegneswaran[1], J Payrat[2], D Hanson[1], B Donnelly[1], A Erickson[1] and N Mufti[1]

[1]Cerus Corporation, Concord, CA, United States of America [2]Cerus Corporation, Amersfoort, Netherlands

Background: Platelet transfusions are important for support of thrombocytopenia during cancer therapy and organ transplant. Platelets are stored at 22–24°C for up to 5 day to limit the risk of bacterial contamination. A substantial amount of platelet components (PCs) are discarded because they expire during storage before use. Bacterial contamination and platelet storage lesions are two major issues that

continue to limit storage of platelets beyond 5 days in many geographies. Storage of PC at 22–24°C allows for proliferation of bacteria and the older PC have been associated with increased incidence of septic transfusion reactions. Amotosalen-UVA pathogen inactivation treatment (INTERCEPT™ Blood System, Cerus Concord, CA) inactivates pathogens and reduces the risk of bacterial growth in PCs during storage and therefore can facilitate storage beyond 5 days while reducing the risk of sepsis. The FDA has approved PC storage of up to 5 days from the time of collection.

Aims: To evaluate the in vitro platelet function and bacterial contamination of Amotosalen-UVA treated pooled buffy coat- and apheresis-derived platelets stored in Plasma-PAS (35:65%) for 7 days.

Methods: Eight studies were conducted in Europe and the US to evaluate platelet function and bacterial contamination of INTERCEPT-treated platelets stored up to 7 days. These studies spanned Small Volume (SV), Large Volume (LV), and Dual Storage (DS) PC processing set configurations and encompassed both buffy coat- and apheresis-derived platelets. PCs were evaluated in two different platelet additive solutions (InterSol™ and SSP+). The collection platforms for buffy coat platelets were Tacsi™ (Terumo BCT) and manual pooling methods. The Amicus™ (Fresenius Kabi) and Trima™ (Terumo BCT) separators were evaluated as collection platforms for apheresis platelets. The PC were assessed using the following parameters during storage: pH, volume, mean platelet volume (MPV), platelet count, residual leukocyte content, pO_2, pCO_2, supernatant glucose, supernatant lactate, supernatant LDH, p-selectin (CD62P) expression and swirling scores.

Results: Irrespective of the source of the platelets (apheresis or buffy coat) or manufacturing methodology, 100% of the 105 evaluated INTERCEPT-treated platelets met the EDQM pH requirement of $pH_{22°C} > 6.4$ after 7 days of storage. Secondly, 100% of the 73 treated PCs (100%) across all approved configurations met EDQM's minimum transfusable dose requirement of 2 x10^{11} platelets/unit. In vitro characterization of platelet metabolism, physical properties, activation and quality demonstrated that PCs treated with Amotosalen-UVA with SV, LV and DS processing sets displayed in vitro characteristics consistent with acceptable post-transfusion in vivo quality and hemostatic function after 7 days of storage. Bacterial cultures were performed on whole blood derived buffy coat platelets (N = 17) and apheresis platelets (N = 15), at the end of 7 days of storage using the BD Bactec™ incubation system. All PCs analyzed for the presence of bacterial contamination after 7 days of storage showed negative results, confirming the sterility of the samples.

Summary/Conclusions: These studies, combined with published clinical trials and bacterial spiking inactivation studies show that INTERCEPT treated platelets are viable and provide safety against septic risks after 7 days of storage.

P-300

COST–EFFECTIVENESS OF PATHOGEN REDUCTION TECHNOLOGY FOR PLATELETS AND PLASMA IN QUEBEC

Y Grégoire[1], G Delage[2], B Custer[3] and M Germain[1]

[1]Medical Affairs and Innovation, Héma-Québec, Québec [2]Medical Affairs and Innovation, Héma-Québec, Montréal, Canada [3]Research and Scientific Programs, Blood Systems Inc, San Francisco, United States of America

Background: Cost-effectiveness of pathogen reduction technology (PRT) for platelets and plasma was previously evaluated for Canada in 2007. One method of PRT for plasma has been approved by regulatory agencies in Canada but not yet implemented: the process for platelets is under review. An updated cost-effectiveness analysis was required for decision making in Quebec, Canada.

Aims: Evaluate the cost-effectiveness of PRT for platelets and plasma in Quebec based on recent data for costs, residual risks and medical procedures.

Methods: Cost-effectiveness of PRT was compared with current screens using Markov models to track the long term consequences of the following adverse events: human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus (HCV), human T-lymphotropic virus, syphilis, West Nile virus (WNV), bacteria, Chikungunya virus, cytomegalovirus, Trypanosoma cruzi, graft-versus-host disease, febrile non-hemolytic transfusion reactions, and transfusion-related immunomodulation. Effectiveness is evaluated in terms of quality-adjusted life-year (QALY) of recipients after transfusion. The initial model used for Canada was updated to reflect the current situation. New submodels were developed for bacteria, and for HCV (to reflect advances in medical treatment). Costs of other medical procedures were adjusted for inflation. Cost of current screens and PRT was assessed in 2015 $CAN. Residual risks for transmissible diseases, which are now estimated to be lower, were updated. Cost for lost productivity for blood recipients was included. Percentage of single-donor platelets was updated to reflect 2016 data. Two scenarios were added to evaluate the potential impact of emerging pathogens, for HIV-like and WNV-like pathogens. Residual risks for these emerging pathogens were calculated to represent multiple hypothetical scenarios based on historical data in the absence of screening tests. Cost of medical procedures for HIV-like pathogen was based on literature review for HIV and adjusted for inflation. Cost savings related to cessation of certain screening tests and of bacterial culture of platelets were included in the model.

Results: Platelets and plasma PRT was estimated to have a cost-effectiveness of $ 9.086.000/QALY (95% confidence interval (CI) approximation: 4 492 000–23 498 000) compared to currents screens for the base case model without emerging pathogens. With a peak risk similar to that in 1984 for HIV in Canada, platelet and plasma PRT was estimated to have a cost-effectiveness of $ 137.000/QALY (95% CI approximation: 86.000–215.000). For a WNV-like emerging pathogen, based on screening results for 2012–2014 in Quebec, platelet and plasma PRT was estimated to have a cost-effectiveness of $ 7.380.000/QALY (95% CI approximation: 4.201.000–15.717.000).

Summary/Conclusions: The results of this analysis found a base case value 6.5 times higher than the one reported in 2007. According to the results of the base model, platelets and plasma PRT is not a cost-effective solution in Quebec, mainly because of lower residual risks for transmissible diseases and high percentage of single-donor platelet use in Québec. However, in the event of the introduction of an emerging HIV-like pathogen, the cost-effectiveness ratio is greatly improved.

P-301

EFFECT OF ANTIOXIDANTS FOR INHIBITING BACTERIAL GROWTH IN PLATELET PRODUCTS

Y Cho[1,2,3], M Handigund[1], N Kim[1], J Lee[1], D Kim[1], H Lee[1] and S Choi[1]

[1]Laboratory Medicine, Chonbuk National University Medical School [2]Research Institute of Clinical Medicine, Chonbuk National University [3]Biomedical Research Institute, Chonbuk National University Hospital, Jeonju, Korea

Background: Bacterial contamination is known as the major infectious hazard of platelet transfusion. The patients receiving bacterially contaminated platelets are at risk depending on bacterial count in platelets. Although low numbers of bacteria contaminate platelet products initially, storage at 22°C for 5 days can allow growth, with high bacterial loads present at the time of transfusion. Many approaches to reduce infectious risk have been tried ever using blood donor screening and blood product testing to eliminate products at risk of carrying infectious microorganisms.

Aims: We evaluated the ability and effectiveness of antioxidants as platelet additive solution for inhibiting bacterial growth in platelet products.

Methods: N-acetylcysteine (NAC) and vitamin C (VC) were used as antioxidants in the study. Ten species of bacteria were used for contamination of platelets including Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mitis, Enterococcus faecalis, Enterococcus faecium, Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa. Antioxidants with variable concentrations (0 to 100 mM) were mixed with Muller-Hinton broth for measuring minimal inhibitory concentration (MIC) and maximal bactericidal concentration (MBC) following CLSI guidelines. Platelet-rich plasma (PRP) was prepared to small 30 ml platelet-storing bags from whole blood collected from normal healthy donors. While PRP spiked with 10–30 CFU/ml of each bacteria were incubating at 22°C for 5 days, small amount (100μl) of PRP were collected at 0, 2, 5 days and cultured on blood agar plates.

Results: 50 mM of NAC and 100 mM of VC were identified respectively as optimal MIC in the study. There was no difference in MIC between gram-positive and negative bacteria species. Bacterial growing was increased significantly in PRP spiked with bacteria without any antioxidants after 2 days. The growth of bacteria were inhibited by antioxidants in PRP. But depending on platelet counts, effective concentration of antioxidants was different.

Summary/Conclusions: NAC and VC can be effective materials for inhibiting bacterial growth in platelet products. For clinical use of them as component of platelet additive solutions, it is necessary for further evaluation related to platelet function and post-transfusion recovery.

P-302

PLASMA-REDUCED SINGLE DONOR APHERESIS PLATELET CONCENTRATES MANUFACTURED UNDER ROUTINE CONDITIONS FOR THE CAPTURE TRIAL: A ONE YEAR EXPERIENCE

A Doescher[1], H Baume[1], E Petershofen[1], P Schenck[1], W Gebauer[1], P Pohler[2] and A Seltsam[2]

[1]BSD-NSTOB, Oldenburg [2]BSD-NSTOB, Springe, Germany

Background: Treatment of apheresis platelet concentrates (PCs) with UVC may enhance transfusion safety of platelets with respect to contamination with pathogens.

Aims: For use in a clinical trial (CAPTURE; EudraCT No.: 2015-001035-20) single donor apheresis platelet concentrates were produced under routine conditions. Here we present the quality data of untreated, UVC-treated and y-irradiated platelet units.

Methods: 405 PCs were prepared from single donors with standard operation procedures (Amicus) using SSP+ (Macopharma, Mouvaux; France) as additive solution from February 2017 to February 2018. UVC-PCs were treated with UVC within 6 h after preparation using the THERAFLEX UV-Platelets system (Macopharma); y-PCs were y-irradiated with a minimum of 25 Gy; and control PCs (AP-PCs) were left untreated. Sampling for quality control parameters was done on day of preparation (n = 44) and at the end of shelf life (AP-PCs: n = 35, UVC-PCs: n = 44; y-PCs: n = 22). The following parameters were examined on day 0: PC volume, platelet concentrations, plasma content, residual erythrocyte and leucocyte counts. Determination of platelet concentration, pH, swirling and sterility testing was done at the end of shelf life.

Results: Mean volumes were 344 ± 16.9 ml in AP-PCs, 355 ± 8.0 ml in γ-PCs and 344 ± 14.9 ml in UVC-PCs with platelet counts of 3.1 ± 0.3/unit, 3.2 ± 0.3/unit and 3.0 ± 0.2/unit, respectively. Residual plasma concentration ranged between 30% and 39%. Residual erythrocyte and leucocyte counts met the standard specifications for PC products in Germany. At the end of shelf life, the pH value of UVC-PCs (7.27 ± 0.05) was comparable to γ-PCs (7.31 ± 0.08) and AP-PCs (7.29 ± 0.09). Tests for bacterial contamination were negative for all tested PCs.

Summary/Conclusions: Quality control data demonstrate that plasma-reduced UVC-treated apheresis PCs meet the standard specifications for PC products in Germany. No differences in quality control were observed between AP-PCs, y-PCs and UVC-PCs. The safety and efficacy of UVC-treated PCs is being evaluated in CAPTURE trial.

P-303

EFFICIENT INACTIVATION OF TRANSFUSION-RELEVANT BACTERIA SPECIES IN PLATELET CONCENTRATES USING THE THERAFLEX UV-PLATELETS SYSTEM

U Gravemann[1], F Tolksdorf[2], W Handke[1], T Müller[3] and A Seltsam[1]

[1]Research and Development, Red Cross Blood Service NSTOB, Springe [2]Macopharma, Langen [3]Red Cross Blood Service NSTOB, Springe, Germany

Background: The THERAFLEX UV-Platelets system (Macopharma) is a pathogen inactivation system for platelet concentrates (PCs) that uses UVC light only (wavelength: 254 nm) without the need of any additional photoactive compound. Inactivation efficiency has been shown for a broad range of viruses, bacteria, and protozoans. In previous studies with the first set of bacteria species of the WHO International Repository of Platelet Transfusion Relevant Bacterial Reference Strains a high inactivation capacity for clinically relevant bacteria was shown.

Aims: Aim of the current study was to investigate the bacteria inactivation efficacy of the THERAFLEX UV-Platelets system for a number of strains which have recently been added to the WHO International Repository.

Methods: PCs were produced from buffy coats using the additive solution SSP+ (Macopharma) with a residual plasma content of 35%. For inactivation kinetics, PCs (n = 3) were spiked with bacteria (Enterobacter cloacae, Morganella morganii, Proteus mirabilis Pseudomonas fluorescens, Serratia marcescens, Staphylococcus aureus or Streptococcus bovis) to a final concentration of approx.10^6 colony forming units (CFU)/ml and irradiated with increasing doses until the standard UVC dose was achieved. Samples were taken for bacterial titer determination after each irradiation step. In order to show sterility after UVC treatment, two PCs were pooled and inoculated with bacteria to a final concentration of approximately 0.3 CFU/ml. Bacteria were allowed to grow for 6 h in the PCs at 22 ± 2°C under agitation. After splitting, one PC remained untreated (growth control) while the other one was UVC-treated. After storage for seven days, samples were taken from both bags for sterility testing

by BacTALERT (Biomerieux) and for determination of the bacterial titer in the untreated control units.

Results: Dose-dependent inactivation of bacteria in PCs by treatment using the THERAFLEX UV-Platelets system was shown. Mean $\log_{10}$ reduction factors ranged from 6 to 7 for seven different investigated bacteria species. Spiked PCs (n = 12 for each bacteria species) were efficiently sterilized by UVC treatment (12/12 tested). PCs treated by the THERAFLEX UV-Platelet system remained sterile during storage for 7 days, while bacteria grew to high titers of $10^6 - 10^9$ CFU/ml in non-treated PCs.

Summary/Conclusions: The THERAFLEX UV-Platelets system efficiently inactivates a broad range of different bacteria species, including the WHO reference strains. PCs remained sterile over a storage period of 7 days. These results suggest that the UVC-based pathogen inactivation technology can significantly improve the bacterial safety of platelet transfusions.

P-304

HEMOSTATIC EFFICACY OF PATHOGEN-INACTIVATED BUFFY COAT–DERIVED PLATELET CONCENTRATES IN HEMATO-ONCOLOGICAL PATIENTS: OUTCOMES OF THE PREPARES TRIAL

P Van Der Meer[1], P Ypma[2], N van Geloven[3], R van Wordragen-Vlaswinkel[3], J van der Bom[3] and J Kerkhoffs[2]

[1]Sanquin Blood Bank, Amsterdam [2]HagaZiekenhuis, The Hague [3]Leiden University Medical Center, Leiden, Netherlands

Background: Pathogen inactivation (PI) of platelet (PLT) concentrates shows good efficacy against a broad array of viruses, bacteria and parasites. Moreover, animal studies have shown that the technology reduces alloimmunization due to HLA alloantibody formation.

Aims: As bleeding is considered to be the pivotal outcome for PLT transfusion trials, we conducted a trial comparing PI-treated PLT concentrates using the Mirasol technology (Terumo BCT, Lakewood, CO) with standard untreated PLT concentrates, with the percentage of transfusion episodes in which a > grade 2 bleeding complication (World Health Organization grading) occurred as primary outcome.

Methods: The PREPAReS study was designed as a randomized multicenter non-inferiority study using a parallel arm design. Patients aged 18 years or older were eligible if they were expected to require at least two PLT transfusions. Patients were assigned to the Control group receiving standard plasma-stored PLT concentrates, or the Study group receiving Mirasol-treated PLTs. Patients could be re-enrolled, thereby adding multiple transfusion episodes to the trial. A Transfusion Episode was defined as the time from randomization until the time the patient went off trial. PLT concentrates were prepared from pooled buffy coats, resuspended in plasma and leukoreduced by filtration. For pathogen reduction, 35 ml (500 μM) riboflavin was added within 8 h of preparation of the platelets, and exposed to UV light. PLT products were stored with gentle agitation at 20–24°C up to five days in Canada and for a maximum of seven days in the Netherlands and Norway. The Intention To Treat (ITT) analysis included all bleeding episodes from the moment of randomization on, the Per Protocol (PP) analysis included only bleeding episodes that occurred after the first platelet transfusion. Patients who were actively bleeding on the day of the first transfusion, or received more than 25% off-protocol transfusions were excluded. The PREPAReS trial was powered to demonstrate non-inferiority in the ITT analysis.

Results: Between November 2010 and April 2016, 567 transfusion episodes were randomized (283 in the Control group and 284 in the Study group; 469 unique patients), of which 11 were excluded due to active bleeding at the time of randomization, or due to gross incompliance. For the PP analysis, 37 episodes were excluded due to active bleeding at the time of the first platelet transfusion (Control, 21, Study, 16), because the patient did not receive a platelet transfusion, or because more than 25% were off-protocol transfusions (Control, 38, Study, 56), rendering 425 episodes evaluable. ITT, 51% of the patients in the Control group versus 54% in the Study group had a WHO grade ≥2 bleeding (difference 3 percentage points, 95% CI, −6 to 11), P value for non-inferiority 0.012. PP, 44% of the patients in the Control group versus 52% in the Study group had a WHO grade≥2 bleeding (difference 8 percentage points, 95 CI −2 to 18), P value for non-inferiority 0.19. No significant difference was observed for percentage of days with a grade ≥2 bleeding irrespective of type of analysis.

Summary/Conclusions: For Mirasol-treated platelets compared with untreated platelets with bleeding as primary study outcome, the non-inferiority criterion was met in the ITT analysis, but not in the PP analysis.

P-305

AMOTOSALEN/UVA TREATMENT CAN INACTIVATE KLEBSIELLA PNEUMONIAE IN WB-DERIVED PC TO EFFECTIVE STERILITY, AFTER 7 DAYS OF STORAGE

N Patel, K Tucker, S McNally, O Aguilera, P Bringmann and A Stassinopoulos

Cerus Corporation, Concord, United States of America

Background: The INTERCEPT™ Blood System for Platelets has been developed for the efficient inactivation of pathogens and leukocytes in platelet concentrates (PC). The system utilizes amotosalen and UVA light and is available for the treatment of apheresis and Whole Blood (WB) derived platelets (mostly buffy coat pools) in Europe, and the treatment of apheresis platelets in the US (TRIMA™ in 100% plasma or AMICUS™ for 65% PAS). The INTERCEPT treatment of WB-derived platelet pools is not approved in the US, where the majority of WB-derived platelets are manufactured as PRP with the Acrodose™ systems. We report here the inactivation of the fast growing, gram negative bacterium K. pneumoniae, that is commonly found in contaminated PC. K. pneumoniae was inoculated at "realistic" titers usually found in healthy volunteers in non-leukoreduced PRP pools, was allowed to proliferate and inactivation treatment was performed post-leukoreduction (Acrodose PL™). The platelets were then stored at 22C for 7 days on a platelet shaker.

Aims: The objective of the study is to evaluate the inactivation of K. pneumoniae in RRP platelets to the sterility measured by prolong storage on the units using the INTERCEPT Blood System for Platelets.

Methods: Five to six RDP units were pooled to an average platelet dose of $4.7 \pm 0.5 \times 10^{11}$ yielding approximately 315 ml of RDPs in plasma (N = 3). K. pneumoniae was grown in LB broth and each unit was spiked with ~100 cfu (Colony Forming Units). After inoculation, the contaminated units were stored in a platelet shaker incubator at 22°C for ~24 h, and were then treated in an INTERCEPT SV kit. Samples were taken: Before and after bacterial inoculation, after 24 h storage (pre and post- leukoreduction), pre and post-inactivation treatment, and at 3, 5 and 7 Days of storage. The samples were analyzed by plating on LB plates (100 μl-10 ml).

Results: Initial titers were 67–211 cfu/unit. K. pneumoniae grew to ~5.6 $\log_{10}$ cfu/ml after 24 h. Following leukoreduction, and prior to the INTERCEPT treatment, the titer was ~5.3 $\log_{10}$ cfu/ml. Following the inactivation treatment, no live bacteria were detected, corresponding to a > 6 $\log_{10}$ inactivation. No bacteria were detected after 3, 5 and 7 Days of storage, corresponding to a > 7.7 $\log_{10}$ inactivation per unit.

Summary/Conclusions: Amotosalen/UVA effectively inactivated K. pneumoniae in WB-derived platelet PRP pools manufactured with Acrodose, with effective sterility demonstrated by no detectable bacteria after 7 Days of storage. Data for pathogen reduction of Whole Blood Derived PRP Platelet by the INTERCEPT Blood System, or storage for 7 Days, has not been submitted for FDA review.

P-306

CHARACTERIZATION OF S-303/GSH PATHOGEN INACTIVATED RED BLOOD CELLS AND CONVENTIONAL RED BLOOD CELLS IN A CHRONIC TRANSFUSION CLINICAL TRIAL OF THALASSEMIA MAJOR PATIENTS

A Erickson[1], Y Aydinok[2], C Sonar[2], A Bordiga[3], L Labanca[3], M Pani[4], M Tronci[4], K Waldhaus[1] and N Mufti[1]

[1]Cerus Corporation, Concord, United States [2]Ege University Hospital Blood Bank, Izmir, Turkey [3]Blood Component Production Center, AO Citta della Salute e della Scienza di Torino [4]Azienda Ospedaliera Brotzu, Cagliari, Italy

Background: The pathogen inactivation (PI) process using amustaline (S-303) and GSH is used ex vivo to prepare red blood cell (RBC) components (RBCC) for transfusion to reduce the risk of transfusion-transmitted infection (TTI). A Phase 3 clinical trial (SPARC) was conducted in Italy and Turkey to compare the safety and efficacy of PI-RBCs compared to conventional RBCs for transfusion support of thalassemia major patients. Lifelong transfusion therapy carries the risk of transfusion transmitted infections, including HIV, hepatitis and emerging pathogens (Zika, West Nile, chikungunya, dengue viruses). The S-303/-GSH PI process robustly inactivates a broad spectrum of blood-borne pathogens and leukocytes. Validation of the PI process at the three blood centers that supported the SPARC study was completed prior to initiating production of RBC study units.

Aims: To characterize PI-RBC (Test) and conventional RBC (Control) manufactured at the three participating blood centers in Italy and Turkey for the SPARC study.

Methods: On the day of collection, CPD whole blood was processed to RBCC using manual or automated (Reveos System, Terumo BCT) methodologies for both Test and Control RBCC. Leukocyte-reduced SAG-M RBCC were stored at $4 \pm 2°C$ prior to PI treatment. RBCC were added to processing solution containing GSH followed by S-303 (final nominal concentration: 20 mM GSH/0.2 mM S-303). After 18–24 h hold at 20–25°C, RBCC were centrifuged and the treatment solution was expressed and replaced with SAG-M. RBCC were stored at $4 \pm 2°C$ prior to transfusion for up to 35 days. All Test units were sampled pre- and post-PI treatment and QC RBCC were also sampled on Day 35. Control RBC units were sampled post-production of RBCC in SAG-M.

Results: 2,210 RBCC were manufactured for the SPARC study, including 1,202 Test (178 RBCC were stored 35 days for QC, and 1,024 Test RBCC were placed in transfusion inventory) and 1,008 Control (all Control RBCC were placed in transfusion inventory). Mean component volume post-treatment was 269.4 ± 19.6 ml (Test) and 278.9 ± 22.2 ml (Control) with mean total hemoglobin content of 54.2 ± 6.0 g [37–73 g] for Test and 55.6 ± 5.9 g [35–74 g] for Control. All study units had hematocrit values within 50–70% (Test 50.4 to 68%; Control 47.4 to 68.7%). The mean RBC cell volume (MCV) was 65 to 99.9 fl for Test and 63.3 to 99.9 fl for Control. To be noted, RBCC that had an MCV <75 fl would indicate that donors with thalassemia minor or iron deficiency may have been included in the donor population for this study. After 35 days of storage, mean hemolysis was $0.21 \pm 0.15\%$ for Test QC RBCC with 1 QC RBCC exceeding 0.8%.

Summary/Conclusions: There was minimal loss of volume and hemoglobin for Test RBCC compared to Control RBCC. The range of RBCC characteristics for both Test and Control showed a large variability in product parameters such as volume, hemoglobin content and MCV. Given that each gram of hemoglobin results in transfusion of 3.7 mg of Fe, knowing the hemoglobin dose per RBCC may improve transfusion treatment and patient management for thalassemia major patients. INTERCEPT Blood System for Red Blood Cells is not approved for use.

P-307

Abstract has been withdrawn

P-308

EVALUATION OF WHOLE BLOOD DERIVED PLASMA PREPARED WITH THE AMOTOSALEN–UVA PATHOGEN INACTIVATION WITH REDUCED DEHP PLASTICS PROCESSING SETS

F Varfaj, K Waldhaus, H Evans and A Erickson

Cerus Corporation, Concord, CA, United States of America

Background: The INTERCEPT™ Blood System for Plasma is a class III medical device approved in the EU and US for the ex vivo pathogen reduction and storage of plasma for therapeutic use. The system utilizes amotosalen, with UVA light to inactivate pathogens and leukocytes. To reduce the proportion of DEHP materials in the processing set, we evaluated several materials for the manufacture of the sets with reduced levels of DEHP. Additionally, minor modifications were made to the design of the compound adsorption device (CAD) housing inlet port and plasma storage container shape.

Aims: To evaluate the in vitro function of pathogen inactivated (PI)-plasma prepared using processing sets consisting of alternate plastic materials and design changes (Test) compared to the currently approved CE marked sets (Control).

Methods: For each replicate (n = 12), 4–5 ABO-matched, whole blood derived plasma components were pooled, and 585–600 ml of the pool was processed into either Test or Control PI-plasma, and frozen within 24 h of collection. In vitro plasma function was evaluated at pre-treatment (pool), post-treatment and after ≥14 days of storage at ≤-18°C. Post-treatment residual amotosalen and twenty-four plasma function parameters were evaluated, with P-values ≤0.05 indicating a statistically significant difference between Test and Control components. Results were evaluated for conformity to the EDQM quality requirements for Fibrinogen and Factor VIII.

Results: The CAD design change resulted in lower post-CAD amotosalen in Test compared to Control (0.6 ± 0.1 vs 0.8 ± 0.2 μM, P = 0.04). Modification of the storage container reduced the thawing time of frozen plasma by approximately 2 min. After 15 ± 1 days of frozen storage, Test and Control PI-plasma, met the EDQM requirements for pathogen reduced plasma for Fibrinogen (mean ≥60% of fresh plasma) and Factor VIII (mean ≥0.5 IU/ml), with Fibrinogen retention of $84 \pm 4\%$ (Test) and $87 \pm 4\%$ (Control) relative to the pool and Factor VIII activity of 0.8 ± 0.1 IU/ml in both Test and Control components. Among all the plasma function parameters assessed, only Prothrombin Time (PT), pH, Fibrinogen, and

Factor V (FV) showed a statistically significant difference (P ≤ 0.05) between Test and Control, however the differences were not clinically relevant (mean levels for Test vs. Control were: PT, 12.2 vs 12.1 sec; pH, 7.47 vs 7.45; Fibrinogen, 2.22 vs 2.28 g/L; FV, 0.96 vs 0.93 IU/ml). Despite these differences, thrombin generation (with 5 pM tissue factor), a global coagulation function measurement, was similar between Test and Control (2014 ± 121 vs 2046 ± 84 nM*min). Additionally, key pro-coagulant and anticoagulant proteins were similar in Test and Control: mean Protein C (0.85 vs 0.86 IU/ml), Protein S (0.85 IU/ml in both), Antithrombin III (0.91 vs 0.93 IU/ml), and alpha-2-plasmin inhibitor (0.88 vs 0.90 IU/ml).

Summary/Conclusions: This evaluation demonstrated that plasma treated with amotosalen-UVA using processing sets manufactured with plastics components containing reduced levels of DEHP had lower post-treatment amotosalen levels and improved thawing times compared to currently licensed PI plasma. Test PI-plasma components retained coagulation and anticoagulation parameters and were comparable to paired Control PI-plasma, indicating that the processing sets with alternate plastics maintained plasma quality and critical in vitro hemostatic functions indicative of therapeutic efficacy.

P-309

PATHOGEN INACTIVATED DOUBLE DOSE BUFFY –COAT PLATELET CONCENTRATES OBTAINED WITH NEW PROCESSING SETS SHOW IMPROVED IN VITRO QUALITY OVER 7-DAY STORAGE

L Larsson[1], S Ohlsson[2], B Diedrich[3], M Uhlin[1] and P Sandgren[3]

[1]*Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet* [2]*Clinical Immunology and Transfusion Medicine, Karolinska University Hospital* [3]*Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden*

Background: A cost effective approach for pathogen inactivation (PI) of buffy coat (BC) pooled platelets is to treat a double dose (DD) platelet concentrate (PC) from 7–8 BC, and then split into two therapeutic transfusion doses. An "I-Platelet Pooling" (IPP) set (Kansuk, Turkey), integrating a Sepacell™ PLX-5 leukodepletion filter (Asahi Kasei, Japan) was specially designed for this purpose with 9 tubing leads, a large pooling bag (700 ml) and a temporary storage final platelet bag. Double Storage (DS) processing sets used for PI with the amotosalen/UVA light photochemical treatment (INTERCEPT™, Cerus, The Netherlands) were modified with new EVA storage bags and a larger Compound Adsorption Device (CAD) container (1.3 L versus 1 L) for the amotosalen reduction step.

Aims: An in vitro storage study was conducted over a 7-day storage period to assess platelet processing and quality improvements with later generation of disposable sets.

Methods: DD PC were obtained from pools of 8 buffy coats in additive solution (SSP+) using either standard (Fenwal) or IPP pooling sets and PI processing sets in current (1 L CAD) or new (1.3 L CAD) plastics. Platelets were treated with INTERCEPT then stored for up to 7 days. 3 study arms were compared, standard pooling set/DS current (n = 8), IPP/DS current (n = 8) and IPP/DS new (n = 14). Metabolic, functional and activation parameters were tested at days 2, 5 and 7.

Results: All tested PCs (n = 30) were in conformity with EDQM guidelines. Platelet content per split unit in the IPP/DS new series was $3.00 \pm 0.33 \times 10^{11}$, not statistically different from other product configurations tested. When compared with the current sets, the PI treatment set in new plastics more effectively maintained glucose reserves (P < 0.01), reduced lactate production (P < 0.01) resulting in higher pH (22°C) at day 7, 7.347 ± 0.034 (P < 0.01). CD62P levels were reduced (P < 0.01) throughout storage. JC-positive cells percent were maintained (P < 0.01 on day 7) and platelet responsiveness (PAC-1) expression was retained (P < 0.01 on day 7). There was, overall, no decline in ATP values and the measured platelet derived factors sCD40L, and PGDF accumulated based on their original concentration in an equivalent way in current and new plastics.

Summary/Conclusions: Processing of DD PC from 8 BC with IPP sets resulted in two therapeutic units of platelets. In vitro quality was improved over the 7 days of storage with DS sets made of new plastic materials. The shift towards anaerobic glycolysis was less pronounced and accompanied by better platelet quality and reduced activation markers.

P-310

ROBUSTNESS OF THE AMUSTALINE/GSH PATHOGEN INACTIVATION SYSTEM FOR RED BLOOD CELLS COMBINED WITH IRRADIATION

M Schott, B Warbington, G Villegas, N Mufti and A Erickson

Cerus Corporation, Concord, CA, United States of America

Background: The pathogen inactivation (PI) system using amustaline and glutathione (GSH) is being developed for the inactivation of pathogens and leukocytes in red blood cell (RBC) components. Amustaline forms adducts with nucleic acids and prevents the replication of contaminating pathogens and leukocytes. Amustaline/GSH treated RBCs are currently being evaluated in a clinical trial in Puerto Rico and the mainland US. Although leukocytes are inactivated in PI RBCs, some facilities may irradiate (IR) PI RBCs based on existing institutional practices.

Aims: To characterize the in vitro function of PI and Control RBCs with and without IR on Day 7 post donation (PD) and throughout 28–35 days of storage.

Methods: Leukocyte reduced RBCs in AS-5 were prepared from CPD whole blood collections within 24 h of donation. For each replicate (n = 6), ABO matched AS-5 RBC were pooled and split to prepare 2 Test (T) and 2 Control (C) components. T RBCs were treated with 20 mM GSH/0.2 mM amustaline while C RBCs were untreated and stored at 2–6°C. On Day 7 PD 1 T and 1 C from each replicate were gamma or x-ray IR using 25 to 50 Gray (IR-T and IR-C), the remaining T and C from each replicate was not irradiated and remained in 2–6°C storage. Sampling for analysis of in vitro parameters was done throughout storage.

Results: On Day 2, all T and C components met the EDQM criteria and contained ≥40 g Hb (C = 53–54 g, IR-C = 53 g, T = 51–54 g, IR-T = 52–53 g) and had 50–70% hematocrit (Hct) (C = 58–61%, IR-C = 58–61%, T = 61–63%, IR-T = 62–64%). After 28 and 35 days of storage all RBCs met the EDQM hemolysis criterion of ≤0.8% (Day 28: C = 0.1–0.3%, IR-C = 0.4–0.8%, T = 0.1–0.2%, IR-T = 0.2–0.5%; Day 35 C = 0.2–0.4%, T = 0.1–0.2%); hemolysis was lower in all T versus C components and IR-T was significantly lower than IR-C (P = 0.014). On Day 28 ATP values exceeded 2 μmol/g Hb for all components and T and IR-T were significantly higher than C and IR-C, respectively (C-4.6 ± 0.3; IR-C 4.3 ± 0.3; T-6.0 ± 6.5; IR-T 5.7 ± 0.5). Day 28 Extracellular K+ (mmol/L) was increased in IR components compared to non-IR components; levels were similar between IR-C and IR-T (C-47 ± 2; IR-C 72 ± 2; T-42 ± 2; IR-T-69 ± 2). IR components had similar Day 28 post-rejuvenation 2,3-DPG (μmol/g Hb; IR-C 30 ± 1 and IR-T 30 ± 2), and p50 (mm Hg; IR-C 41 ± 4 and IR-T 42 ± 3) levels. Non-IR components had Day 35 post rejuvenation 2,3-DPG (μmol/g Hb; C 31 ± 2 and T 32 ± 2), and p50 (mm Hg; C 41 ± 2 and T 43 ± 2) levels.

Summary/Conclusions: Although IR is not expected to be required in routine use, this study demonstrated the robustness of PI treatment when combined with irradiation. Irradiated PI RBC components met the EDQM guidelines for leukocyte depleted RBCs in additive solution with respect to Hct, Hb content and hemolysis at end of storage. All measured in vitro parameters of INTERCEPT treated RBCs, including ATP and glucose levels, indicate suitability for transfusion. The amustaline/GSH PI system for RBCs is not approved for use. This project has been funded in whole or in part with Federal funds from the DHHS; ASPR; BARDA; Contract No. HHSO100201600009C.

P-311

PRODUCTION OF PATHOGEN INACTIVATED PLATELET CONCENTRATES FROM POOLS OF 8 BUFFY-COATS AND DOUBLE DOSE APHERESIS

C Naegelen[1], H Isola[2], N Marpaux[3], A Dupuis[4], P Morel[5] and C Gachet[6]

[1]*Production, EFS BFC, Besançon* [2]*Production, EFS Grand EST, Strasbourg* [3]*Quality control, EFS BFC, Besançon* [4]*Quality control, EFS Grand EST, Strasbourg* [5]*EFS BFC, Besançon* [6]*EFS Grand EST, Strasbourg, France*

Background: Pathogen inactivation (PI) is an option to further reduce microbiological risks of transfusion. EFS adopted (November 2017) PI of PC with a photochemical treatment (PCT) combining Amotosalen and ultraviolet light A (UVA) (INTERCEPT™ Blood System, Cerus) at the national scale and for the entire production. Small volume (SV) and large volume (LV) processing sets are used. A Dual Storage processing set (DS) allows the preparation of 2 PC for transfusion from 7–8 Buffy-Coat (BC) pooled platelets or double dose apheresis platelets.

Aims: The objective was to evaluate in two blood centres the quality of double dose BC and apheresis platelet concentrates (BC-PC and A-PC) with a panel of in-vitro markers pre and post PCT and after storage for up to 7 days.

Methods: BC characteristics using Macopress (Macopharma) were adapted to reach an 8 BC pool volume of approximately 600 ml (including 280 ml InterSol (Fresenius

Kabi)) and 22% hematocrit before separation and leukodepletion of the PC. Apheresis (Trima, Terumo BCT) settings were adjusted to double dose collections. PC were inactivated by PCT on Day 1 and incubated with the compound Adsorption Device for 6 h (A-PC) or 16 h (BC-PC). After split into two containers, PC were stored for 7 days and assayed at days 2, 3, 5, 7 for the evaluation of platelet characteristics and quality markers.

Results: 17 BC-PC and 15 A-PC were produced and split in two storage containers. EDQM and ANSM requirements were met. Platelet content per split unit was 3.2 ± 0.4 and $3.0 \pm 0.3 \times 10^{11}$ for BC-PC and A-PC respectively. All units studied retained homogeneous and conforming pH (≥ 6.4, on average ≥ 7.0) that was stable during post PCT storage. The concentrations of glucose on day 5 for BC-PC and A-PC were 1.4 ± 0.8 mM and 3.2 ± 1.5 mM respectively. On day 7, the detection limit (<0.3 mM) was reached for BC-PC while the residual concentration was 1.3 ± 1.0 mM for A-PC. Lactate concentration increased regularly in both types of PC until day 7. MPV remained stable while LDH concentration increased from 101 ± 18 U/l on day 1 (pre-PCT) to 218 ± 43 U/l on day 7 for BC-PC and from 100 ± 26 to 180 ± 41 U/l for A-PC during the same period. P-selectin concentration increased from 25.5 ± 8.6 ng/ml on day 1 (pre-PCT) to 125.8 ± 16.6 ng/ml on day 7 for BC-PC and from 45.0 ± 13.0 to 176.8 ± 60.0 ng/ml for A-PC during the same period. Swirling was retained in all units throughout storage.

Summary/Conclusions: Using the DS processing set for PI allows obtaining two transfusion doses of about 3×10^{11} platelets each, both with buffy coat and apheresis preparation techniques. The platelet quality during storage is comparable to routinely prepared PCT PC with SV or LV sets and the use of DS reduces consumables and labor time.

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IN–VITRO STORAGE QUALITY OF PLATELET CONCENTRATES PATHOGEN INACTIVATED USING TRIPLE STORAGE PROCESSING SETS MADE OF ALTERNATE PLASTICS

L Infanti, N Tschopp-Weber, A Plattner and A Buser
Blood Donation Center Swiss Red Cross Basel, Basel, Switzerland

Background: The INTERCEPT Blood System for Platelets for pathogen reduction in platelet concentrates (PC) is routinely used in Switzerland. Suitable kits for the treatment of triple dose platelet products collected by apheresis were so far not available. The Triple Storage (TS) set for the processing of such apheresis products with large volume and high platelet content was developed to meet this need and was recently updated with alternate plastics made of EVA material with improved gas transfer properties.

Aims: The objective of this study was to evaluate the in-vitro quality parameters of PC obtained by apheresis collections of a platelet dose sufficient for 3 therapeutic units (8.0 to 10.0×10^{11} platelets) and treated using the INTERCEPT TS processing sets including containers made of alternate plastics.

Methods: Twelve triple dose collections (9.0–9.5×10^{11} platelets in 640 ml) were performed, 6 with Amicus (Fresenius Kabi) and 6 with Trima (Terumo BCT), obtaining 36 single dose PC suspended in 40% plasma/60% PAS (SSP+) and stored up to 7 days after treatment in the TS sets. Six apheresis products were treated on the day of collection with addition of 15 ml of 6 mM amotosalen and illumination with 3 J/cm² of UVA, incubated in a container with a double compound adsorption device (CAD) wafer overnight (close to 16 h) and finally split into 3 storage containers. Six apheresis products were stored overnight then treated in the same way on day 1 with subsequent short CAD incubation (slightly above 4 h). In-vitro parameters were tested pre-treatment (day 0 or 1), post-CAD incubation and split (day 1) and at days 5 and 7 of storage.

Results: The mean platelet content per single PC was $2.89 \pm 0.35 \times 10^{11}$ and the mean volume was 188 ± 10 ml (recovery through processing of 92%), meeting the EDQM requirements. pH values at 22°C ($n = 12$) at day 7 did not differ significantly from those at day 0/1 pre-processing (7.0 ± 0.1 vs. 7.1 ± 0.1). pO$_2$ increased from 11.3 ± 2.4 to 18.3 ± 3.5 mmHg ($P < 0.001$) and pCO$_2$ decreased from 4.1 ± 0.8 to 1.5 ± 0.7 mmHg ($P < 0.001$) between day 0/1 (pre-treatment) and day 7. Glucose was 26.1% of the initial concentration at day 5 and 6% at day 7. Lactate concentration increased from 3.6 ± 1.7 at day 0/1 to 12.1 ± 1.5 mg/dl at day 7 ($P < 0.001$). Bicarbonate reserves were at 40.4% of initial at day 7. Normalized ATP concentration was 68% of initial. LDH increased from 201 ± 119 at day 0/1 to 324 ± 203 U/L at day 7 ($P < 0.001$). All measured residual amotosalen concentrations post-short and long CAD incubation were <2 μM.

Summary/Conclusions: Triple dose platelet products collected by apheresis and processed with the INTERCEPT TS sets made of alternate EVA plastics exhibited satisfactory metabolic activity during 7-day storage. The EDQM requirements of platelet content, volume and pH values were met. INTERCEPT TS sets allow reducing the number of procedures, materials and labor time for pathogen inactivation treatment of PC while preserving product quality.

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EVALUATION OF AMOTOSALEN/UVA PATHOGEN INACTIVATION FOR PLASMA AND PLATELETS

MA Al-Johani, T Al-Deek, P Govindan and M Abdulmajeed
Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Center- Jeddah, Jeddah, Saudi Arabia

Background: Despite improvements in the last decades, there is still a certain risk of transfusion-transmitted pathogens in platelet concentrates. Especially the relatively high risk for bacterially contaminated platelets gives rise to concerns, but also the threats by emerging arboviruses. Pathogen inactivation technology was shown to significantly reduce the risk of transfusion-transmitted infectious diseases, specifically reducing or eliminating pathogens in platelet units, while keeping the platelet function intact. We evaluated such a technology for introduction in our blood center to enhance the blood safety for our patients.

Aims: To evaluate the quality of Amotosalen/UVA pathogen-reduced platelets and plasma as well as the bacterial inactivation efficacy of that technology in platelet units.

Methods: 4 pools of 3 whole-blood derived plasma units respectively were inactivated with the INTERCEPT Blood System (Cerus Corporation, Concord, U.S.A.), samples were taken pre- and post-inactivation to analyze the fibrinogen content, the factor VIII content by and the volume. 7 apheresis platelet units in 100% plasma and 1 pooled PRP platelet unit in 100% plasma (non-leucoreduced) were inactivated by the INTERCEPT blood system and subsequently analyzed for the platelet and volume loss, RBC and WBC content and pH. Four of these units were stored until day 7 to analyze the pH. Two additional double-dose apheresis platelet units were spiked with 300 cfu per unit with E.coli (ATCC#25922) or S.aureus (ATCC#25923), and separated into a test- and a control unit. Test units were pathogen-inactivated 24 h post spiking and analyzed for bacterial growth on agar plates until day 7 of storage to assess the inactivation efficacy. Positive controls were not treated. The species were confirmed by biochemical testing before spiking and for positive culture plates.

Results: After inactivation of plasma units the average volume loss was $8.8\% \pm 1.8$, the average fibrinogen loss was 6.3% with an average content of 1.78 g/L ± 0.26 and the factor VIII average loss was 18.3% with an average content of 0.67 IU/ml ± 0.08. The average volume loss of apheresis units post treatment was $5.0\% \pm 1.8$, the volume loss of pooled PRP platelets 4.2%. The average platelet loss post inactivation was $12.6\% \pm 2.5$ in apheresis units and 10.0% in the pooled PRP unit. The pH of all platelet units was not significantly affected by the treatment and never dropped below 6.8 at day 7 of storage. The inactivation efficacy of S.aureus was $>2.2 \times 10^8$ cfu per unit, the inactivated platelets were negative at day 7 of storage. The inactivation efficacy of E.coli was $>5.2 \times 10^7$ cfu per unit, the inactivated platelets were culture-negative at day 7 of storage. The control units had a bacterial load of 3.6×10^{10} cfu/unit for *S. aureus* and 2.4×10^9 cfu/unit for E.coli at day 7 of storage.

Summary/Conclusions: Amotosalen/UVA inactivated plasma, apheresis platelets and pooled PRP platelets passed all quality requirements with an average 7.5% loss of plasma coagulation factors and an average platelet loss of 12.3% compared to untreated controls respectively. Bacterial inactivation efficacy was fully sufficient, pointing towards enhanced safety regarding bacterial contamination.

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PATHOGEN INACTIVATION (PI) IN 100% OF PLATELET COMPONENTS AND FRESH FROZEN PLASMA TRANSFUSED IN A BRAZILIAN HOSPITAL

S Wendel, R Fontao-Wendel, M Amaral, C Oliveira, V Nunes, L Souza, R Achkar, P Scuracchio, M Brito and R Fachini
Blood Bank, Hospital Sirio Libanes, São Paulo, Brazil

Background: The INTERCEPT Blood System™ is used to inactivate a broad spectrum of viruses, bacteria, protozoan parasites, and contaminating donor leukocytes in platelet products.

Aims: We present the implementation of Intercept for all platelets and fresh frozen plasma (FFP) transfused in our hospital from March 2017 to January 2018 as a routine procedure.

Methods:

1. Apheresis: 598 single low volume (SLowV), 546 double dose (DD) and 273 single large volume (SLV) plateletapheresis were collected using a Trima® device, all leukocyte reduced (LR). Each two SLowV apheresis (same ABO) were pooled before treatment.

2. Random Donor Platelets (RDP): a total of 2201 RDP were produced from 450 ml ± 10% whole blood donation using the platelet rich plasma method. Pools of RDP with same ABO were prepared and LR with BioP 10 plus filter (Fresenius®). Both SLV and pools of 6 RDP were treated using Large Volume disposables for single INTERCEPT treatment (LV). Pools of SLowV, DD and pools of 11 RDP were treated using Dual storage disposables for double dose treatments (DS). A platelet dose has been defined as containing, as average, a total of 3.0×10^{11} platelets.

3. FFP: a total of 1694 whole blood derived plasma was prepared as FFP according to local procedures and frozen within 8 h of collection. Before treatment each 3 units of FFP (same ABO) were thawed at 37°C, pooled and treated following Intercept protocol. After treatment the pool was divided again in 3 units and re-frozen immediately at −30°C. All platelet and FFP products were treated with 150 µM and 6 mM amotosalen respectively, and 3 J/cm² UVA.

Results: A total of 1960 Intercept treatments (1399 for platelets and 561 for FFP), totalizing 2352 platelet doses (average of $3.3 \pm 0.3 \times 10^{11}$ platelets in 210 ± 22 ml, per dose) and 1683 FFP (average of 198 ± 11 ml for unit) were prepared. Only 8% of all treated platelet doses were below 3.0×10^{11} platelets. pH values were well preserved during storage (7.22 ± 0.05, 3rd day of storage as average), and all bacterial tests performed were non reactive performed on the 7th day of storage (n = 15). The platelet count increment (CCI) was analyzed after transfusion in 90 platelet doses. The CCI was $9,283 \pm 6,400$ for apheresis (n = 60) and $10,293 \pm 7,242$ for RDP (n = 30), with no statistical difference (P = 0.49). CCIs were considered very well satisfactory by our standards. There was a loss of 27 ± 9 ml, around 20% less of factor VIII activity and 10% less of fibrinogen for FFP after treatment; still they were in accordance with PI products.

Summary/Conclusions: In addition to the improved microbiological safety to our receptors and blood supply, we've achieved a better standardization for all platelet and FFP components due to a more homogeneous product. In addition, we were also able to suspend routine bacterial contamination tests and more recently, Brazilian regulatory agency approved replacement of gamma irradiation to Intercept for prevention of graft-versus-host disease.

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Abstract has been withdrawn

P-316
EVALUATION OF THE AMOTOSALEN/UVA PATHOGEN INACTIVATION METHOD FOR PLATELETS FOR ROUTINE USE

TT Mustafa

Transfusion Medicine, National Guard – Saudi Arabia, Alhasa, Saudi Arabia

Background: Bacterial contamination of platelets is one of the major threats for blood safety, approx. 1 of 1500 platelet units is potentially contaminated. That risk may even be higher since evaluations were conducted with culture based methods, which are known to have a high false negative rate. Even receiving a contaminated unit does not necessarily cause a bacterial sepsis, the recipients of platelet transfusions are often immunocompromised or critically ill, so bacterial contaminations may have problematic consequences for the health status. Pathogen inactivation is a technology developed to reduce the risk of transfusion-transmitted infections. National hemovigilance data of several France, Belgium and Switzerland, as well as several hemovigilance studies, show efficient prevention of transfusion-transmitted bacterial sepsis.

Aims: Evaluation of the amotosalen/UVA pathogen inactivation technology to mitigate the risk of transfusion-transmitted bacterial contamination of platelets using a gram-negative and a gram-positive organism playing an important role in transfusion-transmitted bacterial sepsis.

Methods: Three therapeutic apheresis platelet units ($>3 \times 10^{12}$ platelets/unit) in 100% plasma were collected. 1 h post collection, two units were spiked with approx. 2×10^3 cfu per bag with S.aureus (ATCC# 25923) and E.coli (ATCC# 25922) respectively. The third unit served as control. At day 1 post collection (16–20 h post spiking) samples for testing were taken followed by pathogen inactivation of all units with the INTERCEPT Blood System (Cerus Corporation, U.S.A.) using the Large Volume Processing Kit for Platelets. Post inactivation, the units were incubated until

day 7, taking samples for further analysis at day 5 and day 7. Bacterial growth was detected with a BacT/ALERT automated blood culture system (Biomerieux, France). Platelet count, platelet volume and pH were assessed at day 1, day 5 and day 7 with standard procedures.

Results: The average pH at day 5 was 6.9 ± 0.1 (drop of 2% from day 1), at day 7 6.5 ± 0.3 (drop of 7.8% from day 1); the pH of each unit never dropped below 6.2 during the course of 7 d storage. The platelet count per bag did not change significantly during 7 d storage, the average volume loss was negligible ($1 \pm 0.3\%$ at day 5 and $2 \pm 0.1\%$ at day 7). Bacterial growth was detected at day 1 before pathogen inactivation in the E.coli and S.aureus units, but not in the control unit. At day 5 and 7 of storage, no bacterial growth was detected in blood cultures of all units, showing sterility of the units formerly spiked with bacteria.

Summary/Conclusions: Units spiked with E.coli and S.aureus were successfully inactivated by amotosalen/UVA pathogen inactivation, staying sterile for 6 more days of storage post inactivation. The quality parameters of all units were within specifications, but we recognized a significant drop of pH between day 5 and day 7 of storage.

P-317
ANALYSIS OF 1000 PLATELET CONCENTRATES (PCS) USED AS CLINICAL INVESTIGATIONAL PRODUCTS FOR THE CAPTURE CLINICAL TRIAL TESTING UVC TREATED (THERAFLEX) PCS VS. UNTREATED CONTROL PCS

V Brixner[1], S Dombos[1], M Karatas[1], H Pfeiffer[1], M Schmidt[1], F Tolksdorf[2], P Pohler[3], A Seltsam[3] and E Seifried[1]

[1]German Red Cross Blood Donation Center Baden Wurttemberg – Hessen gGmbH, Frankfurt [2]Maco Pharma International, Langen, [3]German Red Cross Blood Service NSTOB, Springe, Germany

Background: Pathogen reduction technology may enhance microbial safety of platelet transfusion by reducing bacterial and viral contamination. We established the manufacturing of UVC-treated buffy coat derived platelet concentrates under routine conditions.

Aims: The objective of this study was to evaluate potential differences in product characteristics between UVC treated (TEST group) and non UVC treated (CONTROL group) platelet concentrates (PCs) used as clinical investigational products for the CAPTURE (Clinical Assessment of Platelets Treated with UVC in Relation to Established Preparations) clinical trial.

Methods: For this study, leukoreduced and plasma-reduced PCs were prepared from five buffy coats (BCs) using 280 ml SSP+ additive solution (Macopharma). We established the preparation of TEST PCs treated with the THERAFLEX UV-Platelets system (Macopharma) within 6 h after PC preparation and untreated CONTROL PCs stored in the THERAFLEX UV Storage Bag. In vitro parameters (volume, thrombocyte concentration, total protein concentration) were compared by an unpaired t-test. A P value of ≤0.05 was considered statistically significant.

Results: UVC-treated PCs [n = 445] showed no significant differences compared to untreated CONTROL PCs [n = 555] regarding thrombocyte concentration [TEST 957 ± 128 x10⁹/ml, CONTROL 950 ± 127 x10⁹/ml] and total protein concentration [TEST 21.7 ± 1.4 g/dl, CONTROL 21.6 ± 1.6].UVC treated PCs showed a small but significant [P < 0.001] lower volume [TEST 353 ± 9 ml vs CONTROL 356 ± 8 ml] than untreated PCs. There was no significant difference in storage time until transfusion between TEST and CONTROL PCs [total n = 116]. Mean age at time of transfusion was 2.6 days for TEST-PCs versus 2.5 days for CONTROL-PCs.

Summary/Conclusions: The differences between TEST and CONTROL PCs for platelet concentration, total protein concentration and storage duration are not statistically significant. The average difference in volume between TEST and CONTROL PCs was statistically significant, however with a difference of 3 ml this is considered to be non-significant from a clinical point of view.

P-318
ASSESSMENT OF CRYOPRECIPITATE PRODUCED FROM MIRASOL-TREATED PLASMA

S Yonemura[1], M Shipps[1], M Cardoso[2] and S Marschner[1]

[1]Scientific Affairs, Terumo BCT, Lakewood, United States of America [2]Medical Affairs, Terumo BCT, Zaventem, Belgium

Background: Cryoprecipitate was first developed in the 1960s to treat congenital clotting factor deficiencies such as hemophilia A and von Willebrand disease, but its

use declined as recombinant factors and virus-inactivated single-factor concentrates became available. Today, its primary indication is for control of bleeding associated with fibrinogen deficiency. Because fibrinogen is one of the first clotting factors to become depleted during major bleeding from trauma, there is renewed interest in the role cryoprecipitate can play in massive transfusion protocols (Curry, BJA, 2015). As with any other blood product, cryoprecipitate carries the risk of transfusion-transmissible disease. Technologies such as the Mirasol® System have been introduced to mitigate this risk. The Mirasol system uses riboflavin (vitamin B2) and ultraviolet light to modify nucleic acids so that pathogens and white blood cells are rendered unable to replicate (Kumar, Photochemistry and Photobiology, 2004; Marschner, Transfusion, 2010). Pathogen reduction of plasma used to manufacture cryoprecipitate can improve the safety profile, but the effect of additional processing on the end product must be considered. Specifically, an effective dose of procoagulant factors must be assured.

Aims: This feasibility study evaluated the protein content of single units of cryoprecipitate produced from Mirasol-treated plasma against European Directorate for the Quality of Medicines & Health Care (EDQM) criteria for factor VIII (FVIII) and fibrinogen.

Methods: A total of 20 type-matched, whole blood-derived fresh plasma units from healthy donors were pooled and split to produce N = 10 paired 250 ml Test and Control units. Control units were held on ice while Test units were processed according to the Mirasol System Instructions for Use. Test and Control units were simultaneously flash-frozen within 8 h of collection to produce fresh frozen plasma (FFP). Test units were protected from ambient light, but otherwise the standard operating procedures for cryoprecipitate production (Bonfils Blood Center, Denver, CO) were followed to produce paired cryoprecipitate units. Briefly, FFP units were thawed overnight in a standard blood banking refrigerator, cryoprecipitate was harvested by centrifugation, and individual cryoprecipitate units were flash-frozen and stored at −80°C until analysis. Thawed units were analyzed for FVIII and fibrinogen measurement.

Results: FVIII levels were 104 ± 21 (range 77–147) and 188 ± 31 (155–260) IU/unit for Test and Control units, respectively. Fibrinogen was measured at 184 ± 41 (139–265) mg/unit for Test and 251 ± 52 (198–339) mg/unit for Control. All Test units met the EDQM criterion for FVIII (≥70 IU/unit), while 9/10 met the criterion for fibrinogen (≥140 mg/unit). All control units met both EDQM criteria.

Summary/Conclusions: Although FVIII and fibrinogen levels were lower in Mirasol-treated cryoprecipitate units compared to their paired controls, all units met the EDQM criterion for FVIII and 90% met the criterion for fibrinogen; the unit not meeting the fibrinogen criterion was short by 1 mg. Since cryoprecipitate is typically pooled, it is expected that quality control criteria can routinely be met for the end product. Further characterization and optimization of Mirasol-treated cryoprecipitate is warranted.

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Abstract has been withdrawn

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RETENTION OF THROMBIN GENERATION ACTIVITY IN POOLED WHOLE BLOOD-DERIVED PLASMA AFTER AMOTOSALEN–UVA PATHOGEN INACTIVATION AND STORAGE IS INDEPENDENT OF ABO BLOOD GROUPS

C Ravanat[1], A Dupuis[1], N Marpaux[2], C Naegelen[2], G Mourey[2,3], H Isola[1], M Laforêt[1], P Morel[2,3] and C Gachet[1]

[1]Université de Strasbourg, INSERM, EFS Grand Est, BPPS UMR-S1255, FMTS, Strasbourg [2]EFS Bourgogne-Franche-Comté, UMR 1098 [3]Université Bourgogne-Franche-Comté, INSERM, Besançon, France

Background: Small batch-pooled whole blood (WB)-derived plasma is an important source of therapeutic plasma (TP), but carries an increased risk of transfusion-transmitted infection due to multiple donor exposures. This risk can be mitigated by amotosalen-UVA pathogen inactivation (AUVA-PI). However, a reduction of up to 17–30% in specific coagulation factors has been described for all known methods of PI in plasma (Ramsey, Sem Thromb Hemost, 2016), FVIII being the most strongly affected. Currently, no test is used routinely to assess if a reduction in coagulation factors due to PI has a real impact on the global hemostasis potential of TP.

Aims: Measurement of thrombin generation (TG) provides an integrated assessment of the hemostatic potential of plasma. Our objective was to characterize TG in

AUVA-plasma prepared from WB collections stored 19 h before PI, in order to determine its therapeutic efficacy. The ABO blood group type is known to affect FVIII levels with a 20% decrease in plasma from group O compared to non-group O individuals. Therefore, we evaluated TG in AUVA-plasma from group O donors, as compared to non-group O donors, to assess the impact of lower FVIII levels on the hemostatic capacity.

Methods: WB donations stored overnight were processed to prepare leukocyte-depleted plasma pools (5 units, 1,300 ml), which were divided into two batches and treated with AUVA. The resulting 6 plasma units per pool (200 ml) were frozen and stored (−25°C) within 19 h of WB collection. Pools (10 group O and 30 non-group O donors) were prepared and hemostatic quality was evaluated before and after PI treatment and storage (1–14 days, 6 and 12 months). TG was performed with a low concentration of tissue factor (1 pM) to increase the sensitivity of the detection of potential effects of AUVA treatment, in particular for FVIII activity.

Results: At all-time points tested, the 40 pools prepared from WB met the French guidelines for TP. FVIII levels were 20% lower in the blood group O as compared to the non-group-O plasma units (0.80 ± 0.11 vs 1.01 ± 0.12 IU/ml) and a similar decrease of approximately 30% after AUVA treatment and 12 months storage was observed in both cases (0.50 ± 0.06 vs 0.65 ± 0.09 IU/ml). The total amount of thrombin generated reflected by the endogenous thrombin potential (ETP, nM thrombin × min), were nevertheless not significant, (ETP group O vs non-group O: before AUVA 1531 ± 133 vs 1548 ± 114 P = 0.725; after AUVA and 12 months storage 1480 ± 124 vs 1519 ± 117 P = 0.398). Although a trend to decrease was observed over 12 months, the values of ETP lay within the reference range (ETP: 1170 - 2182).

Summary/Conclusions: Despite diminished FVIII activity in group O donor plasma, the TG capacity was conserved equally as well as in non-group O donor plasma, demonstrating no significant effect of photochemical treatment and storage on the global hemostatic properties. Whatever the ABO blood group, pathogen-inactivated WB-derived plasma prepared and frozen within 19 h of collection represents an alternative or supplement for apheresis plasma prepared as fresh frozen plasma, and conforms to the criteria of the French regulatory authorities.

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LOCAL PREPARATION OF VIRUS INACTIVATED CRYOPRECIPITATE IN DEVELOPING COUNTRIES: AN UPDATE ON THE GLOBAL INITIATIVE

J Faber

Luxembourg Haemophilia Association, Luxembourg, Luxembourg

Background: In developing countries (with low Human Development Index, l-HDI), treatment of patients with bleeding disorders is inadequate or absent and this critical situation has not changed significantly in the past 20–30 years despite several initiatives set up by different national and international organizations. Past experience has shown that industrially manufactured clotting factor concentrates (CFC) cannot solve the problems in l-HDI, if they are used as the sole mean in the treatment of bleeding patients.

Aims: Recently, in many resource limited countries significant developments have occurred which have the potential to change the existing situation in therapy delivery: blood systems (e.g. blood services and blood centers) in many l-HDI countries have tangibly improved and novel technologies for virus inactivation (VI) of blood components are marketed (using amotosalen, riboflavin, solvent-detergent,. . .).

Methods: In a few l-HDI countries, local preparation of virus inactivated cryoprecipitate (Cryo-VI) has been introduced and it has proven to be a safe, effective therapeutic for patients with bleeding disorders, at an affordable cost. Nevertheless, the use of VI-technology rendering cryoprecipitate safe remains very limited; therefore, major coordinated actions are undertaken to promote Cryo-VI in l-HDI and to facilitate implementation of local preparation of safe cryo. End of 2016, a Global Initiative on local production of safe haemostatic products to treat patients with bleeding disorders in l-HDI countries has been launched: it is based on collaboration with international partnering organizations (like WHO, ISBT and others) and national stakeholders in l-HDI (e.g. authorities, blood suppliers, patient associations). The core interventions in the Global Initiative are: 1. revise and update standards and guidelines on "anti-hemophilic" treatment; 2. give high priority in existing blood policies and strategies to "local preparation of virus inactivated cryoprecipitate in developing countries" ("Local Cryo-VI in l-HDI"); 3. organize strong advocacy and promotion of it; 4. run a pilot project in six pilot sites on three continents; 5. establish an expansion program; 6. support activities for implementation and sustainability of "Local Cryo-VI in l-HDI".

Results: Most of the standard setting organizations have taken up Cryo-VI in their standards and guidelines for the treatment of patients with bleeding disorders: an update will be given. The pilot study has started in January 2018 with recruitment of 6 pilot sites on 3 continents. Audits and training are underway, individual production targets have been agreed,... The most recent information on progress is being presented.

Summary/Conclusions: The Global Initiative on "Local Cryo-VI in l-HDI" is complementary to existing relief activities (e.g. product donations by industry) and will result in additional supply of safe and effective haemostatic products to treat patients with bleeding disorders in resource limited countries. At the same time, it will contribute to significantly lower the incidence of inhibitor formation (neutralizing allo-antibodies to injected F.VIII) in previously untreated patients with severe hemophilia A. The Global Initiative on "Local Cryo-VI in l-HDI" is an ongoing programme, it is making stepwise progress and updates will be given at regular intervals.

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FELINE CALICIVIRUS, A MODEL VIRUS FOR HEPATITIS E VIRUS, IS EFFICIENTLY INACTIVATED BY THE THERAFLEX UV-PLATELETS SYSTEM

U Gravemann[1], W Handke[1], F Tolksdorf[2] and A Seltsam[1]

[1]Research and Development, Red Cross Blood Service NSTOB, Springe [2]Macopharma, Langen, Germany

Background: Hepatitis E is a viral hepatitis caused by infection with a small, non-enveloped, single-stranded RNA virus called hepatitis E virus (HEV). It was shown in the past that HEV is transfusion transmissible. Although most cases of HEV genotype 3 infection are asymptomatic or mild and self-limiting, severe cases of hepatitis and chronic liver disease were reported in immunosuppressed patients.

Aims: Up to now, a reliable in-vitro infectivity system for HEV has not yet been established. In this study, we used the feline calicivirus (FCV), a non-enveloped single-stranded RNA virus, as model for inactivation of non-enveloped viruses, in order to assess the inactivation capacity of the UVC-based THERAFLEX UV-Platelets pathogen inactivation system for HEV-like viruses in platelet concentrates (PCs).

Methods: Plasma reduced PCs from buffy coats (35% plasma in additive solution SSP+, Macopharma) were spiked with virus suspension (10% v/v). PCs (n = 6, 350 ml) were then UVC-irradiated on the Macotronic UV machine (Macopharma) and samples were taken after spiking (load and hold sample) and after illumination with different tlsb light doses (0.05, 0.1, 0.15 and 0.2 (standard) J/cm^2). The titre of the FCV (strain FCV-2280, ATCC VR-2057) was determined as tissue culture infective dose (TCID$_{50}$) by endpoint titration in microtitre plate assays on feline kidney cell line CRFK (ATCC CCL-94).

Results: FCV was dose-dependently inactivated by the THERAFLEX-UV Platelets system. After spiking a titer of 5.5 ± 0.5 log$_{10}$ TCID$_{50}$/ml was received in the PCs. At a UVC dose of 0.2 J/cm^2 the titer was reduced to 2.5 ± 0.5 log$_{10}$ TCID$_{50}$/ml, resulting in a log$_{10}$ reduction factor of 3.0 ± 0.2.

Summary/Conclusions: Several non-enveloped viruses are not inactivated by currently available pathogen-inactivation systems for PCs. It was shown in this investigation that the THERAFLEX-UV Platelets system has the potential to inactivate non-enveloped viruses like FCV.

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MERS CORONAVIRUS IS EFFICIENTLY INACTIVATED IN PLATELET CONCENTRATES BY UVC LIGHT USING THE THERAFLEX UV PLATELETS TECHNOLOGY

U Gravemann[1], M Eickmann[2], W Handke[1], F Tolksdorf[3] and A Seltsam[1]

[1]Research and Development, Red Cross Blood Service NSTOB, Springe [2]Institute of Virology, Philipps-Universität, Marburg [3]Macopharma, Langen, Germany

Background: Middle East Respiratory Syndrome coronavirus (MERS-CoV) was first identified in 2012 and was most likely a zoonotic transmission event from camels. MERS-CoV causes severe lower respiratory tract infections that can result in pneumonia and multiorgan failure, particularly in patients with underlying comorbidities and the elderly. Most cases of MERS-CoV infections have arisen in the Middle East, particularly the Kingdom of Saudi Arabia and in the Republic of Korea but two documented cases in travelers have been reported in the United States. Thus, it can be expected that MERS-CoV will continue to emerge in Western countries being imported by travelers entering the countries or returning home.

Aims: This study aimed to investigate the efficacy of the THERAFLEX UV-Platelets system to inactivate MERS-CoV in platelet concentrates (PCs). The THERAFLEX UV-Platelets system (Macopharma) uses UVC light only without the need of any additional photoactive compound.

Methods: Plasma reduced PCs from 5 BCs (35% plasma in additive solution SSP+) were spiked with virus suspension (10% v/v). PCs (n = 2, 375 ml) were then UVC-irradiated on the Macotronic UV machine (Macopharma) and samples were taken after spiking (load and hold sample) and after illumination with different light doses (0.05, 0.1, 0.15 and 0.2 (standard) J/cm^2). The titre of the MERS-CoV (strain HCoV-EMC, Ron A. Fouchier) was determined as tissue culture infective dose (TCID$_{50}$) by endpoint titration in microtitre plate assays on Vero E6 cells (ATCC CCL-22).

Results: The results of the infectivity assay demonstrated that UVC irradiation dose-dependently inactivated MERS-CoV. After spiking a MERS-CoV titer of 6.43 (bag no. 1) and 6.37 (bag no. 2) log$_{10}$ TCID$_{50}$/ml was received in the PCs. At a UVC dose of 0.15 J/cm^2 and higher MERS-CoV was inactivated down to the detection limit of the system (2.67 log$_{10}$ TCID$_{50}$/ml), resulting in log$_{10}$ reduction factors of ≥3.8 (bag no. 1) and ≥3.7 (bag no. 2).

Summary/Conclusions: Our results demonstrate that the THERAFLEX UV-Platelets procedure is an effective technology to inactivate MERS-CoV in contaminated PCs.

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MERS CORONAVIRUS IS EFFICIENTLY INACTIVATED IN HUMAN PLASMA BY MB/LIGHT USING THE THERAFLEX MB PLASMA TECHNOLOGY

W Handke[1], M Eickmann[2], U Gravemann[1], S Reichenberg[3] and A Seltsam[1]

[1]Research and Development, Red Cross Blood Service NSTOB, Springe [2]Institute of Virology, Philipps-Universität, Marburg [3]Macopharma, Langen, Germany

Background: Middle East Respiratory Syndrome coronavirus (MERS-CoV) was first identified in 2012 and was most likely a zoonotic transmission event from camels. MERS-CoV causes severe lower respiratory tract infections that can result in pneumonia and multiorgan failure, particularly in patients with underlying comorbidities and the elderly. Most cases of MERS-CoV infections have arisen in the Middle East, particularly the Kingdom of Saudi Arabia and in the Republic of Korea but two documented cases in travelers have been reported in the United States. Thus, it can be expected that MERS-CoV will continue to emerge in Western countries being imported by travelers entering the countries or returning home.

Aims: This study aimed to investigate the efficacy of the THERAFLEX MB Plasma system to inactivate MERS-CoV in human plasma. The THERAFLEX MB Plasma system (Macopharma) uses methylene blue (MB) in combination with visible light for reduction of pathogen infectivity in plasma.

Methods: Leukodepleted plasma was prepared from whole blood using standard blood banking technology. Plasma units (n = 2) were spiked with virus suspension (10% v/v). MB/light treatment was done according to the manufacturer's instructions using the Macotronic B2 illumination device. Samples were taken after spiking (load and hold sample) and after illumination with different light doses (30, 60, 90 and 120 (standard) J/cm^2). The titer of MERS-CoV (strain HCoV-EMC, Ron A. Fouchier) was determined as tissue culture infective dose (TCID$_{50}$) by endpoint titration on Vero E6 cells (ATCC CCL-22).

Results: After spiking a MERS-CoV titer of 5.95 (bag no. 1) and 6.13 (bag no. 2) log$_{10}$ TCID$_{50}$/ml was received in the plasma units. Already with the lowest tested light dose of 30 J/cm^2 MERS-CoV was inactivated down to the detection limit of the system (2.67 log$_{10}$ TCID$_{50}$/ml), resulting in log$_{10}$ reduction factors of ≥3.3 (bag no. 1) and ≥3.5 (bag no. 2).

Summary/Conclusions: Our results demonstrate that the THERAFLEX MB-Plasma procedure is an effective technology to inactivate MERS-CoV in contaminated plasma units.

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EBOLAVIRUS IS EFFICIENTLY INACTIVATED IN HUMAN PLASMA BY MB/LIGHT USING THE THERAFLEX MB PLASMA TECHNOLOGY

W Handke[1], M Eickmann[2], U Gravemann[1], S Reichenberg[3] and A Seltsam[1]

[1]Research and Development, Red Cross Blood Service NSTOB, Springe [2]Institute of Virology, Philipps-Universität, Marburg [3]Macopharma, Langen, Germany

Background: Ebolavirus (EBOV) disease is a severe, often fatal illness, with a death rate of up to 90% caused by EBOV, a member of the filovirus family. The recent outbreaks of EBOV disease in West Africa had devastated Guinea, Liberia, and Sierra Leone, causing almost 30,000 human infections with over 11,000 fatalities.
Aims: This study aimed to investigate the efficacy of the THERAFLEX MB Plasma system to inactivate EBOV in human plasma. The THERAFLEX MB Plasma system (Macopharma) uses methylene blue (MB) in combination with visible light for reduction of pathogen infectivity in plasma.
Methods: Leukodepleted plasma was prepared from whole blood using standard blood banking technology. Plasma units (n = 2) were spiked with virus suspension (10% v/v). MB/light treatment was done according to the manufacturer's instructions using the Macotronic B2 illumination device. Samples were taken after spiking (load and hold sample) and after illumination with different light doses (30, 60, 90 and 120 (standard) J/cm^2). The titer of Zaire EBOV (strain Mayinga-76) was determined as tissue culture infective dose (TCID50) by endpoint titration on Vero E6 cells (ATCC CCL-22).
Results: After spiking an EBOV titer of 6.85 (bag no. 1) and 6.99 (bag no. 2) $\log_{10}$ $TCID_{50}$/ml was received in the plasma units. Already with a light dose of 30 J/cm^2 (bag no. 1) or 60 J/cm^2 (bag no. 2) EBOV was inactivated down to the detection limit of the system, resulting in $\log_{10}$ reduction factors of ≥ 4.7 for both bags.
Summary/Conclusions: Our results demonstrate that the THERAFLEX MB-Plasma procedure is an effective technology to inactivate EBOV in contaminated plasma.

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EBOLAVIRUS IS EFFICIENTLY INACTIVATED IN PLATELET CONCENTRATES BY UVC LIGHT USING THE THERAFLEX UV PLATELETS TECHNOLOGY

U Gravemann[1], M Eickmann[2], W Handke[1], F Tolksdorf[3] and A Seltsam[1]

[1]Research and Development, Red Cross Blood Service NSTOB, Springe [2]Institute of Virology, Philipps-Universität, Marburg, [3]Macopharma, Langen, Germany

Background: Ebolavirus (EBOV) disease is a severe, often fatal illness, with a death rate of up to 90% caused by EBOV, a member of the filovirus family. The recent outbreaks of EBOV disease in West Africa had devastated Guinea, Liberia, and Sierra Leone, causing almost 30,000 human infections with over 11,000 fatalities.
Aims: This study aimed to investigate the efficacy of the THERAFLEX UV-Platelets system to inactivate EBOV in platelet concentrates (PCs). The THERAFLEX UV-Platelets system (Macopharma) uses UVC light only without the need of any additional photoactive compound.
Methods: Plasma reduced PCs from 5 BCs (35% plasma in additive solution SSP+) were spiked with virus suspension (10% v/v). PCs (n = 2, 375 ml) were then UVC-irradiated on the Macotronic UV machine (Macopharma) and samples were taken after spiking (load and hold sample) and after illumination with different light doses (0.05, 0.1, 0.15 and 0.2 (standard) J/cm^2). The titre of the Zaire EBOV (strain Mayinga-76) was determined as tissue culture infective dose ($TCID_{50}$) by endpoint titration in microtitre plate assays on Vero E6 cells (ATCC CCL-22).
Results: The results of the infectivity assay demonstrated that UVC irradiation dose-dependently inactivated EBOV. After spiking an EBOV titer of 6.84 (bag no. 1) and 6.96 (bag no. 2) $\log_{10}$ $TCID_{50}$/ml was received in the PCs. At a UVC dose of 0.15 J/cm^2 and higher EBOV was inactivated down to the detection limit of the system (2.37 $\log_{10}$ $TCID_{50}$/ml), resulting in $\log_{10}$ reduction factors of ≥ 4.5 (bag no. 1) and ≥ 4.6 (bag no. 2).
Summary/Conclusions: Our results demonstrate that the THERAFLEX UV-Platelets procedure is an effective technology to inactivate EBOV in contaminated PCs.

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CRYOPRESERVED PLATELETS – A NOVEL APPROACH FOR DELIVERY

R Charlewood[1], S Kirwan[1] and V Slyshkov[2]

[1]New Zealand Blood Service, Auckland, New Zealand [2]National Component Development Laboratory, New Zealand Blood Service, Auckland, New Zealand

Background: Platelets can be cryopreserved using 5% dimethylsulphoxide (DMSO), the same cryoprotectant used in stem cell cryopreservation. To minimise DMSO toxicity, the initial platelet component with added DMSO is centrifuged and the supernatant removed, leaving a platelet plug and 15–20 ml plasma with 5% DMSO. The frozen platelets are thawed but are too concentrated to infuse, requiring reconstitution in either plasma or platelet additive solution (resuspending fluid). Current methods require either that the resuspending fluid be sterile docked onto the platelet bag, or that the bags are spiked and the resuspending fluid run into the platelet bag. This has implications for storage, ease of use and regulatory compliance.
Aims: To demonstrate that cryopreserved platelets, frozen in the same bag as plasma but separated by a clip, are equivalent in platelet surface markers by flow cytometry and by functional clot formation using thromboelastography (TEG); and to demonstrate no temperature differences between the two compartments when thawing the component.
Methods: Twelve apheresis irradiated platelet doses were processed following bacterial testing at 36 h post-collection. Immediately prior to cryopreservation, each platelet dose was sampled and tested for AnnexinV and CD62p expression as well as R time (time to clot) and maximum amplitude (MA) (clot strength). Six doses were processed using standard techniques using MacoPharma dry bags for frozen storage and without resuspension of the platelet plug post centrifugation prior to freezing. The second set of six doses were processed in the same way but
using Cryostore bags for frozen storage
the platelet plug was resuspended prior to freezing (in 15–20 ml 5% DMSO)
a WeLoc clip was applied, isolating the resuspended platelet plug in the bottom half of the bag
100 ml of plasma run into the top half of the bag via sterile docking prior to freezing.
The first set of six doses were thawed and reconstituted with FFP. The second set of six doses were thawed and reconstituted in the contiguous plasma. Post-thaw samples from each bag were tested for platelet count, CD62p, Annexin V, R-time and MA assays. Separately, two units of platelets were frozen then thawed using the WeLoc® bag clips with temperature probes in the smaller (platelet) and larger (plasma) portions of the bag, monitoring the temperature during thawing.
Results: All components of both arms met the volume and post-thaw recovery criteria. The second arm had a better post-thaw recovery (83% vs 70%). There were no significant differences between the two arms for CD62P and AnnexinV on flow cytometry, nor MA on TEG, between the two arms. R-time trended towards being slightly longer in the second set of doses (mean of 4.4 min vs 3.8 in the standard arm, P = 0.06) (normal: 5–10 min). Thawing showed no difference in temperature between the two portions in the bags separated by the WeLoc clip.
Summary/Conclusions: This study has shown no significant changes in moving from a standard preparation to the novel method, where the platelets are resuspended prior to freezing and are frozen in the same bag as the plasma for resuspension.

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FLOW CYTOMETRIC MEASUREMENT OF CD41/CD61, CD42B PLATELET RECEPTORS AND PLATELET FACTOR 3 ACTIVITY DURING LYOPHILIZED INFUSIBLE PLATELET MEMBRANE PREPARATION

S Nasiri and K Tekeh

IBTO-Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: The short life time of human platelet units has led to a chronic shortage of fresh platelets in blood transfusion centers. Many approaches have been investigated experimentally to produce new hemostatically active platelet products that are capable of long term storage. Infusible platelet membrane (IPM) prepared from fresh or outdated human platelets have been developed as an alternative to standard platelet concentrates, with the additional advantage of long shelf life.
Aims: The aim of this study was to measure presence of CD41/CD61, CD42b platelet receptors and platelet factor 3 (PF3) activity during IPM preparation.
Methods: After pooling of fresh platelet concentrates, freeze-thawing procedure was performed for lysis of platelets. For removal of contaminants washing step was

applied and then IPM was formulated with sucrose 1 M and human serum albumin 1% before lyophilization in a sterile condition. Flow cytometric analysis and PF3 assay were carried out.

Results: Flow cytometric analysis of CD41, CD61 and CD42b found 45.9%, 51.3% and 44.4% with PF3 activity of 39% after lyophilization step of IPM in contrast to starting fresh pooled platelet concentrates with 81.5%, 87.5% and 81.1% respectively with 100% PF3 activity.

Summary/Conclusions: The results showed that lyophilized IPM product can preserve major adhesion (CD42b) and aggregation (CD41/CD61) platelet receptors and may retain PF3 activity at acceptable level which demonstrates hemostatic property of the lyophilized IPM. In brief, although much remains to be investigated, the success of such investigations will affect patients' care in transfusion medicine.

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DUALITY OF CRYOPRESERVED PLATELETS AND PLATELET CONCENTRATES IS RELATED TO PLASMA CLOTTING FACTOR ACTIVITY

I Vysochin[1], A Berkovskiy[2], V Khvatov[1], E Kobzeva[1] and A Kostin[1]
[1]Sklifosovsky Research Institute of Emergency Medicine [2]Research Center for Hematology, Moscow, Russia

Background: A technique for cryopreservation of human platelets was developed and patents on it were obtained in the Russia in 2017. The procedure for cryopreservation of platelet concentrates includes storage of both cells (platelets) and plasma. To our knowledge, there have been no prior studies of plasma quality in platelets concentrates (PC) or cryopreserved platelet concentrates (CPC) so far. That context dictates the relevance of investigating plasma clotting factor activity in PC and CPC.

Aims: We sought to evaluate the activity of plasma coagulation factors in PC and CPC.

Methods: PC were harvested on the Trima Accel automated blood collection system. The patented technology was employed to cryopreserve PC within a closed system with the use of DMSO as a cryoprotectant. The residual plasma factor VIII activity in PC and CPC was measured by the one-stage clotting assay using a reagent set for FVIII activity testing in-vitro. The method applied consisted in adding a deficient substrate plasma to a dilution of the test plasma and determining the clotting time of the mixture in the APTT assay which implies correction of all clotting factors, except factor VIII, so that the APTT of that mix is only dependent on the factor VIII activity in the plasma being tested. It was determined against a calibrated plasma reference preparation with the factor VIII activity certified to the International Standard. Fibrinogen concentration in the residual plasma remaining with CPC was assayed with the aid of an in vitro diagnostic kit of reagents for determining fibrinogen content. That involves noting the clotting time after excess thrombin has been added to the specimen of plasma diluted 1:10. In this system, the time it takes the fibrin clot to form depends solely on the plasma fibrinogen concentration.

Results: The residual plasma analysis in PC showed the factor VIII activity to decrease throughout the PC storage period. The lowest factor VIII activity level, 195–134 IU, was revealed within 24 h of PC storage. The activity of factor VIII was found to reach another trough (81 IU) after 96 h of PC storage. However, there was no significant change in the fibrinogen concentration seen to be as high as 2.2–3.5 g/l. The cryopreservation process was demonstrated to nearly halve the factor VIII activity, as compared to its activity in the original PC. The activity in CPC was heavily dependent on the original PC storage times. The peak activity of factor VIII, 125 ± 55 IU, was detected in CPC from PC stored within 24 h. A significant decline in the activity of factor VIII (84 ± 38 IU) was noted in CPC, obtained from PS after 24 h storage. With longer storage of the original PC and CPC being produced from them, the factor VIII activity level fell to 40 IU. A fibrinogen level of 2.0–2.7 g/l in CPC was unaffected by freezing and prolonged storage of PC. Plasma was additionally assayed after prolonged storage of CPC at − 85–196°C. While being frozen, all PC exhibited a twofold reduction in factor VIII activity, but afterwards, it hardly changed over 2 years of storage.

Summary/Conclusions: Not only platelets, but also active plasma clotting factors (factor VIII and fibrinogen) being recovered in PC and CPC confer some dual properties to the blood components under review. The high activity of factor VIII is still found in CPC over a two-year refrigerated storage period. In the setting of the patients being transfused with PC and CPC, both platelet dose and the activity of clotting factors, influencing haemostasis in a hypo- or hypercoagulable state, should be taken into account.

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THE EFFECT OF COLD STORAGE ON PLATELET QUALITY

A Morrison[1], L McMillan[1], L Agnew[2], A Fraser[1] and J Campbell[1]
[1]Tissues, Cells & Advanced Therapeutics Development [2]Component Testing, Scottish National Blood Transfusion Service, Edinburgh, United Kingdom

Background: Room temperature Storage (22°C) of platelet components are not without problems, such as increased storage lesions, metabolism and pH leading to reduced storage time. This combined with the potential for bacterial growth at ambient temperature allows for platelets to be stored for only 7 days. Over the last decade platelet production in the UK has increased by 17% (SHOT Report 2007 – 2017) but is contrasted with a 3.2% wastage rate due to products expiring. Thus storage once again at 4°C has been re-investigated. Cold stored platelets can reduce bacterial growth, slow down metabolism and potentially allow for increased storage time. There are also suggestions that these platelets may be more efficient at binding due to platelet 'priming' in the cold. However, circulation in vivo of these transfused platelets is suggested to be short lived. Recently there has been evidence emerging suggesting that these cold induced changes may however be reversible by periodic warming during cold storage and therefore may allow transfused platelets to stay in circulation longer.

Aims: To evaluate cold and temperature cycling conditions with that of our standard practice and determine whether quality and functionality is maintained.

Methods: Briefly 3 × O+ buffy coat platelet units in SSP+ (day 2) were pooled and then split back into fresh bags and stored at the following temperatures/conditions A) Control/standard (S) 22°C, B) Cold 4°C (C) and C) Temperature cycled between 4°C for 11 h and 37°C 1 h (TC). Samples were analysed for quality and functionality on days 2, 5, 9 and 12.

Results: All platelet parameters measured still had functional platelets by end of storage despite the loss of swirl in both cold and TC stored platelets. Although we noted both cold and TC stored platelets pH to decrease over storage compared to the standard platelets, all samples measured were above the European and UK guidelines of ≥ 6.4. Morphology of the platelet surface changed for all parameters measured over time, with Annexin V levels increasing from 1.6 ± 1.2% on day 2 to 13.6 ± 2.5% (S), 9.9 ± 2.0% (C), 17.4 ± 4.8% (TC) by end of storage. We also noted GP1bα sites were maintained best on TC platelets by end of storage reducing from 98.3 ± 1.2% to 93.5 ± 4.2% compared to 82.1 ± 6.4% (S) and 92.2 ± 4.2% (C). Haemostatic ability was retained for all units measured by thromboelastography (TEG), with stronger clot strength being observed for both cold and TC stored platelets 67.0 ± 2.4 mm (TC), 67.9 ± 3.6 mm (C) and 65.6 ± 3.4 mm (S)

Summary/Conclusions: Our data suggests that platelets can be as effectively stored in the cold as under standard temperatures (22°C). Although swirl disappeared for the cold and TC stored components, platelets still retained haemostatic ability. Due to changes in platelet surface markers, survival time of these components in vivo would require further assessment. Storage in the cold may therefore allow for longer storage time and reduce platelet wastage.

Novel Blood Products

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THAWED PLATELETS AND THAWED PLASMA CAN BE STORED FOR 2 WEEKS AT 4 DEGREES CELSIUS, A POSSIBLE NEW ASSET TO THE TREATMENT OF MAJOR HAEMORRHAGE IN THE PREHOSPITAL SETTING

F Noorman[1], A Bek[1], P Pun[2], J Lu[2], R Hoencamp[3,4,5] and M Zoodsma[1]
[1]Quality, Research and Development, Military Blood Bank, Leiden, Netherlands [2]Research, DSO National Laboratories, Singapore, Singapore [3]Research Operational Medicine, Defense Health Organisation, Utrecht [4]Vascular and Trauma Surgery, Alrijne Hospital [5]Vascular and Trauma Surgery, Leiden University Medical Center, Leiden, Netherlands

Background: The Netherlands Armed Forces have shown that −80°C frozen blood products are safe and effective in the treatment of trauma casualties in military treatment facilities. Survival improved from 56% to 86% in massively transfused patients, when the frozen blood products were used in combination with a "4:3:1 red blood cells: plasma: platelets" massive transfusion policy. Pre-hospital transfusion of blood products may further improve survival. Thawed red blood cells can be stored for 2 weeks and thawed plasma for 1 week at 4°C before use. Thawed platelets can only be stored for 6–24 h at 22°C which makes it not practical to use this product in a prehospital setting.

Aims: The primary aims is to assess the cut-off point of cold storage of thawed platelets or plasma, according to European guidelines. The secondary aim is provide evidence to prolong storage of a readily available, universal donor type, blood component stock for the prehospital setting.

Methods: Platelet units (type O) were concentrated in 5–6% dimethyl sulfoxide/plasma (15–20 ml), frozen to −80°C (DTC). After thaw, platelets were resuspended in thawed plasma (300 ml, type AB), that was first pooled and split; the other plasma unit (DFP) was stored separately at 4°C. DTC and DFP were compared on days 0, 7, 10, 14 of post-thaw 4°C storage. These products were compared to fresh buffy coat platelets (type B) stored in autologous plasma (BCTC, days 2, 7 at 22°C; days 7, 10, 14 at 4°C). Product volume was determined by weight, platelet concentration was measured with Sysmex XS1000i and pH was measured with i-STAT®. Coagulation factor activities (IU/ml), fibrinogen (gr/L) and phospholipid activity (PPL, sec) were measured with Stago Max® coagulation analyser; In vitro coagulation was assessed with Kaolin Thromboelastography (TEG®). In vitro data and compliance to European guidelines were evaluated.

Results: DTC platelet content remained stable at ±300*10^9/Unit and pH decreased during storage (pH 7.5 ± 0.0 to pH 7.3 ± 0.1). Most coagulation factors were similar for DTC and DFP, slightly reduced or remained stable during storage (day 14 fibrinogen (2.6 ± 0.3), factor VII (0.9 ± 0.1), factor VIII (0.6 ± 0.1), Protein C (1.1 ± 0.1), anti-thrombin III (1.2 ± 0.0)). In DTC, Factor V was reduced stronger (Day0 to 14: DFP 1.0 ± 0.1 to 0.7 ± 0.1; DTC 0.4 ± 0.1 to 0.2 ± 0.0) and Protein S decreased stronger during 4°C storage (DFP 1.2 ± 0.2 to 0.5 ± 0.2, DTC 1.0 ± 0.4 to 0.2 ± 0.0). Similarly Factor V and Protein S decreased in BCTC (4°C: FV 0.9 ± 0.3 to 0.3 ± 0.1, PS 0.8 ± 2 to 0.5 ± 0.1; day 7 22°C:FV 0.6 ± 0.2, PS 0.2 ± 0.1). Phospholipid activity was highest in DTC and decreased during 4°C storage (PPL 12 ± 0 to 15 ± 1 sec; TEG R-time 4 ± 1 to 7 ± 2 min). PPL activity of BCTC started low and increased during storage (4°C: PPL 35 ± 4 to 20 ± 0 sec; TEG R-time 10 ± 1 to 7 ± 0 min; 22°C: PPL 36 ± 4 sec to 31 ± 0 sec; TEG R-time 9 ± 1 to 8 ± 1 min). Activity was higher compared to DFP (day 14: PPL 63 ± 4 sec; TEG R-time 9 ± 1 min). BCTC produced stronger clots during storage (4°C: TEG MA 67 ± 1 to 61 ± 2 mm; 22°C: TEG MA 68 ± 10 to 47 ± 10 mm) compared to DTC (TEG MA 65 ± 1 to 50 ± 6 mm), which produced stronger clots compared to DFP (TEG MA 25 ± 6 to 27 ± 3 mm) throughout storage.

Summary/Conclusions: Thawed plasma and platelet storage can be prolonged to 2 weeks when stored at 4°C, according to the European guidelines, which suggests that these products can be used in a pre-hospital setting. Cold stored (thawed) platelets in plasma, support in vitro coagulation stronger compared to (cold stored) thawed plasma and may be more effective in the treatment of major haemorrhage. Future research should focus on their effectiveness during resuscitation in vivo.

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CRYOPRESERVED SHEEP PLATELETS ARE HEMOSTATICALLY FUNCTIONAL: A SUITABLE PRECLINICAL TRANSFUSION MODEL

G Simonova[1,2,3], S Pedersen[1,3], M Reade[2,4], L Johnson[5], M Dean[1,2], D Marks[5] and J Tung[1,2,3]

[1]Research and Development, Australian Red Cross Blood Service [2]School of Clinical Medicine, The University of Queensland [3]Critical Care Research Group, The Prince Charles Hospital, Brisbane [4]Joint Health Command, Australian Defence Force, Canberra [5]Research and Development, Australian Red Cross Blood Service, Sydney, Australia

Background: Cryopreservation, as an alternative to standard room temperature storage of platelet units, offers an extended shelf-life and provides significant logistic and supply advantages, especially for rural areas and military settings. However, clinical studies are yet to conclusively establish their safety and efficacy as a resuscitation therapy. While ethical constraints limit the design of these studies, using animal models of transfusion provides several advantages, including the capacity to investigate any implicated factors responsible for adverse events. Sheep are a valuable model of blood transfusion research as their size, anatomy and blood volume are similar to humans.

Aims: The aims of this research project were to investigate the feasibility of cryopreserving sheep platelet units, optimise protocols for their manufacture and to determine the hemostatic function in sheep platelet concentrates pre-freeze and post-thaw.

Methods: Buffy-coat derived sheep platelet units (n = 6) were prepared in 30% plasma/70% SSP+ additive solution with minor modifications to standard procedures for human platelets. Four buffy-coats were pooled and platelets were separated by centrifugation, leukodepleted by filtration and stored in the associated storage bag at 22°C with agitation overnight. Sheep platelets concentrates (sPCs) were cryopreserved (cryo-sPCs) within 24 h of manufacture with the gradual addition of 5–6% DMSO. The supernatant, containing DMSO, was removed by centrifugation and sPCs were stored at −80°C for 57–154 days. Cryo-sPCs were thawed at 37°C and resuspended in pre-warmed pooled sheep plasma. Thawed and reconstituted cryo-sPCs were sampled immediately post-thaw. The platelet count was determined using a hematology analyser and post-thaw recovery was calculated. Platelet hemostatic function was assessed by rotational thromboelastography (ROTEM, HaemoVIEW Diagnostics) using EXTEM (extrinsic coagulation pathway) and INTEM (intrinsic pathway) tests. In decalcified samples, EXTEM test measures changes of the extrinsic coagulation pathway, while INTEM test measures alterations with intrinsic coagulation pathway and both provide information on clot formation and stability.

Results: Mean post-thaw recovery of cryo-sPCs was 72.7% (range: 60–84.7%). Cryopreservation resulted in prolonged EXTEM clotting time (CT (s), 73 ± 2.4 pre-freeze vs. 78 ± 4.3 post-thaw, P = 0.0004) but faster clot formation (CFT (s), 86 ± 11 pre-freeze vs. 80 ± 10 post-thaw, P = 0.7359) with decreased maximum clot firmness (MCF (mm), 45 ± 9.0 pre-freeze vs. 37 ± 3.4 post-thaw, P = 0.0162) compared to pre-freeze platelets. INTEM results indicated that cryopreservation shortened clotting time (190 ± 19 s pre-freeze vs. 186 ± 13 s post-thaw, P = 0.3456) and increased clot formation time (87 ± 14 s pre-freeze vs. 109 ± 22 s post-thaw, P = 0.1921) time but the overall strength of clot formed was decreased (52 ± 12 mm pre-freeze vs. 39 ± 4.5 mm post-thaw, P = 0.0085). These results are in line with characteristics of human cryopreserved platelets.

Summary/Conclusions: Sheep platelet units were successfully cryopreserved and were hemostatically effective. Based upon this evidence, sheep biomedical models should be able to incorporate transfusion of cryo-sPCs, and provide a suitable preclinical model to address knowledge gaps regarding transfusion with cryopreserved blood product.

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QUANTIFICATION AND CHARACTERIZATION OF EXTRA-CELLULAR VESICLES AND MICROVESICLES IN VARIOUS HUMAN PLATELET LYSATES FOR CLINICAL USE

L Delila[1], Y Wu[1], M Chou[2], D Devos[3] and T Burnouf[1]

[1]Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering, Taipei Medical University, Taipei, Taiwan, Republic of China [2]Centre de Recherche Saint-Antoine (CRSA), INSERM UMRS 938, Paris [3]Pharmacologie Médicale & Neurologie, INSERM U 1171, Lille, France

Background: There is an increasing interest in the clinical use of various human platelet lysates (HPL) preparations in regenerative medicine, including soft tissues healing, bone augmentation, treatment of osteoarthritis, and, even, neuroprotection. HPL is also increasingly used as a supplement of growth media for human cell propagation and cell therapy. The scientific rationale supporting the clinical benefits of the platelet preparations is usually thought to be their content in numerous growth factors such as PDGF, TGF-b, EGF, VEGF, HGF, or BDNF released by the platelets. However, there is preliminary evidence that platelet lysates contain extra-cellular vesicles (EVs), including microvesicles (MVs) (collectively called here EVs/MVs), that can potentially contribute to their functional activity by being a potent cargo of bio-active molecules facilitating cell-cell communication. Little is known about the presence and content of MVs in different types of HPLs used in regenerative medicine, and more exploration is needed.

Aims: To compare the content, characteristics (size and size distribution), and morphology of EVs/MVs in various types of platelet lysates preparations used for regenerative medicine applications.

Methods: Apheresis platelet concentrates (PC) were obtained from Taipei Blood Center upon IRB approval. PC were aliquoted and processed into different platelet lysates: PPL (Platelet Pellet Lysate); HPPL (Heat-treated Platelet Lysate); SCPL (Serum-converted Platelet Lysate using calcium chloride/glass bead treatment); and HSCPL (Heat-treated Serum-Converted Platelet Lysate). The mean population size and Zeta potential of EVs/MVs in the platelet lysates before and after fractionation on qEVoriginal size exclusion chromatography (SEC) column (Izon Science) was analyzed by Dynamic light scattering (DLS). Additional exploration of morphology, individual particle size and counting was done by transmission electron microscopy (TEM) and Nanoparticle tracking analysis (NTA).

Results: All HPLs were found to contain numerous EVs/MVs with a content ranging from approximately 10^{10} (SCPL) to 10^{12}/ml (HPPL). DLS analysis showed that EVs/MVs in crude PPL, HPPL, SCPL, and HSCPL have a mean population size of 192.4 ± 1.48 nm; 196.8 ± 2.53 nm; 153.7 ± 1.65 nm; and 176.2 ± 3.50 nm, respectively. Exploration of EVs/MV after fractionation by the Izon column revealed

a mean population size in PPL from 104.4 ± 0.90 to 257.0 ± 6.18 nm bigger than in SCPL where the range was 45.3 ± 0.34 to 241.7 ± 2.76 nm. In the heat-treated fractions, HPPL and HSCPL, the mean population size of fractionated EVs/MVs ranged from 145.4 ± 2.17 to 227.0 ± 7.2 nm and 54.8 ± 0.10 to 186.6 ± 2.24 nm respectively. The estimation of EVs/MVs size range in the HPL was confirmed by TEM observations and supported by NTA.

Summary/Conclusions: The size and number of EVs/MVs differ in different types of platelet lysates preparations used for regenerative medicine applications. The physiological implications, if any, of these differences deserve further in vitro, cell-based and pre-clinical animal model explorations.

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PLATELET–RICH PLASMA FOR DENTAL EXTRACTIONS IN PATIENTS WITH HAEMOPHILIA

V Molina, M Parreira, D Neme, B Rode, C Vázquez, L Elhelou, E Honnorat and M Alba

Foundation of Haemophilia, Buenos Aires, Argentina

Background: The management of patients with bleeding disorders such as haemophilia is a significant challenge to dental providers and requires collaboration with the patient's haematologist as well as an awareness of local haemostatic measures and techniques. The use of platelet-rich plasma (PRP) has been associated with the improvement of the tissue healing process in different procedures.

Aims: The main goal of this study is to evaluate the reported potential benefits of the use of PRP after dental extractions, in a population of patients with haemophilia.

Methods: Autologous PRP was used to fill the sockets after exodontias. Specific coagulation replacement therapy was administered as a pre-procedure bolus injection, followed by 2–3 daily doses. 13.5–18 ml of blood were drawn from each patient using 4.5 ml tubes containing 3.8% trisodium citrate solution, 10 min after the infusion of FVIII/FIX. The tubes were centrifuged at 1,600 rpm for 10 min (table centrifuge) at room temperature. The PRP was obtained by aspirating with a pipette the lower third of the plasma fraction and was transferred into a sterile glass Petri dish. The Platelet-Poor Plasma (PPP) was obtained from the upper third of the plasma and placed into another glass Petri dish. To each 1 ml plasma fraction placed in the dishes, 40 µl of 10% calcium chloride were added. The dishes were kept in a 37°C water bath. These fresh products were malleable and ready to be introduced in to the alveolar socket. Bleeding was evaluated using the post exodontia alveolar bleeding index (PEABI). A score of 0 to 03 was used, where 0 represented total absence of bleeding. Healing was determined using the healing index (HI). A score of 1 to 5 was given, where 1 was associated with a very poor healing. The assessment of inflammation was done using a 0 to 3 score. 0 was absence and 3 was facial planes blurring with affectation of nasolabial folds and eyes. Pain was evaluated using the Faces Pain Rating Scale. Bone healing was studied using a longitudinal radiographic assessment technique, performed on days 1, 30 and 90 postoperatively.

Results: 30 consecutive patients with haemophilia (20 patients with severe) underwent 39 exodontias. Mean age was 35 years old (15–69). The bleeding score (PEABI) was 0 in 20 patients, 01 in six, 02 in four. No bleedings after 7 days of procedure were reported. The Healing index was 1 in one patient, score 2 in one, 3 in eight, and 5 in twenty patients. The inflammation score was 0 in twenty-five patients, 1 in three, and 2 in two. Twenty four (80%) patients reported no pain and only four patients used analgesic therapy. No surgical complications, trismus, dental alveolitis or infection were reported. Radiographic assessment showed a significant vertical bone mass increase through all observation periods.

Summary/Conclusions: The reported potential benefits of the PRP after dental extractions could also be obtained in patients with haemophilia, with the appropriate replacement therapy

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NEUROPROTECTIVE AND NEURORESTORATIVE EFFECTS OF A TAILOR–MADE HUMAN PLATELET LYSATE IN IN VITRO MODELS OF TRAUMATIC BRAIN INJURY

O Nebie[1], C Peng[2], D Devos[3], D Blum[4] and T Burnouf[1]

[1]*Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering* [2]*School of Biomedical Engineering, College of Biomedical Engineering, Taipei medical University, Taipei, Taiwan, Republic of China* [3]*Pharmacologie Médicale & Neurologie, INSERM U1171,* [4]*Jean Pierre Aubert Research Centre, UMR INSERM 1172, Lille, France*

Background: Cell-based and animal models suggest that human platelet lysate (HPL) can emerge as effective biotherapy of neurodegenerative diseases. We have developed one particular HPL, depleted of plasma proteins and heat-treated (HPPL) to remove fibrinogen and avoid thrombogenic, inflammatory, and proteolytic activity. This HPPL protects dopaminergic neurons in a differentiated Lund human mesencephalic (LUHMES) cell model and, using intranasal administration, in an animal model of Parkinson's disease. Neuroprotective activity of this HPPL may result from its content in multiple neurotrophic growth factors (PDGF, VEGF, BDNF, TGF-b, etc.), known to exert beneficial impacts on neuron survival, and from the removal of neurotoxic blood components. HPL protects against cell death pathways and oxidative stress inducers, and its mechanism of protection in neuronal cell models involves the activation of the Akt and MEK pathways. The capacity of HPL to exert neurorestorative potential in traumatic brain injury (TBI) has not been explored yet.

Aims: Evaluate the neurorestorative activity of HPPL in in vitro models of TBI

Methods: HPPL was prepared from fresh therapeutic-grade platelet concentrates formulated in 100% plasma (PC). A platelet pellet lysate was first obtained by centrifugation ($3,000 \times g$, 22°C, 30 min) of PC. The platelet pellet surface was washed to remove residual plasma, re-suspended in PBS and subjected to 3 freeze-thaw cycles (-80°C/37°C), followed by centrifugation ($4\ 500 \times g$, 22°C, 30 min). The supernatant was recovered and heat-treated at 56°C for 30 min. HPPL total protein concentration was determined and growth factors assessed by ELISA. Functional activity was evaluated using 5% (v/v) HPPL compared to 5% fetal bovine serum (FBS). Impact on viability, proliferation, and apoptosis of neuroblastoma (SH-SY5Y), microglia BV-2 and human endothelial (EA-hy926) cells was assessed by WST-8, BrdU and Western blot respectively. Inflammatory activity on BV-2 was investigated by tumor necrosis factor-alpha (TNF-a) release. HPPL capacity to stimulate wound healing and protect from mechanical damage was evaluated by scratch assay and transection model, respectively. Its capacity to stimulate neurites extension was evaluated in a SH-SY5Y differentiation test.

Results: The mean HPPL (N = 3) protein concentration was 10 mg/ml. The mean content in neurotrophic factors was: BDNF: 36.4 ng/ml; PDGF-AB: 82.2 ng/ml; EGF: 2 ng/ml); and VEGF: 0.5 ng/ml. 5% HPPL stimulated SH-SY5Y and EA-hy926 growth without affecting viability nor stimulating apoptosis. It did not induce detectable (<0.007 ng/ml) TNF-a release by BV-2 compared to LPS control (1.2 ng/ml). The mean viability of SH-SY5Y and EA-hy926 treated with HPPL was 115% and 116% of that obtained with 5% FBS after 48 h of culture respectively. HPPL exhibited potent wound healing efficacy in the scratch assay with a wound closure index of 0.9 for SH-SY5Y and 0.98 for EA-hy926 after 24 h. HPPL induced SH-SY5Y neurite outgrowth and the average neurites length was 70 µm. In a transection model, HPPL exhibited a significant (P < 0.001) protective effect compared to untreated cells.

Summary/Conclusions: In vitro data confirms that HPPL is not toxic to neuronal cells, not inflammatory, and exerts neuroprotective and neurorestorative activities warranting further evaluation in in vivo models of TBI.

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SERUM EYE DROPS FOR PATIENTS UNABLE TO DONATE BLOOD: THE ALLOGENEIC PERSPECTIVE

M Mrotzek[1], V Petrescu-Jipa[1], M Störmer[1], V Tahmaz[2,3], P Steven[2,3], C Cursiefen[2,3] and B Gathof[1,3]

[1]*Transfusion Medicine* [2]*Department of Ophthalmology* [3]*Ocular GvHD Competence Center, University Hospital of Cologne, Köln, Germany*

Background: Treatment with blood derived serum eye drops (SED) is a highly effective therapy for patients suffering from some severe ocular surface disorders. Preparation from the patient's own blood (Auto-SED) is the most common procedure. Since > 5 years this autologous approach is well established in our centre. Due to some patient's inability to donate Auto-SED cannot be manufactured. Results for allogeneous SED reported in the literature encouraged us to evaluate this option.

Aims: The aim was to re-evaluate our Auto-SED donors regarding their prospective ability to donate blood and to gain experience with allogeneous serum eye drops.

Methods: All Auto-SED donors were evaluated for potential factors, which could prevent their blood donation like underlying disease, poor venous access, low haemoglobin, infections, circulatory disturbances, as well as very old or young age. The local authority agreed upon "individual healing attempts" according to each patient's individual setting. This was necessary because this procedure, in contrast to other countries (Taiwan, Korea, Denmark, New Zealand), is not performed regularly in Germany yet. AB0-identical male donors without blood borne diseases, that never received blood products and not taking any kind of medication will be selected within our regular blood donors. Additionally donors must pass a questionnaire excluding any form of dry eye syndrome. Allo-SED manufactured are directed for each patient according to the process for Auto-SED in a closed system (Meise, Schalksmühle, Germany) Petrescu V, Transfusionsmedizin, 2014. Therapeutic results are evaluated by subjective measures and ocular surface disease index (OSDI).

Results: Out of 370 SED-donating patients 20 patients were identified: 14 not eligible anymore, 6 temporarily to donate blood. Most frequently contraindications were underlying disease: 9 pt (45%), poor venous access, low haemoglobin: 7 pt (35%), circulatory disturbances: 5 pt (25%), very young age/low body weight: 3 pt (15%) and 1 case of hepatitis B infection (5%). Some patients presented more than one contraindication. According to medical urgency 3 patients was given priority. A 2 year old child suffering from neurotrophic keratopathy in both eyes already received Allo-SED twice. Follow-up examinations showed a distinct shrinking of lesions in both eyes. The other 2 patients, suffering from ocular GvHD and dry eye syndrome have received Allo-SED, follow-up examinations will be performed quarterly. All other patients will be provided with Allo-SED when their stock of Auto-SED is expired.

Summary/Conclusions: Considering the literature and our first experience, the treatment with allogeneic SED may be an effective, if not even equally efficient, alternative to autologous manufacturing if donation is impossible. A direct comparison between both settings, Auto- versus Allo-SED, regarding the effectiveness is missing yet. In the future we will need to explore advantages, disadvantages and therapeutic effect of both approaches and most desirably in a direct comparison in the same group of patients.

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IN VITRO FUNCTIONALITY TEST OF SERUM EYE DROPS

J Lorinser[1], S Groot[1], A van Stalborch[2], J van Buul[2], P van der Meer[1] and D De Korte[1,3]

[1]Product & Process Development Blood Bank, Sanquin [2]Plasma Proteins Molecular Cell Biology Lab [3]Blood Cell Research, Sanquin Research, Amsterdam, Netherlands

Background: Human serum eye drops (SEDs) are used for treatment of dry eye syndrome. The hypothesis is that active components of serum, such as growth factors, have an active effect on dry eyes because the adhesion between cells in the cell layers of the eye strengthen, thereby improving the barrier function. However, until now there is no in vitro model to test the effectiveness of SEDs.

Aims: To develop a standardized in vitro system to test the healing effect of SEDs on human endothelial/epithelial cells, representing the cell layers of the eye. Also to investigate at which concentration of serum the healing effect is optimal.

Methods: Two heat-inactivated serum pools were tested on cell layers of Human Umbilical Vein Endothelial Cells or human lung epithelial cells H292 and A549. Measuring the resistance across the cell layers, caused by the adhesion of the cells, was carried out in triplicate for each serum pool in 8-well Electric Cell-substrate Impedance Sensing (ECIS) arrays with 1.0×10^6 cells per well. After formation of a cell monolayer, 200 µl of serum was pipetted per well in duplicate, with 10, 20 and 40% final concentration and as 0% serum control 200 µl of EGM-2 growth medium. Results were calculated and normalized from the time of serum addition and measured during 16 h.

Results: Very reproducible results were obtained with the various cell lines and serum pools. For endothelial cells, the highest difference in resistance was measured with 10% serum, indicating a strengthening of the barrier function of the cell layer and improved adhesion of the cells. The effect for the various concentrations was almost the same and was maintained the full 16 h. For epithelial cells, the highest resistance difference was measured with 40% serum, with a dose-response relationship. With 40% serum, a long activity was measured, while the lower percentages serum returned to the level of 0% serum after an initial effect within the 16 h measurement.

Summary/Conclusions: With ECIS a reproducible in vitro model has been developed to test serum pools with the used endothelial and epithelial cells. There is a direct and reproducible activity measured at all dilutions. For endothelial cells, the improved adhesion between the cells remains for all concentrations during the full

measurement time. For epithelial cells this is only the case with 40% serum.ECIS is very suitable for follow-up research in which wounding can be applied to the cell layers, in order to determine the maximum healing effect of SEDs.

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Abstract has been withdrawn

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A SIMPLE PROCEDURE TO ACHIEVE A SPECIFIC PLATELET CONCENTRATION IN CORD BLOOD PLATELET GEL

P Rebulla, I Scaramuzzino, G Bertelè, C Biadati, D Forlani and N Greppi

Blood Transfusion Service, Foundation Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy

Background: Allogeneic cord blood platelet gel (CBPG) is a blood component rich of tissue regenerative factors used for topical treatment of skin ulcers. CBPG can be prepared from CB units collected for hemopoietic transplant which show insufficient cell dose for this use. Units with volume ≥50 ml and platelet count ≥150 × 10^9/L are suitable for CBPG production. Platelet rich plasma (PRP) is obtained by soft CB centrifugation, followed by PRP hard spin and platelet resuspension in a plasma volume appropriate to achieve a specific platelet concentration. For therapeutic applications, a gel is formed by adding calcium to the platelet concentrate (CBPC). CBPG clinical efficacy studies require careful product standardization, in particular of platelet concentration in the CBPC. This can be achieved by performing a platelet count in the PRP, which is then used to determine the appropriate volume reduction to ensure a specific platelet concentration in the CBPC. As recommended by several PG experts, in our standardization studies we chose a target mean platelet concentration in the CBPC of 1000 (SD 200) × 10^9/L.

Aims: We aimed to determine the PRP volume reduction factor using only the platelet count × 10^9/L from the complete blood count routinely performed by the CB bank on a whole CB unit sample, thus avoiding workload, inaccuracies, costs and contamination risks associated with the intermediate step of PRP sampling and platelet count. This objective was supported by previous evidence that percent platelet recoveries through CB fractionation steps showed limited variations.

Methods: In a preliminary study on 39 CB units (study 1) we determined CBPC volume and platelet concentration by empirically using PRP discrete volume reduction factors of 0.50, 0.40, 0.33 and 0.25 for units with initial whole CB platelet count of ≥300, 250–299, 200–249, and 150–199 × 10^9/L respectively. We then performed a simulation study (study 2) by imposing a constant platelet concentration in the PC of 1000 × 10^9/L in the database obtained from study 1 and determined the linear regression of initial platelet count in whole CB versus the imposed constant value of 1000 × 10^9/L in the CBPC. This simulation yielded the following equation: y (CBPC volume, ml) = 0.0863 × (CB platelet count, × 10^9/L) − 5.9209. Finally (study 3), we experimentally evaluated the platelet concentration in 44 newly prepared CBPC whose volume was determined (by weight) using the equation obtained in study 2.

Results: Setting the CBPC volume with the equation from study 2, we obtained a mean platelet count of 1021 × 10^9/L (SD 182) in the 44 CBPC of study 3, a value very close to our standardization target.

Summary/Conclusions: The procedure reported in this study can facilitate the standardization of platelet count in CBPG, reduce the workload and improve the quality of comparative evaluations of its clinical efficacy.

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IN VITRO QUALITY OF FREEZE–DRIED PLASMA

LY Dimberg, A Parr, T Khat, R Bates, N Hovenga, N Johnson and S Marschner

SC&L, Terumo BCT, Lakewood, Colorado, United States of America

Background: Traumatic injury is the leading cause of death for persons under the age of 45 in the United States, and overall the fifth leading cause of death. Hemorrhage is the most preventable direct cause of death by trauma. Studies have shown that early administration of plasma improves clinical outcomes after trauma. However, the storage requirements and thawing time of fresh frozen plasma (FFP) can be operationally challenging in the prehospital setting, for small hospitals and on the battlefield. Lyophilized or freeze-dried plasma (FDP) that can be stored at room

temperature and reconstituted rapidly for immediate use as a point-of-injury resuscitation fluid is a potential solution to these issues. An FDP product that is stored in a rugged, light-weight plastic package suitable for field use is being developed.

Aims: The aim of the present study was to compare the in vitro quality of a reconstituted FDP prototype to that of FFP.

Methods: Ten units of liquid plasma were derived from whole blood collected in citrate phosphate dextrose anticoagulant. Aliquots were removed from each unit and were frozen within 8 h of collection to serve as paired FFP controls and the remaining volume of each unit was freeze-dried. After freeze-drying, the FDP was reconstituted in water for injection. The reconstituted FDP and the paired thawed FFP controls were tested for coagulation factor activity and clotting properties at baseline (time = 0). To characterize the stability of the reconstituted product, the reconstituted FDP and paired FFP controls were stored at 4°C and retested at 24 h and at 120 h for the same parameters.

Results: The average reconstitution time of the FDP was 1 min, 52 s. As a comparison, a unit of FFP is typically thawed in about 30 min at 37°C. The pH of the reconstituted FDP was physiologic (average = 7.4) and similar to the pH of FFP (average 7.3). At the time of reconstitution (t = 0) there were no significant differences observed between FDP and paired FFP controls for Factor V, Factor VIII, fibrinogen, PTT, PT, activated partial thromboplastin time (aPTT), prothrombin time (PT), Protein S, Protein C, or parameters measured by ROTEM and thrombin generation assay (P > 0.05). These quality parameters of reconstituted FDP remained statistically similar to paired FFP controls even after storage at 4°C with two exceptions: FDP prothrombin time was slightly (0.8 s) higher at 24 h, and FDP Protein S activity was lower at 120 h (72% vs 84%). However, values remained within normal plasma reference ranges.

Summary/Conclusions: Reconstituted FDP maintained similar in vitro quality compared to thawed FFP for up to 5 days at 4°C. The data from this pilot study suggest that reconstituted FDP has sufficient plasma quality to serve as an alternative to FFP. Rapid reconstitution time and the possibility of room temperature storage provides a significant operational advantage compared to FFP in certain settings. Additional studies are ongoing. This material is based upon work supported by the United States government under contract no. H92222-16-C-0081.

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Abstract has been withdrawn

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DEVELOPMENT OF AMINO ACID–BASED ICE RECRYSTALLIZATION INHIBITORS TO CRYOPRESERVE RED BLOOD CELLS

J Meyer and R Ben

Department of Chemistry and Biomolecular Sciences, University of Ottawa, Ottawa, Canada

Background: Cryopreservation provides a solution for the long-term storage of red blood cells (RBCs). This is currently achieved by using high concentrations of glycerol (40% in North America) as a cryoprotectant; however, the glycerol must be removed to <1% prior to transfusion to avoid intravascular hemolysis. This is a lengthy process which increases patients' wait time prior to receiving a transfusion. Furthermore, glycerol does not prevent cryoinjury due to ice recrystallization. Our laboratory has developed carbohydrate-based small molecule ice recrystallization inhibitors (IRIs) capable of cryopreserving RBCs using 15% glycerol. Many of these IRIs have issues which preclude their use clinically, including hemoglobin oxidation and inducing hemolysis during the deglycerolization process. This indicates the need for the development of a new class of IRIs suitable for RBC cryopreservation which would allow for rapid deglycerolization.

Aims: To design non-toxic amino acid-based IRIs capable of successfully cryopreserving RBCs using reduced glycerol concentrations.

Methods: Amino acids and synthesized derivatives were assessed for IRI activity using a modified splat-cooling assay. Cytotoxicity in HepG2 cells was assessed using a conventional resazurin assay.

Results: Phenylalanine, tyrosine, methionine, and isoleucine were identified as the only proteinogenic amino acids exhibiting significant IRI activity, with IC_{50} values ranging from 0.3 mM to 69 mM. Several structural modifications of the amino acids were assessed in order to determine their effects on IRI activity. The IC_{50} of phenylalanine decreases from 25 mM to <1 mM with the introduction of an N-isopropyl

substituent, although N-ethyl and N-propyl derivatives led to a significant loss in activity. Oxidation of methionine (IC_{50} = 24 mM) to the sulfoxide significantly decreased activity whereas oxidation to the sulfone ($MetSO_2$) retained similar activity (IC_{50} = 34 mM). Importantly, incubation of HepG2 cells for 48 h with 100 mM $MetSO_2$ resulted in cell viability of $104.0 \pm 7.7\%$, whereas 100 mM methionine resulted in only $45.9 \pm 10.2\%$ viability under the same conditions.

Summary/Conclusions: The rational design of amino acid derivatives can both increase IRI activity and reduce cytotoxicity compared to their parent compounds. This novel class of IRIs is promising for the cryopreservation of RBCs using lower glycerol concentrations, ultimately allowing shorter processing times prior to transfusion.

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THE USE OF NOVEL SMALL MOLECULE ICE RECRYSTALLIZATION INHIBITORS TO FACILITATE −80°C STORAGE OF RBCS WITH 15% GLYCEROL

TR Turner[1], J Poisson[2], J Meyer[2], R Ben[2] and J Acker[1,3]

[1]Centre for Innovation, Canadian Blood Services, Edmonton [2]Department of Chemistry and Biomolecular Sciences, University of Ottawa, Ottawa [3]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

Background: Red cell concentrates (RCCs) cryopreserved using a low glycerol method are not as commonly used in clinical medicine due to the need for rapid cooling and thawing systems, storage and shipment in liquid nitrogen and the higher incidence of blood bag breakage. Red blood cells (RBCs) in low concentrations of glycerol are highly susceptible to the damage induced by transient warming events (TWEs) which allow for ice recrystallization to occur. Novel small molecule ice recrystallization inhibitors (IRIs) have been shown to control ice crystal size and growth throughout the cryopreservation process affording improved protection to RBCs.

Aims: The purpose of this study is to use a small scale model that mimics the freezing and warming profile of a full size 15% glycerolized RCC to evaluate the effectiveness of an IRI to protect RBCs from TWEs and afford storage at −80°C.

Methods: Samples were prepared by adding glycerol with and without an IRI to RBCs. Glycerol-only controls were frozen by either placement directly into a −80°C freezer, or in the vapor phase of liquid nitrogen followed by −80°C storage or liquid nitrogen storage. Test samples with glycerol and an IRI were frozen in the vapor phase of liquid nitrogen to mimic the freezing rate of a full size RCC frozen directly in liquid nitrogen. A set of samples were thawed and tested for hemolysis by the Drabkin's method at 24 h, 7, 14, 21 and 28 days post glycerolization. A second set of samples were exposed to either a fast "TWE" (exposed to room temperature) or a "slow" TWE (exposed to −20°C) until the samples reached −40°C. After the exposure the samples were returned to −80°C storage before being thawed and tested at multiple storage time points. A third set of samples were exposed to a set of 5 "slow" TWEs from −75°C to −20°C to −75°C and tested after each cycle.

Results: 15% glycerol control samples without TWEs at 28 days post-glycerolization had hemolysis of $4.1 \pm 1.0\%$ when stored in liquid nitrogen, $10.3 \pm 0.7\%$ when frozen in liquid nitrogen vapor and stored at −80°C, and $91.8 \pm 1.0\%$ when frozen and stored at −80°C. A 40% glycerol control frozen and stored at −80°C had hemolysis of $2.0 \pm 0.4\%$. When 15% glycerol was supplemented with an IRI, frozen in liquid nitrogen vapor and stored at −80°C, post thaw hemolysis was $3.0 \pm 0.2\%$, an improvement in RBC stability over 15% glycerol alone. After exposure to either a "fast" or "slow" TWE, glycerol samples had hemolysis of $82.2 \pm 2.1\%$ and $76.7 \pm 3.7\%$ respectively. However, with the addition of an IRI, hemolysis decreased to $27.8 \pm 0.4\%$ and $44.1 \pm 1.5\%$ for a "fast" and "slow" TWE. After multiple "slow" TWEs to −20°C, hemolysis in samples containing an IRI stabilized and remained lower than non-IRI samples.

Summary/Conclusions: With the addition of an IRI into the glycerolization process, RBCs can be cryopreserved with a fast freezing rate followed by −80°C storage and demonstrate comparable results to those stored in liquid nitrogen. IRIs can protect RBCs from damage that can occur during multiple TWEs.

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A NOVEL CLASS OF CRYOPROTECTANTS FOR HUMAN RED BLOOD CELLS

J Poisson[1], T Turner[2], J Acker[2] and R Ben[1]

[1]University of Ottawa, Ottawa [2]Canadian Blood Services, Edmonton, Canada

Background: The storage time of refrigerated blood is limited to 42 days. The cryopreservation of red blood cells (RBCs) is a desirable method as it can extend storage time to 10 years. RBCs cryopreserved with 40% (w/v) glycerol is the current method; however, it is not routinely utilized to manage large supplies of blood. Prior to transfusion, frozen blood must be thawed and deglycerolized – a time-consuming process that requires specialized equipment. As a result, using frozen blood remains impractical. During freezing and thawing, a significant amount of cells experience cellular damage as a result of ice formation and recrystallization. This process occurs as large ice crystals grow larger at the expense of smaller ones. Ice recrystallization inhibitors (IRIs) have the ability to inhibit this process and can protect RBCs from cryo-injury during freezing and thawing. The use of IRIs as cryoprotectants allows for a reduction in the amount of glycerol, which can significantly reduce deglycerolization times. This would allow frozen RBCs to be rapidly prepared for emergency transfusions and may aid in managing blood supply.

Aims: This project involves the use of small molecule IRIs as cryo-additives for the cryopreservation of RBCs using reduced glycerol. While it has been shown that carbohydrate derivatives, PMP-Glc and pBrPh-Glc, exhibit IRI activity and have the ability to increase the percentage of intact RBCs post-thaw in the presence of 15% glycerol, these IRIs yield very low cell recoveries. The aims of this project are (a) to design a new class of IRIs that are more hydrophilic and (b) to cryopreserve and deglycerolize RBCs using these IRIs as a means of improving cell recovery.

Methods: Nine azide-based small molecule carbohydrate derivatives were synthesized using conventional procedures and tested for IRI activity. RBCs were cryopreserved using IRI-active molecules in combination with 15% (w/v) glycerol and were frozen either to −40°C (1°C/min) or to −80°C (dry ice), thawed immediately in a 37°C water bath and percent hemolysis was determined using the Drabkin's assay. Prior to deglycerolization, osmotic fragility studies were performed to determine optimal saline wash conditions. RBC samples were deglycerolized manually using centrifugation with supernatant removal between washes and the remaining packed RBCs were resuspended in SAGM or AS-3 solution. Percent cell recovery was calculated based on changes in RBC volume and hematocrit.

Results: After thawing, one IRI showed an increase in the percentage of intact RBCs post-thaw compared to the 15% glycerol control (95% vs 40%). Osmotic fragility studies showed that RBCs suspended in a cryosolution containing an IRI had a high osmotic tolerance and a 2-step wash could be used for deglycerolization. In combination with 15% glycerol, this IRI afforded a RBC recovery of 57% compared to the 15% glycerol control (26%).

Summary/Conclusions: Azide-based small molecule IRIs represent a novel class of cryprotectants that have the ability to successfully cryopreserve RBCs using reduced glycerol concentrations (15%), with significantly improved recoveries. This work demonstrates that the structure of an IRI can be rationally modified for a specific in vitro application.

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HUMAN PLATELETS LABELED AT MULTIPLE BIOTIN DENSITIES: A PROMISING APPROACH FOR MONITORING IN VIVO PLATELET SURVIVAL IN CLINICAL TRIALS

C Ravanat, V Heim, A Pongérard, A Dupuis and C Gachet

Université de Strasbourg, INSERM, EFS Grand Est, BPPS UMR-S1255, FMTS, Strasbourg, France

Background: Biotin (Biot) is an alternative to radioactive blood cell tracers. It allows one to concurrently track in vivo multiple cell populations labeled at different Biot densities. So far, multi-labeled red blood cells have been safely transfused in man to assess their survival (Mock, 2014). Concerning platelets, the Biot method has been utilized to simultaneously monitor the survival of low- and high-Biot PLTs in animals (Franco, 1994; Alberio, 1997). However, only one study in man has described the tracking of a Biot-platelet population (Stohlawetz, 1999).

Aims: Our aim was to label human platelets (PLTs) with different levels of Biot to determine whether biotinylation affects their function. This was a preliminary study to explore the feasibility of multi-labeled Biot-PLT production for clinical trials.

Methods: PLTs in Tyrode's albumin (TA) were treated with Biot-sulfo-NHS (0, 4.5, 45 and 180 μM), washed twice to remove the excess of Biot and re-suspended (3×10^8/ml) in a mixture of TA/PPPcit (v/v). Biot densities were controlled by flow cytometry analysis with streptavidin-PE labeling and PLT functions by assessing parameters such as secretion, glycoprotein (GP) integrity and aggregation.

Results: Various Biot-PLT populations could be distinguished by flow cytometry: Biot 0 (MFI 0.7 ± 0.3), Biot 4.5 μM (MFI 3.7 ± 0.2), Biot 45 μM (MFI 35 ± 1.2), Biot 180 μM (MFI 168 ± 27). All Biot-PLT populations displayed swirling. GPIb and GPIIbIIIa expression was normal for all Biot-PLTs. Using TRAP (60 μM), quantitation of P-selectin externalization was stable from 0 to 45 μM Biot labeling but slightly lower for 180 μM Biot: Biot 0 (P-selectin 7086 ± 631), Biot 4.5 μM (P-selectin 6244 ± 709), Biot 45 μM (P-selectin 6156 ± 868), Biot 180 μM (P-selectin 3040 ± 492). PLTs aggregability using arachidonic acid (1 mM) was well preserved in all Biot-PLTs: Biot 0 (amplitude 100%), Biot 4.5 μM (amplitude 101 ± 0.7%), Biot 45 μM (amplitude 96 ± 3%), Biot 180 μM (amplitude 80 ± 9%), whereas biotinylation impaired the response to ADP (5 μM) and collagen (2.5 μg/ml) in a dose dependent manner with an aggregation of the Biot180-PLTs almost abolished. ADP: Biot 0 (amplitude 100%), Biot 4.5 μM (amplitude 97 ± 5%), Biot 45 μM (amplitude 51 ± 6%), Biot 180 μM (amplitude 4 ± 1.6%). Collagen Biot 0 (amplitude 100%), Biot 4.5 μM (amplitude 101 ± 2%), Biot 45 μM (amplitude 88 ± 6%), Biot 180 μM (amplitude 36 ± 21%).

Summary/Conclusions: The main PLT functions tested, i.e., secretion, GP integrity and aggregation in response to the strong agonist arachidonic acid, were fully preserved for all the Biot densities used. In contrast, Biot labeling affected the response to ADP and collagen. We conclude that multi-Biot labeling would be suitable to trace PLTs in clinical trials provided low Biot densities (<45 μM) are used when full PLT function is critical. This approach should be helpful to evaluate new PLT products and fulfill the need for non-radioactive tracers.

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SELECTION OF BLOODSTAINS AT THE CRIME SCENE DEVELOPMENT OF AN IN-SITU DISCRIMINATION METHOD BASED ON BLOOD TYPING

V Carlier, A Bécue and O Delémont

Ecole des Sciences Criminelles, University of Lausanne, Lausanne, Switzerland

Background: Blood sampling at a crime scene is a crucial investigative step aiming at collecting a set of bloodstains to help reconstructing the past events, mostly through DNA profiling. It represents a challenge for crime scene investigators who must balance the number of stains to be collected without missing relevant samples. To reach that goal, they usually rely on their experience or on a blood pattern analysis.

Aims: Discriminating bloodstains from different sources directly at the crime scene would represent a third approach, providing the investigators valuable information such as a minimal number of distinctive sources and distinctive bloodstains to be sampled.

Methods: Our approach is based on the use of antibodies to discriminate bloodstains. To reach that goal, it was first necessary to determine if the distributions of blood antigens are correlated between individuals and which blood antigen represents the highest discriminatory power. Twenty-four blood antigens were identified from the literature (several ethnic groups) and from a set of fifteen individuals (mainly Caucasians) by using 'MDMulticards®' (Grifols) and 'ID-Antigen Profile' kits (Bio-Rad®). The second step was to determine if the selected antigen was stable with time and available for immunodetection. Bloodstains from twelve individuals (i.e., three donors per blood group of the ABO model) were left on five substrates (i.e., glass, tile, paper, fabric and wood). The stains were dried for a month at room temperature in a laboratory. The dot blot technique was carried out to detect the presence of the chosen antigen in A and AB bloodstains and to assess the specificity of the approach using B and O bloodstains as negative controls. The third step consists in establishing an application protocol compatible with a crime scene use.

Results: Results of the discriminatory power calculation indicated that the A antigen (ABO blood group) was the most discriminatory antigen among the twenty-four antigens that were tested. The correlation measurements showed that the antigen distributions among the experimental set are not correlated. The dot blots successfully detected the A antigen into A and AB bloodstains after a month, confirming that this antigen is stable enough with time. The current approach requires to solubilize the bloodstains, which could hinder its application at the crime scene. This issue illustrates one of the difficulties of the forensic investigation: bloodstains are most likely dried and must be processed as such. Our efforts are currently focused on a way to locally solubilize the bloodstains, using anticoagulants and thrombolytic agents, promoting by the same way the interaction with the antibodies.

Summary/Conclusions: To conclude, this research aims at providing crime scene investigators a new method supporting their selective process of bloodstain

sampling. The A antigen (ABO blood group) has been identified as a promising and discriminating target. Results showed that it is still possible to detect this antigen after a month in dried bloodstains, which is required to consider blood typing at the crime scene. This research also illustrates how antibodies and blood antigens can be used in forensic science, to help police investigations.

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COLD STORAGES PROVOKES BIOMECHANICAL CHANGES AND AGGREGATE FORMATION IN PLATELET CONCENTRATES

K Aurich[1], R Palankar[1], O Hartwich[1], M Ulbricht[1], J Wesche[1], A Greinacher[1] and O Otto[2]

[1]Transfusion Medicine, University Medicine Greifswald [2]Innovation Center – Humoral Immune Responses in Cardiovascular Disorders, University of Greifswald, Greifswald, Germany

Background: Platelet concentrates (PC) are currently stored at room temperature (RT) for 4 days. PC storage at 4°C is an attractive option to reduce bacterial proliferation, reveals no differences in standard quality tests for platelet metabolism, aggregation and activation, but platelet function is impaired in in-vivo assays. To understand this contrast, we analyzed in detail platelet cytoskeleton and aggregation behaviour on different surfaces of cold stored PC. For a deeper insight in platelet biomechanical properties, we introduce real-time deformability cytometry (RT-DC), as a label-free functional platelet assay based on cell mechanical properties. As RT-DC measurements can be carried out without sample preparation based on intrinsic material properties only, we highlight the potential of cell mechanics as a label-free biomarker in platelet quality control.
Aims: The aim of this study is to gain a deeper insight into the binding and aggregation behaviour of cold-stored platelets and to characterize their biomechanical properties by RT-DC.
Methods: Platelets from apheresis PC of 8 healthy donors containing 65% additive solution (SSP+, Maco Pharma, France) were stored either at RT or at 4°C for 10 days. Samples were taken at day 1, 4, 7, and 10 after donation. All platelet samples underwent fluorescence microscopy with tubulin staining. Platelet adhesion was assessed on collagen, laminin, fibronectin, and fibrinogen. Real-time deformability cytometry is a hydrodynamic method for mechanical cell characterization, which is based on suspended cells pumped through a microfluidic channel. Cells are being deformed by hydrodynamic shear forces without any physical contact between cell and constriction wall. While cells translocate the channel, a high-speed camera captures images of the steady-state deformation, which allows for an analysis based on intrinsic cell properties with a throughput of approximately 1,000 cells/s on-the-fly. RT-DC allows to carry out label-free assays within seconds and without extensive sample preparation.
Results: RT-DC enables for a clear differentiation between RT and 4°C stored platelets. For cold storage conditions, deformation of platelets was reduced to 0.034 ± 0.004 (SEM of biological replicates), while samples stored at RT show an elevated deformation of 0.133 ± 0.032 ($P < 0.0007$). Platelet size (projected area) decreased during cold storage ($29.0 \pm 2.2 \ \mu m^2$ RT- platelets vs $24.8 \pm 1.5 \ \mu m^2$ 4°C-platelets at day 4; $P < 0.0047$). The cytoskeleton of 4°C stored platelets was assessed to be rapidly degraded as shown by tubulin morphology already after day 1. Most importantly, 4°C- platelets form aggregates on all tested matrices starting between day 1 and day 4 of storage and constantly increasing thereafter. This strongly indicates that cold stored platelets might increase the risk for micro-thromboembolism.
Summary/Conclusions: Platelets stored at 4°C for more than 3 days bear the risk for causing micro-thromboembolism. RT-DC allows capturing underlying alterations in the platelet cytoskeleton after 24 h based on high-throughput analysis of platelet biomechanical properties.

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IMMORTALIZATION OF ERYTHROID PRECURSOR CELLS BY C-MYC AND BCL-XL USING ANTIBIOTIC INDUCIBLE LENTIVIRAL VECTOR SYSTEM

R Kronstein-Wiedemann[1], S Zimmermann[2], E Pasini[3] and T Tonn[1]

[1]Institute for experimental Transfusion Medicine, DRK-Blutspendedienst Nord-Ost, Dresden [2]Institute for Microsystemtechnique– IMTEK, Albert-Ludwigs-University Freiburg, Freiburg, Germany [3]Department of Parasitology, Biomedical Primate Research Centre, Rijswijk, Netherlands

Background: Blood pharming using embryonic, bone marrow or induced stem cells represents a new and fascinating option to warrant the blood supply in the future.

However, little is known about the mechanisms and factors that would allow the most efficient in vitro generation of enucleated blood cells from the above mentioned progenitors.
Aims: We show that overexpression of c-myc and BCL-XL into erythroid precursors enables sustained exponential self-replication of glycophorin A-positive erythroblasts.
Methods: Using an antibiotic inducible lentiviral vector system we transduced erythroid precursor cells derived from CD34 + stem cells from mobilized peripheral blood (blood group AB RhD) with five different oncogenes (c-myc, BCL-XL, SV40 LargeT, Bmi-1, LhX-2) and combinations of each two. 48 h after transduction gene expression was induced by the addition of doxycycline. In the absence of doxycycline oncogene expression is turned-off. Using single cell printing technology single cell colonies were obtained, expanded and analysed for CD235a expression and morphology.
Results: The transduction of each oncogene alone does not lead to immortalization of the cells. Only combined transduction of c-myc and BCL-XL leads to immortalization of erythroid precursor cells and continuously proliferation of them for more than 2 years. Furthermore we obtained single cell colonies from these cells with different morphology and expression pattern for different surface marker (CD71, CD45, CD34, CD235a). After removal of doxycycline a part of these cells were differentiated into normoblasts and reticulocytes within 7 days.
Summary/Conclusions: Immortalization of erythroid precursor cells provides a model of erythrocyte biogenesis that could potentially contribute to a stable supply of erythrocytes for donor-independent transfusion and could pave the way for the development of universal blood (0 Rhd).

Transfusion Transmitted Infections – Screening Strategies for TTI

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EVALUATION OF THE ROCHE COBAS E801 INSTRUMENT: PILOT STUDY FOR ESTIMATING SPECIFICITIES USING SOUTH AFRICAN BLOOD DONOR SAMPLES

CF Coleman, J Jaza, S Machaba and M Vermeulen
Donation Testing, South African National Blood Service, Roodepoort, South Africa

Background: The South African National Blood Service was approached by Roche Clinical Operations to perform a post European Conformity (CE marking) study on the Roche Cobas e801 instrument. The new HIV Duo assay is CE marked but not FDA approved. The novel Duo technology allows for discrimination between antigen and antibody reactivity, adding information on infection recency.
Aims: To evaluate the specificity of HIV, HCV, HBsAg and TPHA assays on the Cobas e801 by screening South African blood donors and to compare this with Abbott Prism and Spinreact assays for the respective markers. Sensitivity was evaluated by comparing confirmed positive donors across systems.
Methods: During September 2017 a subset of approximately 300 randomly selected donor samples were tested daily in parallel using the Roche Elecsys HIV Duo, anti-HCV, HBsAg and TPHA and the Abbott Prism HIV O Plus, anti-HCV, HBsAg and Spinreact TPHA (Beckman Coulter PK7300). Specificity was calculated from testing 4922 donations for HIV, 5109 for HCV, 5135 for HBsAg and 5034 for TPHA. All discordant reactive samples were confirmed by comparing the Nucleic Acid Testing result (Procleix ULTRIO Elite) or performing confirmatory testing for anti-HIV (Biorad Geenius), HBsAg (Elecsys neutralization) or TPHA (recomWell Treponema IgM and IgG).
Results: Of the approximately 5000 donations tested, 16% were from first time and 84% from repeat donors. The specificity for each marker using the Cobas and Prism respectively, was as follows: 1) HIV was 99.90% (CI 99.76–99.97%) and 99.96% (CI 99.85–100%), 2) HBsAg was 99.94% (99.83–99.99%) and 100% (CI 99.93–100%), 3) HCV was 99.78 (99.61–99.89%) and 99.90% (CI 99.77–99.97%). Specificity for TPHA was significantly different at 99.88% (CI 99.74–99.96%) and 99.92 (CI 99.79–99.98%) on the Elecsys TPHA and Spinreact TPHA respectively (P = 0.02). Four HBsAg and nine anti-HIV confirmed positive donations were detected by both assays concurrently. The HIV Duo assay detected three additional antibody and two antigen false positive donations. No HIV antigen only positive donations were confirmed. The Elecsys anti-HCV detected 11 false positive donations, but none were confirmed. There were 36 confirmed Syphilis positive donations, of which the Elecsys TPHA

detected 33 with a sensitivity of 91.67% (CI 77.53–98.25%). The Spinreact TPHA detected 19 positive donations giving a sensitivity of 47.22% (CI 30.41–64.51%). Both Syphilis assays failed to detect one TPHA IgM positive sample each.

Summary/Conclusions: The specificity of the Cobas e801 assays is comparable to the Abbott Prism assays. Comparison between the two assays may be biased as repeat donors were used in the evaluation and therefore false positives on the Abbott Prism assay may have been screened out increasing specificity. The Elecsys HIV, HBsAg and HCV assays were able to detect all confirmed positives during this study. The Elecsys TPHA assay was significantly more sensitive than the Spinreact TPHA for the detection of TPHA IgG antibodies (P < 0.005) but specificity was lower (P < 0.05). The detection of TPHA IgG antibodies is less important to blood services as this indicates resolved infection. Based on results in this study the Cobas e801 could be considered by transfusion services for blood screening.

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PERFORMANCE EVALUATION OF ROCHE ELECSYS SEROLOGICAL SCREENING ASSAYS ON THE NEW COBAS E 801 AMONG BLOOD DONORS IN COMPARISON TO ABBOTT PRISM/ARCHITECT ASSAYS

M Miletic, M Stojic Vidovic, M Strauss-Patko and I Jukic
Croatian Institute of Transfusion Medicine, Zagreb, Croatia

Background: The Croatian Institute of Transfusion Service routinely screens all regular and first-time-donors with serology assays for HIV (HIV antigen/antibody), HCV (anti-HCV), HBV (HBsAg) and Syphilis (anti-TP) in addition to the respective ID-NAT assay. A method comparison between Roche Cobas e 801 and Abbott Prism/Architect on these parameters were carried out between October 2017 and January 2018.

Aims: The aim of the study was to evaluate the specificity as one of the key performance criteria for the platforms, Roche Cobas e 801 and Abbott Prism/Architect on the main four screening serology parameters.

Methods: The following assays were used: Elecsys® HIV Duo, Elecsys® Anti-HCV II, Elecsys® HBsAg II, Elecsys® Syphilis and Prism HIV Ag/Ab Combo, Prism HCV, Prism HBsAg as well as Architect Syphilis TP. The following verification methods were used to decide on false or correct positive results: immunoblot, HIV-1 Ag, 3rd HIV combination assay (HIV); immunoblot, HCV Ag, 3rd anti-HCV assays (HCV); HBsAg Confirmatory tests, hepatitis B serological profile (HBsAg); immunoblot, TPHA, RPR, 3rd syphilis ELISA (syphilis); in addition to triplex ID-NAT (HBV DNA, HCV RNA and HIV 1/2 RNA).

Results: The specificity results on Cobas e 801 Elecsys® HIV Duo were 99.85% (n = 4073), 99.90% for Elecsys® Anti-HCV II (n = 4006), 100% for Elecsys® HBsAg II (n = 4073) and 99.93% (n = 4052) for Elecsys® Syphilis. For Abbott Prism, the specificity for HIV Ag/Ab Combo was 100%, 99.93% for HCV and 99.98% for HBsAg; Abbott Architect Syphilis TP revealed a specificity of 100%.

Summary/Conclusions: The observed specificity performance data of the Roche Cobas e 801 Elecsys screening assays were similar to the respective Abbott Prism/Architect assays which showed a slightly higher specificity, but not statistically different. Taking into consideration, that the tested blood donor population was unselected and comprised of approx. 85% repeat, regular donors and approx. 15% first-time donors, a certain, however very difficult to quantify bias due to a cleaning-out process over many years of routine use can be a putative cause of slightly different specificity results of new and established screening assays. Both platforms can be considered suitable for blood donor screening.

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EVALUATION OF THE ROCHE ELECSYS® INFECTIOUS DISEASES ASSAYS ON THE NEW COBAS® E801 INSTRUMENT: COMPARING SPECIFICITY OF ELECSYS VERSUS ROUTINE BLOOD SCREENING ASSAYS

A Van Weert, M Gorissen-Schutter, L Schippers-Uiterwijk, N Teunissen and E Bakker
National Screening Laboratory Sanquin, Sanquin Blood Supply, Amsterdam, Netherlands

Background: Sanquin Blood Supply continuously investigates new developments to acquire and share knowledge for further improvement of the quality of the blood supply. Towards this purpose the National Screening laboratory Sanquin evaluated a panel of five assays on the new cobas® e801 instrument, including the recently CE-marked Elecsys® HIV Duo assay.

Aims: In this study a comparison is made of the specificity of the new cobas e801 assays with the established routine screening assays when testing whole blood donation and plasmapheresis samples. The panel included HIV, anti-HBc, HBsAg, anti-HCV and Syphilis. Results should demonstrate that the Elecsys assays are state-of-the-art and fulfill the 98/79/EC Directive (specificity >=99.5%).

Methods: In May and June 2017 samples from 2832 whole blood repeat donors, 309 new donors and 1134 fresh plasmapheresis donors were tested with Elecsys HIV Duo (HIVAG and AHIV), Anti-HBc II, Anti-HCV II, HBsAg and Syphilis. Results were compared to routine results: Prism® HIV O plus, HBcore, HCV, HBsAg and Olympus pk7300-TPHA. Discrepant or positive samples were confirmed by the respective NAT-screening assay (cobas MPX; except anti-HBc and Syphilis), confirmatory assays and immunoblots.

Results: Specificity for all samples tested (4275) was: Elecsys HIV Duo 99.93% (HIVAG 99.97%/AHIV 99.94%), Prism Next HIV O Plus 99.95%Elecsys Anti-HBc II 99.98%, Prism Next HBcore 100%Elecsys Anti-HCV II 99.91%, Prism Next HCV 99.95%Elecsys HBsAg 99.95%, Prism Next HBsAg 100%Elecsys Syphilis 99.95%, Olympus pk7300-TPHA 100%. All confirmed positive samples were detected by both assays.

Summary/Conclusions: The results demonstrate that in a routine laboratory environment the Elecsys assays investigated provide the required regulatory demands for ≥99.5% specificity and are comparable with established testing blood screening systems. All confirmed positive samples were detected by both systems as expected. Separate antigen and antibody sub-results (HIVAG and AHIV) provides added information. Depending on the donation testing strategy of the blood donation screening laboratory this may potentially shorten the clarification for a reactive result. One should note that comparing the specificity of a new assay and platform against a routine assay is potentially biased since donors with reactive donations in the past have been ruled in time. Therefore, donors causing false positive results in the past cannot be assessed.

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COMPARISON STUDY OF THE NEWLY LAUNCHED ROCHE ELECSYS INFECTIOUS DISEASE PARAMETERS ON COBAS E 801 IN BLOOD DONOR SCREENING

C Tinguely, M Hotz and C Niederhauser
Infectious Diseases, Interregional Blood Transfusion Service SRC Ltd, Berne, Switzerland

Background: Testing all blood donations for markers of infectious diseases in blood banks plays an important role in maintaining the safety of blood transfusions. Mandatory serological testing is performed for anti-HCV, HIV Ag/Ab, HBsAg and syphilis. Highly specific and sensitive tests with corresponding automation are essential for this purpose.

Aims: To evaluate the performance of the Elecsys HIV Duo, Anti-HCV II, HBsAg II and Syphilis (Roche Diagnostics) infectious disease parameters on the new cobas e 801 instrument a comparative study was carried out with the currently used ELISA methods on the Quadriga BeFree System (Siemens Healthcare Diagnostics).

Methods: The study took place in the Interregional Blood Transfusion Service in Berne, Switzerland. The specificity of the parameters has been studied on 3,066 blood donor sera (using sera from both first time and repeat donors). The samples were tested initially on the Quadriga Be Free System with the Enzygnost HBsAg 6.0, Enzygnost Anti-HCV 4.0, EnzygnostHIV Integral 4 and on the PK7300 (Beckman Coulter) with the newbio-PK TPHA (Newmarket Biomedical). These samples were retested on the same day on the cobas e 801 with Elecsys HIV Duo, Anti-HCV II, HBsAg II and Syphilis. Initial reactive samples were repeated in duplicate. Discriminatory tests were carried out on repeatedly reactive samples using alternative screening tests and neutralisation (for HBsAg) on an Abbott Architect i1000 system, immunoblots (HIV-, HCV-, Syphilis- INNO-LIA, Fujirebio), as well as, individual donation nucleic acid assay ID-NAT (HCV, HIV, HBV, Roche cobas 8800 system).

Results: Based on the results from testing 3,066 blood donations, the observed specificity of Roche Elecsys assays on cobas e 801 (R) and Siemens Enzygnost assays on Quadriga BeFree (S) are comparable: % specificity/% confidence interval: HCV 99.84/99.62 − 99.95 (R), 99.97/99.82−100 (S), HIV 99.77/99.53 − 99.91 (R), 99.97/99.82 − 100 (S), HBsAg 99.90/99.71 − 99.98 (R), 99.84/99.62 − 99.95 (S), Syphilis 99.93/99.76 − 99.99 (R), 100.00/99.88 − 100 (S). The initial reactive (IR) and repeat reactive (RR) % specificity were identical. One sample was positive with Elecsys HBsAg II and confirmed by Elecsys HBsAg Confirmatory assay but negative in the Enzygnost HBsAg 6.0, Architect HBsAg confirmatory, Architect anti-HBc and Roche HBV ID NAT. Further tests with this sample including repetition of the HBsAg

confirmatory assay and Auto-Confirmatory-Prototype assay (Roche Diagnostics) were negative indicating the Roche Elecsys HBsAg result was false reactive.

Summary/Conclusions: The observed performance of Roche Elecsys assays to Siemens Enzygnost assays is comparable in a blood donor screening setting. Due to the insufficient number of donor samples tested in parallel it was not able to analyse the specificity data statistically. It is worth noting that 92% of the samples included in the study derived from repeat donors who had been previously tested with the Enzygnost assays but were "naïve" for the Elecsys assays. The anti-HCV, HIV Ag/Ab, HBsAg and syphilis assays from both systems exhibit a very good specificity and are highly suitable and practicable for routine blood donor screening.

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SEROLOGY EVALUATION STUDY OF ROCHE ELECSYS INFECTIOUS DISEASES SCREENING ASSAYS ON THE NEW COBAS E801 IN A ROUTINE BLOOD DONORS POPULATION

J Burkhart, T Sauer, B Herb and F Weinauer

Blood Donor Service of the Bavarian Red Cross, Munich, Germany

Background: Screening of blood products with HIV antibody or combination assays (HIV antigen/antibody), HCV (anti-HCV) and HBV (HBsAg and anti-HBc) is mandatory in Germany in addition to the respective NAT assays (HIV-NAT and HCV-NAT) and voluntary HBV-NAT.

Aims: To investigate the specificity performance of a new Roche Cobas e 801 platform and the Siemens Quadriga BeFree System, a method comparison on these parameters was carried out between November and December 2017.

Methods: The specificity as one of the key performance criteria for the platforms, Roche Cobas e 801 and Siemens Quadriga BeFree System was evaluated on the main four screening parameters by parallel testing of approximately 5000 blood donations. The following assays were used: Elecsys® HIV Duo, Elecsys® Anti-HCV II, Elecsys® HBsAg II, Elecsys® Anti-HBc II and Enzygnost® HIV Integral IV, Enzygnost® Anti-HBc monoclonal, Enzygnost® HBsAg 6.0 and Enzygnost® Anti-HCV 4.0.

Results: The specificity results on Cobas e801 Elecsys® HIV Duo were 99.87% (n = 5268), 99.94% for Elecsys® Anti-HCV II (n = 5180), 99.92% for Elecsys® HBsAg II (n = 5181) and 99.92% (n = 5120) for Elecsys® Anti-HBc II. The initial reactive (IR) and the repeat reactive (RR) results for these assays were equal. For Siemens Quadriga BeFree system, the respective specificity for Enzygnost® HIV Integral IV was 99.98% (IR = RR, n = 5268); 99.96% (IR)/99.98 (RR) for Enzygnost® Anti-HCV 4.0 and 99.81% (IR)/99.90% (RR) for Enzygnost® HBsAg 6.0 (n = 5181); Enzygnost® Anti-HBc monoclonal revealed a specificity of 99.94% (IR = RR, n = 5120). 1 false negative sample was observed with Enzygnost® Anti-HCV 4.0 with a positive HCV immunoblot/negative HCV-RNA-NAT; 3 samples were excluded from calculations for anti-HBc due to inconclusive results of the confirmatory tests.

Summary/Conclusions: The observed specificity performance data of the Roche cobas e 801 Elecsys screening assays were very similar to the respective Siemens Enzygnost assays on Quadriga BeFree System, which showed a slightly higher specificity for HIV. It has to be noted, that the majority of the tested donations were from regular repeat donors (85–90%). These repeat donors were tested previously with the Siemens Enzygnost assays. Both platforms can be considered suitable for blood donor screening.

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HEV RNA SCREENING OF BLOOD DONATIONS BY A COMMERCIAL TRANSCRIPTION–MEDIATED AMPLIFICATION ASSAY (TMA): LINEAR CORRELATION BETWEEN TMA VALUES AND HEV VIRAL LOAD

M Piron[1,2,3], M Bes[1,2,3], C de la Torre-Rial[3], N Casamitjana[1] and S Sauleda[1,2,3]

[1]*Transfusion Safety Laboratory, Banc de Sang i Teixits, Barcelona* [2]*CIBERehd, ISCIII, Madrid* [3]*VHIR, Vall d'Hebron Hospital Research Institute, Barcelona, Spain*

Background: Hepatitis E virus is a potential threat to blood safety. The Blood and Tissue Bank of Catalonia (Spain) is screening blood donations with a fully automated NAT platform. In contrast to other NAT methods, where nucleic acid amplification reactions are brought to signal saturation, we have observed some variability in the signal to cut-off (S/Co) values of the commercial HEV NAT, paralleling HEV viral load in the samples.

Aims: The objective of this study is to assess whether there is a correlation between the S/Co signal of the TMA method and the HEV viral load in the blood donations.

Methods: HEV RNA positive blood donations and follow-up samples (33 and 21 samples respectively, total N = 54 samples) have been included in this study. All samples were tested individually by a qualitative NAT HEV method (Procleix HEV Assay, Panther, Grifols), with a 95% limit of detection (LOD) of 7.9 IU/ml according to the manufacturer's insert. Two different lots of reagents were used and the S/Co values for the respective positive calibrators were recorded. Viral load of HEV RNA positive donations was assessed by a quantitative in-house real time PCR using the HEV RNA WHO standard PEI 6329/10 and viral load was expressed as log10 IU/ml.

Results: The mean S/Co values for the WHO standard set to final concentration of 40 IU/ml were 13.4 ± 4.6 (CV 34%, N = 26 replicates). As for the HEV RNA positive donations, S/Co values ranged from 1.00 to 58.98. Comparison of S/Co values of the commercial assay with the estimated viral load of the samples showed linear correlation (R2 = 0.815). Low S/Co values correlated nicely with low viral loads and a formula could be obtained to calculate estimated viral load according to the S/Co value in the qualitative commercial assay: Y = 12,027X–7,4911, where Y equals to the S/Co value and X equals to the estimated viral load expressed in log10. The mean S/Co values for the positive calibrators of the commercial reagent were 32.4 ± 1.9 (LOT 1 N = 76 replicates) and 31.8 ± 3.1 (LOT 2 N = 282 replicates), for a coefficient of variation (CV) of 6% in LOT1 and 9.6% in LOT2. Applying the formula obtained previously, the HEV transcript concentration in the positive calibrators of the commercial system would equal to 3.3 log10 IU/ml for both LOT1 and LOT2, which is 2 logs above the claimed 95% LOD of the assay.

Summary/Conclusions: Unlike our previous experience with other TMA reagents for HCV/HIV/HBV NAT screening, HEV NAT performs as semi-quantitative assay and provides a rough estimation of HEV viral load in the sample. On the other hand, quite high variability in S/Co values is observed among replicates, even at HEV RNA concentrations well above the assay LOD, which may lead to a result slightly above 1 S/Co in true positive samples. The addition in the runs of an external positive control set to a concentration closer down to the LOD is advisable.

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SEROPREVALENCE OF HIV, HBV, HCV, SYPHILIS AND MALARIA AMONG BLOOD DONORS AT A LARGE ACADEMIC CENTER IN PAKISTAN: 2005–2016

F Karim[1], K Grabowski[2], H Qadir[3] and E Bloch[4]

[1]*Pathology and laboratory medicine, Aga Khan University Hospital, Karachi, Pakistan* [2]*Johns Hopkins University School of Medicine, Baltimore, United States* [3]*Aga Khan University Hospital, Karachi, Pakistan,* [4]*Pathology, Johns Hopkins University School of Medicine, Baltimore, United States*

Background: Transfusion transmissible infections (TTIs) remain a challenge to low-middle income countries given deficiencies spanning donor selection, testing, hemovigilance and quality systems. Published data on TTIs in Pakistan and other parts of South Asia are lacking.

Aims: We sought to characterize the epidemiology (i.e. seroprevalence by demographic and temporal trends) for the major TTIs (HIV, Hepatitis B [HBV] and C [HCV], Syphilis and malaria) in blood donors at a major academic center in Pakistan.

Methods: A retrospective data analysis was conducted of all donations at the Blood Bank of The Aga Khan University Hospital (AKUH) from 1st January 2005 to 30th December 2016. AKUH, located in Karachi, is one of the largest tertiary care teaching hospitals in Pakistan, offering comprehensive medical and surgical services including hematology-oncology and stem cell transplantation. Karachi is also the largest metropolitan city in Pakistan affording broad donor representation. All donations were routinely screened for HIV [anti-HIV-1/2, third generation automated chemiluminescence immunoassay (CLIA)], hepatitis C (anti-HCV by CLIA), hepatitis B (HBsAg by CLIA), syphilis (VDRL Carbon antigen, RPR kit) and malaria (ICT malaria, Rapid SD malaria antigen test). All reactive tests were repeated on the same sample. Data were collected using an in-house blood bank information system. Total seroprevalence for each infectious marker was estimated annually. Seroreactivity rates were compared between voluntary- non-remunerated and replacement donors (Chi-square test)

Results: A total of 289,066 blood donations were collected over twelve years; 278,509 (96.3%) donors were male. Ninety-two percent of the donors (n = 267,338) were replacement blood donors, the rest (n = 21728; 7.5%) were voluntary donors. No paid donation was reported. The overall donor seroprevalence for any infectious marker was 3.2% (n = 9137). The trend for transfusion transmitted infections

remained static for all five pathogens over the study period. Seroprevalence of each of the infectious markers was as follows: HIV 0.04% [n = 125], HBV 1.14% [n = 3320], HCV 1.54% [n = 4442], syphilis 0.40% [n = 1160] and malaria 0.03% [n = 90]. Most (n = 7747 [84.8%]) seropositive donors were resident in Karachi; the remaining seropositive donors spanned the following provinces: Sindh (10%), Balochistan (2.6%), Punjab (1.07%) and Khyber Pakhtunkhwa (0.14%); residence was not known in 1.2%. The cumulative seroprevalence in replacement donors (3.3% [n = 8944]) versus VNRBD (n = 193 [0.9%]) was not significantly different (P = 0.062). Donor status (i.e. first time vs. repeat vs. lapsed) was not recorded and therefore not available for analysis.

Summary/Conclusions: The findings indicate reliance on a donor pool that is overwhelmingly male and of mostly replacement donors. Replacement donation is widely publicized to portend higher risk of TTIs (as compared to VNRBD); this was not observed. The rates of TTIs in Pakistan have been largely static, with HCV and HBV being the most prevalent (corroborating other studies in Pakistan). However, exclusive use of serological testing algorithms, limited repeated testing and absent molecular evaluation, poses regional risk of transfusion transmission.

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Abstract has been withdrawn

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ANALYSIS OF DISCORDANT RESULTS IN SYPHILIS SCREENING OF BLOOD DONORS

A Varaklioti[1], A Papachronis[1], P Kotsi[1], M Gavalaki[1], T Adraktas[1], A Kontopanou[1], V Tatsi[1], V Kapsimali[2] and O Katsarou[1]

[1]Blood Transfusion Center, Laiko General Hospital [2]Laboratory of AIDS and STD, Andreas Syggros Hospital of Cutaneous and Venereal Diseases, Athens, Greece

Background: The use of the reverse algorithm for syphilis screening of blood donors is increasingly being adopted. Automated treponemal immunoassays have undoubtedly mediated this transition. However, growing number of discordant results between treponemal and nontreponemal tests, impose a challenge towards management and notification of blood donors.

Aims: The aim of the study was to evaluate discordant results during syphilis screening in a blood donor setting.

Methods: From September 2013 to June 2017 serum samples from all blood donors were screened with Architect Syphilis TP Assay (Abbott Diagnostics). All initially reactive samples (signal to cutoff value, S/CO>1) and samples with grey zone results (S/CO: 0.85–0.99) were further tested in a reference laboratory with both a nontreponemal test (Venereal Disease Research Laboratory test, VDRL) and a second confirmatory treponemal test (Treponemal pallidum agglutination assay, TPPA). Results of both VDRL and TPPA tests were reported as negative or positive, while TPPA positive samples were further reported with an end point titer. Statistical analysis was performed with SPSS and included descriptive frequencies, Spearman correlation between S/CO and TPPA titers and ROC (Receiver Operator Characteristic) curve analysis.

Results: A total of 72.448 blood donations were screened for syphilis using the reverse algorithm via an automated chemiluminescent immunoassay (CLIA), of which 231 (0.32%) were characterized initially reactive. 203 samples had S/CO>1 and 28 had grey zone results. Supplemental testing with the nontreponemal VDRL test confirmed CLIA reactivity in only 27 (11.7%) cases. When TPPA was used as a confirmatory test, 81 samples out of 231 (35.1%) were confirmed positive, whereas 150 samples (64.9%) were negative. Among 204 (88.3%) of VDRL negative sera, 58 samples were TPPA positive, which could represent samples from individuals with early primary infection or treated syphilis and should be deferred as blood donors. Median S/CO ratio was higher among TPPA-positive samples compared to TPPA-negative samples (12.87 vs 1.48). Furthermore, correlation analysis revealed a strong positive correlation between S/CO ratios and TPPA titers (Spearman correlation coefficient r = 0.831, P < 0.001). ROC curve analysis exhibited an area under the curve (AUC) of 0.990 (95% CI 0.982–0.998) and revealed that the optimal S/CO cutoff value for the prediction of positive results was 3.6.

Summary/Conclusions: Management of blood donors with positive syphilis screening could be a complicated and delicate issue, therefore confirmatory testing is important. All discordant samples (CLIA positive and VDRL negative) should be corroborated with a confirmatory treponemal test, such as TPPA, to discriminate between false reactivity and blood donors with either treated or early primary

syphilis. Analysis of our data revealed that an S/CO value of 3.6 can potentially discriminate those sera that need further confirmation with TPPA analysis. When initial screening values are above the optimal S/CO value of 3.6, confirmatory TTPA analysis can be omitted. Moreover, discordant treponemal results (CLIA positive and TPPA negative, with lower S/CO values than the optimal cut/off, most likely represent false positive cases.

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DETECTION OF HUMAN T CELL LYMPHOTROPIC VIRUS TYPE 1 BY WESTERN BLOT AND REAL-TIME PCR AMONG BLOOD DONORS IN ZHEJIANG PROVINCE

B Dai[1,2], X Ling[1,2], X Li[1,2], H Zhu[1,2], J He[1,2], F Zhu[1,2] and W Hu[1,2]

[1]Blood Center of Zhejiang Province [2]Zhejiang provincial Key Laboratory of Blood Safety Research, Hangzhou, China

Background: Screening all blood donors for HTLV-1 and HTLV-2 is not mandatory in China. Therefore, the data for HTLV-1/2 prevalence in the Chinese blood donors is rare. Anti-HTLV test was preformed for all blood donors in Zhejiang Province, China from 2016 and currently more than 1,000,000 donations were determined.

Aims: The aim of this study is to evaluate the HTLV prevalence in the Chinese blood donors and compare the results between Western blot and real-time PCR method.

Methods: All donors were preformed a physical examination according to the donation regulations of China and screened with Hb, HBsAg and alanine aminotransferase (ALT) before donation, then deferred donation with HBsAg positive, ALT level abnormal (>50 IU/ml) or Hb level lower (Male<120 g/L, Female<115 g/L). Following donation, the samples were preformed for Anti-HTLV-1/2 using ELISA reagents according to manufacturer's instruction. Samples with anti-HTLV-1 reactive in ELISA were tested by Western blot assay (WB), and HTLV-1 DNA in these samples were also detected using real-time PCR technique. This research was supported by the Science Foundation of Zhejiang Health Bureau (No.2016KYA070 and 2017KY316).

Results: Totally, 128 samples with anti-HTLV-1/2 positive were found in 481312 donation, the initial reactive rate was 0.0266% in the blood donations. Then these initial reactive samples were analyzed by HTLV-1/2 WB, the results were showed that 19 samples were positive (14.8%),9 samples were indeterminate (7.0%) and 100 samples (78.1%) were negative. All of positive individuals were HTLV-1 type. The confirmation anti-HTLV-1 positive rate was 3.95/100,000 in blood donations. HTLV-1 DNA of 128 initial reactive samples were analyzed, all individuals with HTLV-1 WB positive were reactive in the HTLV-1 real-time PCR, but all the individuals with HTLV-1 WB indeterminate or negative were not reactive in the HTLV-1 real-time PCR.

Summary/Conclusions: The HTLV prevalence data was obtained in the Chinese blood donors. The real-time PCR assays may be as a confirmation method substitute for HTLV-1 WB.

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DEVELOPMENT OF ALTERNATIVE PROCEDURES FOR HBV DNA CONFIRMATION IN BLOOD DONORS WITH NON-REPRODUCIBLE REACTIVE NUCLEIC ACID TESTING

X Deng[1], X Guo[1], L Zhou[1], L Zang[1], S Laperche[2], X Liang[1] and D Candotti[2]

[1]Dalian Blood Center, Dalian, China [2]DATS, INTS, Paris, France

Background: Blood donations screening with the Procleix-Ultrio Plus nucleic acid testing assay (Grifols) requires a secondary diagnostic step using separate virus-specific amplification discriminatory assays to identify the origin of the multiplex reactivity. However, non-reproducible reactive (NRR) samples defined as multiplex reactive but discriminatory assay non-reactive and/or repeat multiplex non-reactive are observed. Confirmation of HBV DNA reactivity can prove challenging in donors with occult HBV infection (OBI) especially when anti-HBc testing is not informative due to high prevalence. It is also critical to limit blood product wastage and definitive deferral of potentially safe donors in areas experiencing donor shortage.

Aims: To develop alternative HBV DNA confirmation algorithms using viral particle concentration procedures coupled with optimized sensitive nested PCR assays.

Methods: Blood donors from Dalian, China, were screened pre-donation for HBsAg. Eligible donors were further tested with two HBsAg EIAs and for HBV DNA by using ProCleix-Ultrio Plus assay. Individual samples NAT initially reactive (IR) were

discriminated according to manufacturer's procedure. NAT IR/HBsAg- samples were retested twice and discriminated once using ProCleix Ultrio Plus assay. Viral particle concentration was done by ultracentrifugation (250,000 g for 3 h) or precipitation with 12% polyethylene glycol (PEG) at 4°C of 12 and 6 ml plasma, respectively. Nested PCRs targeting different regions of HBV genome (BCP/PC, preCore/Core, pre-S/S, and S) were developed and optimized to a 95% LOD of 5 IU/ml using the WHO International Standard (10/266). Repeat DNA testing (12 replicates) was performed using the Ultrio Elite assay.

Results: 118/51,247 (0.23%) samples were Ultrio-Plus reactive: 23 (19.5%) HBsAg+ and 94 HBsAg-. Based on repeat and discriminatory testing, 51 (54%) HBsAg- samples were identified as NRR. The 43 (46%) HBsAg-/HBV DNA repeated reactive (RR) samples were further confirmed OBI carriers. Ultrio Elite repeat testing of 15 randomly selected anti-HBc+ NRR and 5 RR control samples was performed: 9 (60%) NRR samples were consistently non-reactive, and 2 (13%) and 4 (27%) showed 1/12 and 2-11/12 reactive replicates, respectively, and 3-12/12 replicates were reactive for all RR controls. HBV DNA was detected by at least one PCR assay in 6 (40%) and 7 (47%) NRR samples following virus concentration by PEG precipitation and ultracentrifugation, respectively. Five of Ultrio Elite non-reactive samples were PCR non-reactive irrespective of the virion concentration procedure. HBV DNA was consistently detected in all RR samples with at least two PCR assays. Additional 64 NRR plasma samples from Dalian blood donors were ultracentrifuged and HBV DNA was detected in 43 samples (67%).

Summary/Conclusions: The combination of highly sensitive NAT and presence of low levels of HBV DNA resulted in a 54% NRR rate in blood donors from Dalian, China. The concentration of viral particles from large volumes of plasma and the development of sensitive HBV nested PCRs confirmed the presence of HBV DNA in 63% (50/79) of HBsAg-/anti-HBc+/NAT NRR donors. Further sequencing of amplified products will definitively confirm HBV infection. PEG precipitation may constitute an alternative method to concentration HBV particles when ultracentrifugation cannot be implemented for technical or economic reasons.

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THE COBAS MPX ASSAY ON THE COBAS 6800 PLATFORM: DIAGNOSTIC PERFORMANCE AND ONE-YEAR ROUTINE EXPERIENCE

I Debruyne, E De Samblanx, M Vanbrabant, A Muylaert and E Lazarova
Blood Services, Belgian Red Cross-Flanders, Mechelen, Belgium

Background: In most countries, blood donations are routinely screened for the presence of HIV, HBV and HCV by nucleic acid testing (NAT). Previous assays were based on the simultaneous detection of viruses, requiring an additional step for discrimination. The introduction of discriminatory NAT assays, combined with a new generation of diagnostic platforms, has resulted in an increased throughput, an ameliorated user friendliness and an improved donor management. One of the new assays, the cobas MPX assay on the Roche cobas 6800 platform, allows discriminatory detection of HBV-DNA, HCV-RNA, HIV-1 Group M RNA, HIV-2 RNA and HIV-1 Group O RNA in human plasma and serum samples.

Aims: We aimed at studying the diagnostic performance of the cobas MPX assay on the cobas 6800 system in comparison with the cobas Taqscreen MPX v1 assay on the cobas s201 system.

Methods: During pre-implementation verification, the diagnostic specificity was determined by testing 280 minipools of 6 donations (MP6) with the cobas Taqscreen MPX v1 assay and the cobas MPX assay in parallel. To assess diagnostic sensitivity, a total of 18 samples reactive for HBV, HCV or HIV were tested with the cobas MPX assay, both individually and in MP6. The limit of detection (LoD) was determined by Probit analysis using a WHO reference standard or an equivalent Roche material. We also implemented the cobas Synergy software, a middleware that connects the Hamilton STAR pooling instrument, cobas 6800 system and laboratory information system and manages the total workflow. One year after the implementation of the assay in January 2017, a total of 363.754 donations had been tested in minipools. To investigate long-term reproducibility, the inter-run precision was calculated for the cycle threshold values of all the assay controls measured during one year.

Results: In the pre-implementation verification, the diagnostic specificity and sensitivity were both 100%. The 95% LoD of HBV, HCV, HIV-1M, HIV-2 and HIV-1O was 1.1, 6.6, 21.9, 4.4 IU/ml and 5.6 cp/ml, respectively. Since the implementation of the assay, 11 samples were NAT reactive when tested individually. Ten of these results were confirmed by serological testing or by NAT testing in an external laboratory, one result was false-positive (99.9997% specificity). However, we also observed 79 pools that were initially reactive, but did not have a reactive result when tested

individually. It is likely that these non-resolved pools are caused by non-specific amplification and are thus false-positives, which lowers the specificity to 99.87%. Long-term %CV's are 2.02, 1.10, 0.98, 0.96, and 1.11 for HBV, HCV, HIV-1M, HIV-2 and HIV-1O, respectively. Since we are the first user of the Synergy software, we frequently encounter teething problems, hampering the workflow.

Summary/Conclusions: The cobas MPX assay on the cobas 6800 shows high analytical and diagnostic sensitivity and good reproducibility. During routine testing we regularly observe reactive pools that cannot be resolved on the individual level, lowering the initial diagnostic specificity of 100% to 99.87% for MP6. Furthermore, the Synergy software currently does not deliver added value compared to its predecessor. These are limitations for which we advise an improvement.

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HCV CORE ANTIGEN ASSAY VS NAT IN BLOOD DONORS

L Sommese[1], C Sabia[1], A Sansone[1], A Sorriento[1], C Iannone[1], M Montesano[1] and C Napoli[1,2,3]

[1]*U.O.C. Division of Clinical Immunology, Immunohematology, Transfusion Medicine and Transplant Immunology, Regional Reference Laboratory of Transplant Immunology, AOU, Department of Internal and Specialty Medicine* [2]*Department of Medical, Surgical, Neurological, Metabolic and Geriatric Sciences, Università degli Studi della Campania "Luigi Vanvitelli"* [3]*IRCCS SDN, Naples, Italy*

Background: Chronic hepatitis C virus (HCV) infection is estimated to affect million individuals worldwide. Screening assays for HCV detection are routinely performed with specific anti-HCV antibodies (anti-HCV) assay in order to guarantee the safety of blood donation. HCV/RNA detection by nucleic acid testing (NAT) is also performed on blood donors in compliance with national law. In many industrial countries, NAT introduction for blood donor screening has decreased the risk of viral transmission via blood transfusion. Unfortunately, HCV transmission by hemocomponents is still a problem in developing countries in which NAT cannot be implemented for its high cost and technical skill requirement.

Aims: The aim of this study was to evaluate the performance of HCV core antigen (HCV-Ag) assay as potential alternative to NAT and determine its clinical utility in the management of blood donors.

Methods: From 2013 to 2017, n = 63 randomized blood donors, aged 25–60 years (average 37.1 ± 10.2) resulted anti-HCV reactive were studied. All serum samples were evaluated for HCV detection by using Architect anti-HCV assay with Chemiluminescent Microparticle Immunoassay (CMIA) platform (Abbott Diagnostics, Wiesbaden, Germany). Besides, all samples were tested also for Architect HCV-Ag assay. Those sera yielding sample/cutoff (S/CO) ratios between 0.80 and 0.99 were scored as gray zone (GZ) while those yielding S/CO ratios ≥1.00 as reactive samples. All reactive and GZ samples for anti-HCV assay were further checked by confirmatory testing such as HCV specific immunoblot assay (Fujirebio, Italia S.r.l.). The relationship between S/CO and confirmed seropositive samples was assessed. All blood donations were screened also by NAT for HCV-RNA by the TaqScreen method on the Cobas s201 system (Roche Molecular Systems, Branchburg, NJ, USA): the assay was performed on mini pools of six samples each and with a nominal sensitivity of <20 International Units per milliliter (IU/ml).

Results: Of 63 samples, n = 50 were anti-HCV reactive with S/CO between 1.00 and 18.65 while n = 13 resulted anti-HCV GZ. Only 10 anti-HCV reactive samples with S/CO between 9.47 and 18.65 were positive with HCV-Ag assay resulting also NAT positive. The correlation between HCV-Ag assay and NAT was 100%.

Summary/Conclusions: Our data highlight that HCV-Ag assay correlate highly with NAT, especially with those samples yielding an anti-HCV S/CO >9.00. Thus, a reliable and easy serological marker such as HCV-Ag assay could support NAT, mainly in those countries where NAT is not currently performed for high cost. Then, the implementation of this serological assay could provide a new scenario for blood safety.

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SERO POSITIVE NAT NEGATIVE SAMPLES IN THAI BLOOD DONORS

K Chaiwong[1], P Thunnok[1], S Oota[2] and U Charoonruangrit[2]

[1]Blood Testing Section [2]National Blood Centre, Thai Red Cross Society, Bangkok, Thailand

Background: National Blood Centre (NBC), Thai Red Cross Society (TRC) has been followed the policy of Thailand blood service that recommended the donated blood screening using both serological test and Nucleic acid testing (NAT) for all blood donation. The blood transfusion service was managed by NBC, TRC about 90% of all blood donations throughout the country. Chemiluminescent immunoassay (CIA) was a serological suggestion for HIV Ag/Ab Anti-HCV HBsAg and Syphilis detection. NAT was suggested for HIV-RNA HCV-RNA HBV-DNA, the method was changed from mini pool of six (MP6) to individual NAT (ID-NAT) since 7 January 2016. From annual report, more than 600,00 samples of donated blood were collected from NBC and about 100,000 samples were collected from hospital blood bank (HBB) that locate in Bangkok and nearby. The HBB donated blood samples were sent to NBC for blood grouping and transfusion-transmitted infection (TTI) screening.

Aims: Are there Sero positive NAT negative (SPNN) samples after implemented the ID-NAT?

Methods: Data of donated blood testing were collected from 7 January 2016 – 31 October 2017. Only blood donors from NBC could be distinguished for sex, first-time donors (FD) and repeated donors (RD). All data were analyzed by Excel program 2013.

Results: Total 1,467,906 samples (1,275,449 from NBC, 192,457 from HBB) were tested with serological test and NAT for HIV, HCV, HBV infection. This study found that total seropositive samples for HBsAg, HIV Ag/Ab, Anti-HCV were 1537, 645 and 1898 respectively, from these 60, 266, 1513 samples were SPNN for HBsAg, HIV Ag/Ab and Anti-HCV respectively. The seropositive samples from HBB were 724 (HBsAg), 171 (HIV Ag/Ab) and 563 (Anti-HCV), from these samples 31 (HBsAg), 64 (HIV Ag/Ab) and 432(Anti-HCV) were SPNN. Whereas, total seropositive samples from NBC were 813 (HBsAg), 474 (HIV Ag/Ab) and 1335 (Anti-HCV), also 29 HBsAg-SPNN samples that as 10 males (6 FD, 4 RD) and 19 females (14 FD, 5 RD), while 202 HIVAg/Ab-SPNN samples separated as 101 males (34 FD, 67 RD) and 101 females (50 FD, 51 RD), furthermore 1081 Anti-HCV-SPNN samples were distinguished as 478 males (227 FD, 251 RD) and 603 females (279 FD, 324 RD).

Summary/Conclusions: This study shows that although using IDNAT some samples could only detected by serological testing. Sensitivity of serologic reagents should be considered for donated blood screening. Some SPNN samples might be false positive serology or false negative NAT. These positive donors should be followed for diagnosis with second testing. From our experience, less than 50% of positive donors came back for followed test. Furthermore, this study has been showed 0.1% of total samples were HBsAg, Anti-HCV positive rate and 0.04% for HIV Ag/Ab, while 1:24465, 1:5518, 1:970 were HBsAg-SPNN, HIV Ag/Ab-SPNN and Anti-HCV-SPNN rate respectively. The minimum-maximum of signal ratio (S/CO) of these SPNN were 1.19–5210.55 (HBsAg), 1.00–1146.5 (HIV Ag/Ab) and 1.00–74.80 (Anti-HCV). Except the false positive samples, these SPNN samples can increase the safety of donated blood by avoid TTI for the recipients.

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NAT TESTING – AN ADDED LAYER OF BLOOD SAFETY

A Verma, P Negi, J Singh, S singh and M Khan

Transfusion Medicine, Max Super Speciality Hospital Vaishali, Ghaziabad, India

Background: One of the main strategies employed and required in ensuring blood safety is donor testing for various pathogens in preventing transfusion transmitted infections (TTI). The efficacy of testing is dependent on the ability to detect certain markers of infection. There are two general testing modalities: the first is nucleic acid testing (NAT), assaying for nucleic acid sequences (RNA or DNA) specific to the infectious agent's genome and the second is assaying for viral protein or antibodies produced by the host specific to the infectious agent. NAT testing is generally more sensitive and decreases the window period of an infectious pathogen when compared to serologic/protein tests

Aims: The main aim of this case study is to highlight the importance of NAT as an effective method for safeguarding the blood supply.

Methods: The study was carried out at Department of Transfusion Medicine for over a period of 2 years from January 2016 to December 2017. A total number of 9,419 blood donor samples were subjected to screening for HIV 1 & 2 Virus, hepatitis B virus (HBV) and hepatitis C virus (HCV) by using fully automated Enhanced Chemiluminescence Immunoassay Assay (ECI) processor of VITROS. The tests performed were HBV surface antigen (HBsAg) to detect HBV, anti-HCV to detect HCV and HIV kits to detect p24 antigen and glycoprotein antibodies against HIV 1 and 2. Rapid cards were used for detection of malaria and Syphilis. During the same period, 9,259 (nonreactive samples for HIV 1 & 2 Virus, hepatitis B virus (HBV) and hepatitis C virus (HCV) by using fully automated Enhanced Chemiluminescence Immunoassay Assay (ECI) processor of VITROS) were subjected for NAT. Plasma was separated and tested using the multiplex polymerase chain reaction (PCR) technology.

Results: Of the 9,419 blood donors screened for HIV, HBV and HCV by using fully automated Enhanced Chemiluminescence Immunoassay Assay (ECI) processor of VITROS 160 (1.70%) were seroreactive for HIV (22, 0.23%), HBV (64, 0.68%) or HCV (74, 0.79%). The NAT yield (Seronegative by ECI and NAT reactive) for HIV-1,HIV-2, HCV and HBV was 5 out of the 9,259 samples tested (0.05%) and included only HBV.

Summary/Conclusions: Blood safety is still a major challenge in India because of the high prevalence of HIV (0.5%), HCV (1.5%), and HBV (4%), the relatively low percentage of voluntary blood donors and the lack of standardization of screening procedures among the multitude of blood collection centers. The NAT yield of 5 out of the 9,259 samples tested (0.05%) in our study is highly significant as single donation is used for generating 3 components that can be further used by 3 different recipients. Hence, in effect the NAT yield becomes 3 times that is 15 in 9,259 and saved 15 recipients from TTI out of 9,259 (0.16%). As reducing the rate of TTI gains momentum more and more countries are adopting NAT testing before release of blood products. NAT can serve as an additional layer of safety in providing safe and high quality of blood and blood components to all patients requiring blood transfusion.

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SEROPREVALENCE OF HIV HCV HBV AND SYPHILIS INFECTION AMONG BLOOD DONORS OF NATIONAL BLOOD CENTRE, THAI RED CROSS SOCIETY: 10 YEARS RETROSPECTIVELY

W Saekram, T Meemook, N Yuttayoth, R Kimilar, P Khamsawang, D Intharasongkroh and K Chaiwong

Blood Testing Section, National Blood Centre, Thai Red Cross Society, Bangkok, Thailand

Background: The blood safety is provided through several processes for minimizing the risk of transfusion-transmitted infections (TTIs). The infected donors are excluded by donor selection and blood screening followed the National guidelines. Serological testing is a major role and important method for blood donor screening in routine laboratories. In Thailand, human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and syphilis are tested on blood samples for the provision of blood safety. The seroprevalence of TTIs among blood donors of the National Blood Centre (NBC), Thailand is different in each year. So, this study aimed to assess the seroprevalence of HIV, HCV, HBV and Syphilis of NBC's blood donors for ten years. These results will useful to know Thailand situation and their trends for developing the national blood donor policy in the future.

Aims: To assess the seroprevalence of HIV, HCV, HBV and Syphilis infection among blood donors of the NBC, Thailand.

Methods: Ten years retrospective of NBC's blood donors serological screening was studying from October 2007 to September 2017. The reports of seroprevalence including HIVAg/Ab, HCV antibody, HBsAg and Treponema pallidum antibody by using chemiluminescent microparticle immunoassay (CMIA) were reviewed and summarized.

Results: Of 6,096,547 volunteer blood donors for ten years ago, 42,444 donors (0.70%) were infected with at least one pathogen. And in these infected donors were positive for HIV 5,894 (0.10%), HCV 8,867 (0.15%), HBV 20,634 (0.34%) and Syphilis 7,049 (0.12%).

Summary/Conclusions: From our data, the HBV infection was the highest in NBC's blood donors of Thailand followed by HCV, Syphilis and HIV respectively. The seroprevalence of HIV, HCV, HBV and Syphilis infection has continuously deceased from the past. So, the result of this study showed that the efficacy of blood donor selection was better than the previous and Thai blood donors realized the importance of self-defer when they have been exposed to any risk before blood donation.

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Abstract has been withdrawn

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BLOOD DONATION AND HEPATITIS SEROPREVALENCE

AS Rezeq and A Rezeq

QA, Palestinian Central Blood Bank, Ramallh, Palestinian Territory, Occupied

Background: Blood transfusion is one of the most important therapeutic procedures in life-threatening conditions. Transfusion-transmissible infections (TTIs) have continued to raise concerns about blood safety. Challenges to safe blood transfusion continue due to new emerging pathogens.
Aims: This study aims to determine the prevalence of only examined infections hepatitis B (HBV), and hepatitis C (HCV) among blood donors at the Palestinian Central Blood Bank (PCBB) to reflect on the current status of transfusion medicine.
Methods: A retrospective cohort of the profiles of 77,360 blood units was conducted including donors between January 2010 and October 2017 at PCBB. The donated units were routinely examined for HBs Ag, anti-HCV, anti-HIV-1/2, and Syphilis. The data were analyzed for HBV and HCV only.
Results: Among the donated blood units (77,360), 52% were voluntary donations, 95.4% were males, and the average age was 30.8 ± 9.8 years. During all study years, around 50% of donors were <30 years old and another about 27% were between 30 and 40 years old. Blood types A positive and O positive constituted the majority of donated samples (36.2% and 31.7% respectively). The seroprevalence of HBsAg was 0.9% and that of anti-HCV was 0.3%. The highest prevalence was seen in 2011 for both HCV and HBV (0.5% and 1.5%). Moreover, the seroprevalence of HBsAg was higher among male donors and A negative blood group, whereas HCV seroprevalence did not differ by any of the demographic factors.
Summary/Conclusions: This study shed light on the high prevalence HBV and HCV among blood donors which might also reflect a high prevalence of other unexamined TTIs. Thus, there is an urgent need to develop blood safety surveillance system and to further introducing a nucleic acid testing for the list of infections that are considered major risk factors in transfusion medicine according to the International Society of Blood Transfusion.

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THE PREVALENCE OF TRANSFUSION TRANSMITTED INFECTIOUS AMONG BLOOD DONORS IN THE LAO PEOPLE'S DEMOCRATIC REPUBLIC

C Souksakhone[1], C Keokhamphoiu[1], V Soinxay[2] and T Mazda[3]

[1]National Blood Transfusion Center [2]National Blood Transfusion Centre, Lao Red Cross, Vientiane, Lao People's Democratic Republic [3]Social Pharmacy, Kitasato University, Tokyo, Japan

Background: Every unit of Blood donation are screened for TTI testing before transfusion which are HIV 1/2, HBsAg, HCV, and Syphilis. Among of these four mandatory tests, HBsAg positives has been shown remaining stable high prevalence, in particular first time blood donors 8.7% and 9.6%.(1,2) Because of this high prevalence of HBV, the Lao government started a HBV vaccination program for newborns in 2002. Recently Xeuatvongsa et al (3) reported that the prevalence of HBsAg is not high in Laos since both mothers (15–45 years) and infants (5–9 years) taken randomly from selected districts in the whole country show positivity of 2.9% and 1.7% respectively. In this report, TTI positivity was analyzed according to occupation age, gender, and number of blood donation during 2015–2017 in National Blood Transfusion Centre, Vientiane, Lao PDR.
Aims: To investigate the trend of TTI prevalence among blood donors in Lao PDR.
Methods: TTI positivities were calculated from routine screening test results for all blood donors (total 54,857 donors: 47,877 volunteer blood donors and 6,980 family donors) at the NBTC in 2015–2017. HIV was screened by HIV Ag/Ab Combo SD Bioline/Aler, HBsAg and HCV was screened by commercial ELISA kits, Monolisa HBsAg Ultra (Bio-Rad Laboratories, Inc.), and Syphilis by Human.
Results: HIV positive cases were significant increased from 0.08%, 0.16% and 0.21% in 2015, 2016, 2017 respectively. Majority of these are young ages. HBsAg positivity for first time donors and repeat donors (2 and more times) was for males higher than females. In particular 17 to 19 year old showed higher than other groups. The average positivity of first-time blood donors was 7.5%. Males were more than 2 times higher than females.

Summary/Conclusions: The increasing of HIV positives cases were showed alarming status for donor selection and screening process to ensure blood transfusion safer. First-time donor positivity of HBsAg in Laos was high (7.5%) but this is dependent on age and gender. The reason for high positivity in young blood donors, especially teenagers, is unknown. Probably it is due to horizontal infection by health problems in their normal social lives, not to mother-child infection. The NBTC introduced a notification system to donors who were found to be TTI positive, those positive are not accepted as future blood donors. The majority of blood donors are from the young generations in Laos, however currently this group has the highest TTI prevalence. Measures for making blood safer should always be considered. 1) Jutavijittum P, et al. Southeast Asian J Trop Med Public Health 38: 674–679, 2007. 2) Jutavijittum P, et al. Vox Sang 106, 31–37, 2014. 3) Xeuatvongsa A, et al. PLOS ONE 9(2): e88829, 2014.

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PREVALENCE OF TRANSFUSION TRANSMITTED INFECTIONS AMONG IRANIAN BLOOD DONORS; SOUTH OF IRAN

M Paridar[1], A Khosravi[2], M Jalalifar[2], A Salah[3], P Paridar[1] and Z Sabzpoush[1]

[1]Deputy of Management and Resources Development, Ministry of Health and Medical Education [2]Transfusion Research center, High Institute for Research and Education in Transfusion Medicine, Tehran [3]Transfusion Research center, High Institute for Research and Education in Transfusion Medicine, Shiraz, Iran

Background: he chief aim of blood transfusion organization is providing adulate and safe blood supply. Major transfusion-transmissible infections (TTIs) including human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis have been considered as a worldwide health concern. The prevalence of TTIs among blood donors could be reflected the safety of blood supply.
Aims: To evaluation of transfusion-transmitted infections prevalence among Iranian blood donors.
Methods: The retrospective study was carried out on blood donors admitted to Fars blood transfusion organization (FBTO) during 2016 to 2017. The viral screening test was conducted on all donations. Initially, reactive donors were repeatedly tested and confirmatory tests were performed for repeatedly reactive donors. Donors with confirmed positive infection considered for analyzing The prevalence of infections were calculated per 100,000 donations.
Results: The overall prevalence of HBV, HCV, and HIV were 43, 23 and 4 (per 100,000).The prevalence of viral infection positive donations slightly increased from 66.5 in 2016 to 75.5 in 2017(HBV; 41 to 46, HCV; 21 to 24, HIV;3.7 to 4.3). Moreover, it has been shown that TTIs prevalence was significantly higher in mobile blood collection sites than fixed sites (108.5 vs 61.5).
Summary/Conclusions: Our findings indicated that TTIs prevalence in the studied region is considerably lower than our neighboring countries. But, we have found that the prevalence is increasing during the studied period. Moreover, It has been seen that donors admitted to mobile blood collection sites carried a higher risk of TTIs. FBTO should be reconsidered the strategies of mobile blood collection sites establishment.

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USE OF A NOVEL TECHNOLOGY TO EFFECTIVELY WASH THE SAMPLE PIPETTOR DURING AUTOMATED BLOOD SCREENING ON THE ALINITY S

LA Martin[1], S Stramer[2], D Krysztof[2], B Weston[1], M Flores[1], M McGowan[1], D House[3], P Soni[3], E Prieto-Ballengee[3] and G Williams[1]

[1]D-09GT, Abbott Laboratories, Abbott Park, IL [2]Scientific Affairs, American Red Cross, Gaithersburg, MD [3]D-8482, Abbott Laboratories, Abbott Park, IL, United States of America

Background: Historically, individual disposable pipettor tips have been used as an alternative to complex sample pipettor washing protocols during automated blood screening. These tips increase cost per test due to the commodity cost, storage, workflow impact (load/unload), and disposal of the associated solid biohazardous waste. The application of induction heating technology to the sample probe is an alternative to individual disposable pipettor tips. It provides a non-contact method to enhance liquid washes on metallic pipettor probes. The induction heating system induces an alternating current on the surface of the metallic probes. The probe's electrical resistance to this current results in localized, highly controlled heating on

the probe's internal and external surfaces. By increasing the temperature of the probe surface, an active liquid wash is greatly enhanced. This heat is then quenched during a thorough washing operation prior to aspiration of the next sample to prevent any temperature related impact to subsequent samples.

Aims: To demonstrate the effectiveness of induction heating as a means of effective sample probe washing during blood screening on the Alinity s.

Methods: The effectiveness of induction heating was evaluated on the Alinity s, a new automated blood screening platform. Worst case conditions were established by quantification of HBsAg concentrations in HBsAg positive donor samples. Negative donor samples were tested under conditions with no positive material present (protected negatives) and compared to negative donor samples that were directly preceded by an extremely high concentration HBsAg positive sample (unprotected negatives).

Results: The HBsAg concentrations were determined in a sampling (n = 448) of the 2,725 HBsAg positive donors identified from 29 million donations. In this sampling, 9 donors with HBsAg concentrations above 125,000 IU/ml were identified. Based on these results, the frequency of finding a donor with an HBsAg concentration above 125,000 IU/ml is approximately 1 in 500,000 thus establishing 125,000 IU/ml as an appropriate worst case condition. Studies were conducted on the Alinity s using induction heating under these worst case conditions comparing protected negatives to unprotected negatives. Two studies were performed using high positive samples greater than 125,000 IU/ml. In each study, 12 or 13 protected negative replicates and 12 or 13 unprotected negative replicates were generated. In the two studies, the means of the unprotected negatives were 0.18 S/CO and 0.21 S/CO versus an assay cutoff of 1.00 S/CO. The S/CO shifts between the means of the protected replicates and the means of the unprotected replicates were 0.01 S/CO and 0.04 S/CO, respectively.

Summary/Conclusions: Induction heating prevented the extremely high positive sample from impacting the subsequent unprotected negative sample results. These results indicate that induction heating provides acceptable sample pipettor washing without having to generate solid biohazardous waste and other negative consequences associated with disposable pipettor tips.

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INDUCTION HEATING: AN ADVANCED WASHING TECHNOLOGY TO PRESERVE SAMPLE INTEGRITY ON ALINITY S FOR TRANSFER TO NAT INSTRUMENTS

P Soni[1], A Olivo[1], M Barber[1], R Whitlatch[1], M Effinger[1], J Mackowiak[1], G Cloherty[1], M Rodgers[1] and A Fischer[2]

[1]Abbott Laboratories, Abbott Park [2]Abbott Laboratories, Irving, United States of America

Background: In automated blood screening, the potential for contamination from a previous sample puts all downstream molecular testing integrity at risk. Single-use pipette tips with filter barriers are commonly used to reduce this risk, although this strategy greatly increases the cost per test due to the additional commodity, storage, workflow impact (load/unload), and disposal costs of the biohazardous waste.

Aims: To meet the critical need of maintaining sample integrity, we evaluate a novel application of induction heating as a means of effectively washing a non-disposable pipettor that handles samples analyzed between serology instruments like Abbott's Alinity s instrument to Nucleic Acid Testing (NAT) instruments in which targets are exponentially amplified through multiple thermal cycles.

Methods: In this application of induction heating, the metallic pipettor warms under its own resistance to coil-induced electrical currents. By sweeping the pipettor through an induction coil, temperatures on the pipettor are elevated throughout its length. The effectiveness of the induction heater was evaluated on a new automated blood screening platform (Alinity s, Abbott Laboratories) with an extremely high viral load HBV sample (8.69 log IU DNA/ml) near the upper limit of quantitation (ULOQ) of the molecular assay (ULOQ 9 log IU DNA/ml, RealTime HBV, Abbott Molecular Diagnostics). Samples such as this one with >8.5 log IU DNA/ml are among the highest of all HBV DNA positive specimens in the Abbott Global Surveillance program, which is biased to include mostly ill patients seeking healthcare. Worst case conditions were evaluated by organizing the high viral load HBV sample immediately before a known HBV DNA negative sample (60217, negative human plasma, Abbott Molecular Diagnostics) and run on the Alinity s platform with induction heated washes between all samples. This loading pattern was replicated 134 times. The known negative samples were then analyzed for the presence of HBV DNA using the Abbott RealTime HBV assay with a limit of detection (LOD) of 15 IU DNA/ml on the Abbott m2000 instrument. Nonconformance was defined as any known negative HBV samples having any amount of detectable HBV DNA.

Results: All negative samples (n = 134) run on an Alinity s immediately after a high-titer (8.69 Log IU DNA/ml) HBV sample, with induction heated washes in between, yielded no detectable amount of the HBV target (<15 IU DNA/ml).

Summary/Conclusions: Induction heating effectively maintains the integrity of samples run on the Alinity s instrument for downstream molecular testing. Given the higher frequency of HBV samples with viral load >8.5 log IU/ml compared to other viruses, our results suggest that these results will likely extend to additional infectious disease markers for HIV and HCV.

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ABBOTT ALINITY S ASSAYS ROBUSTNESS TO BIOTIN INTERFERENCE

LA Martin, J Siregar, S Gawel, S Worobec, X Jiang, J Bryant and G Williams

Blood Screening Assay New Product Development, Abbott Laboratories, Abbott Park, IL, United States of America

Background: The use of biotin as a supplement has increased in recent years and many health care professionals may not be aware of the high dosage intake by their patients or donors of blood products. Specimens collected from patients taking 300 mg/day may have concentrations of biotin up to 1200 ng/ml. Based on guidance from the FDA, the Alinity s assays were tested at a level nearly three times greater than the highest concentration reported or 3500 ng/ml. High levels of biotin in samples have led to inaccurate lab results for assays that utilize the free capture biotin-streptavidin methodology. Although Abbott's Alinity s assays do not utilize this free capture biotin-streptavidin methodology, eight assays developed for blood screening on the Alinity s system were evaluated for biotin interference to ensure there are no unknown consequences of high biotin levels.

Aims: The purpose of this study was to determine if the eight Abbott Alinity s assays would be susceptible to biotin interference by evaluating their performance in the presence of high concentrations of biotin.

Methods: For each of the Alinity s assays evaluated (Anti-HBc, Anti-HCV, Chagas, CMV IgG, HBsAg, HIV Ag/Ab Combo, HTLV I/II, and Syphilis), samples spiked with concentrations of biotin at 1500 and 3500 ng/ml were tested against a control (unspiked) sample preparation to determine if there was a difference between the control and biotin containing samples. Two samples, one negative and one positive, were tested with all assays, except the HIV and HTLV assays, which each tested two positive samples (HIV-1 antibody, HIV-1 p24 antigen, HTLV-I antibody and HTLV-II antibody, respectively).

Results: For the negative samples that were tested with 1500 ng/ml, the sample to cutoff (S/CO) differences between the biotin spiked and control were 0.00 for Anti-HBc, Anti-HCV, Chagas, CMV IgG, HBsAg, HIV Ag/Ab Combo and Syphilis, and 0.03 for HTLV I/II. For the negative samples spiked with 3500 ng/ml, the mean S/CO differences between the biotin spiked and control were either −0.01 or 0.00 for the eight assays. For the positive samples spiked with 1500 ng/ml, the percent differences between the biotin spiked and control ranged from −2.1 to 1.5% for all assays. For the positive samples spiked with 3500 ng/ml, the percent differences between the biotin spiked and control ranged from −1.0 to 2.2% for the eight assays.

Summary/Conclusions: Eight Abbott Alinity s assays were evaluated to determine if they were susceptible to biotin interference. These results indicate that the eight Alinity s assays do not show susceptibility to biotin interference at concentrations of 1500 and 3500 ng/ml.

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Abstract has been withdrawn

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PERFORMANCE OF NEW ASSAYS FOR HTLV I/II, HBC AND CHAGAS ON THE FULLY AUTOMATED ABBOTT ALINITY S SYSTEM

B Marchlewicz[1], R Haley[2], S Jones[3], T Simon[4], G Williams[5], M Paradowski[5], L Martin[5], T Bui[1] and G Chen[1]

[1]D-09TM, Abbott Labs, Abbott Park [2]Medical Director, Bloodworks Northwest, Seattle [3]Scientific Research, Biobridge Global, San Antonio [4]Medical Director, CSL Behring, King of Prussia [5]D-09GT, Abbott Labs, Abbott Park, United States of America

Background: Blood centers require high throughput assays with a high level of reproducibility to assure consistent results and minimize unnecessary retesting of samples and deferral of donors. In addition, continued economic pressures on laboratory operations demand that assays perform on platforms capable of increased walk away time and enhanced automation in areas of reagent management, retest options, and commodity/waste management.

Aims: To evaluate the within-run, within-day, within laboratory reproducibility (which includes the within run, between run, and between day variability) of 3 new automated prototype chemiluminescence immunoassays for the detection anti-HTLV I/II, anti-HBc and anti-T. cruzi antibody on an automated next generation platform, the Abbott Alinity s.

Methods: A 5-day reproducibility study was conducted by testing a reproducibility panel consisting of multiple members (7 for HTLV; 4 for HBc and Chagas) representing different levels of analyte. Testing was done at 3 sites, with 1 instrument per site, using each of 3 lots of assay reagents, calibrators, and controls.

Results: A total of at least 359 results were generated for each panel member and data from the 3 clinical sites and 3 reagent lots were used in the final analysis. For Reactive samples: the within-run % CVs across all 3 assays ranged from 2.2 – 3.6%; the within-day %CVs ranged from 2.2 – 3.7%, and the within laboratory reproducibility %CVs ranged from 2.4 – 3.7%. For the Negative Control sample: the within-run SDs ranged from 0.001 – 0.021; the within-day SDs ranged from 0.001 – 0.021; and the within laboratory reproducibility SDs ranged from 0.001 – 0.022.

Summary/Conclusions: The new automated prototype Alinity s system and assays demonstrated reproducibility values that had less than a 4% CV on reactive samples or a SD < 0.022 for a negative sample. This demonstrates the precision of results generated by this fully automated blood screening analyzer, which helps assure consistent results for the testing and retesting of blood donor specimens.

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PERFORMANCE OF NEW ASSAYS FOR HBSAG, HCV, AND HIV AG/AB COMBO ON THE FULLY AUTOMATED ABBOTT ALINITY S SYSTEM

B Marchlewicz[1], R Haley[2], S Jones[3], T Simon[4], G Williams[5], M Paradowski[5], L Martin[5], J Bryant[5], T Bui[1] and G Chen[1]

[1]D-09TM, Abbott Labs, Abbott Park [2]Medical Director, Bloodworks NorthWest, Seattle [3]Scientific Research, Biobridge Global, San Antonio [4]Medical Director, CSL Behring, King of Prussia [5]D-09GT, Abbott Labs, Abbott Park, United States of America

Background: Blood centers require high throughput assays with a high level of reproducibility to assure consistent results and minimize unnecessary retesting of samples and deferral of donors. In addition, continued economic pressures on laboratory operations demand that assays perform on platforms capable of increased walk away time and enhanced automation in areas of reagent management, retest options, and commodity/waste management.

Aims: To evaluate the within-run, within-day, and within laboratory reproducibility (which includes the within run, between run, and between day variability) of 3 new automated prototype chemiluminescence immunoassays for the detection Hep B Surface antigen, anti-HCV and HIV Ag/Ab Combo on an automated next generation platform, the Abbott Alinity s.

Methods: A 5-day reproducibility study was conducted by testing a reproducibility panel consisting of multiple members (12 for HIV Ag/Ab Combo; 4 for HBsAg and HCV) representing different levels of analyte. Testing was done at 3 sites, with 1 instrument per site, using each of 3 lots of assay reagents, calibrators, and controls.

Results: A total of at least 358 results were generated for each panel member and data from the 3 clinical sites and 3 reagent lots were used in the final analysis. For Reactive samples: the within-run % CVs across all 3 assays ranged from 2.5 – 4.7; the within-day %CVs ranged from 2.7 – 4.7%, and the within laboratory

reproducibility %CVs ranged from 2.7 – 4.9%. For the Negative Control sample: the within-run SDs ranged from 0.004 – 0.023; the within-day SDs ranged from 0.005 – 0.030; and the within laboratory reproducibility SDs ranged from 0.005 – 0.030.

Summary/Conclusions: The new automated prototype Alinity s system and assays demonstrated reproducibility values that had less than a 5% CV on reactive samples or a SD < 0.030 for a negative sample. This demonstrates the precision of results generated by this fully automated blood screening analyzer, which helps assure consistent results for the testing and retesting of blood donor specimens.

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INCIDENCE OF HIV, HBV AND HCV IN UNITED STATES REPEAT BLOOD DONORS FROM 2007–2016: DOES INCIDENCE METHODOLOGY AFFECT RATES?

W Steele[1], L Crowder[1], E Notari[1], J Haynes[1], R Dodd[2] and S Stramer[3]

[1]Scientific Affairs [2]Medical Office, American Red Cross, Rockville [3]Scientific Affairs, American Red Cross, Gaithersburg, United States of America

Background: Monitoring incidence of transfusion-transmitted viral infections (TTI) is a key blood safety activity. Calculations of incidence in repeat donors use different methodologies (Brambilla, Transfusion 2016). When calculating incidence for the most recent 10 years at the American Red Cross (ARC), results of two methods were compared, the conventional method (CM) and the extended lookback method (ELM). In the CM, a repeat donor is included as an incident case or contributes to person-time if at least 2 donations exist within the estimation interval (EI). With ELM, the history of each repeat donor within the EI is traced back the same length of time as the EI to look for prior negative donations (i.e., an EI of 24 months requires a 24-month lookback). Donation data must be available that predate the EI so that each repeat donor can have the appropriate lookback. This allows for the inclusion of more positive and negative donors, but may introduce bias. In either method, repeat donors lacking a prior donation within the EI (CM) or extended lookback (ELM) are censored.

Aims: To present incidence rates for HIV, HBV and HCV in ARC donors for five 2-year estimation intervals (2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016) using two calculation methodologies.

Methods: Incidence rates were calculated as the number of incident cases divided by total time at risk for all repeat donors (expressed per 100,000 person-years, pht). Linear regression was used to test for temporal changes in rates.

Results: Incidence rates for HIV, HBV and HCV decreased between the first and last interval studied using both methodologies, but this decrease was only significant for HIV and HBV (CM: F = 13.42, P = 0.04 and F = 25.99, P = 0.01, respectively; similar data exist for ELM). Using CM, HIV incidence in 2007–2008 was 4.24 pht and with ELM was 2.13 pht. In 2015–2016, HIV incidence using CM was 2.59 pht and using ELM was 1.27 pht. HBV rates decreased from 5.63 to 1.45 pht by CM and 2.74 to 0.66 pht by ELM. For HCV, CM in 2011–2012 was highest at 7.32 pht with the ELM estimate of 3.86 pht. By 2015–16, HCV was 1.75 pht using CM and 1.42 pht using ELM. ELM captured an additional 502 donors that were not characterized as incident using CM including 148, 105, and 245 discrepant donors for HIV, HBV, and HCV, respectively.

Summary/Conclusions: Incidence of all three TTIs in US blood donors are decreasing regardless of calculation method. Although both methodologies show the same temporal patterns, CM consistently had higher rates compared to ELM. Even though ELM identified a greater number of incident donors, the ELM person-time calculation is on average over 200% greater than that used in CM, while the number of incident donors captured in ELM is, in all but two calculations, less than 100% greater. The larger denominator, without the balance of an equally larger numerator, resulted in lower ELM incidence. Comparisons of incidence between blood collectors using different methodologies should be made cautiously. The strengths, limitations, and potential biases must be evaluated to determine the optimal method.

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ESTIMATION OF UNDETECTED TRANSFUSION TRANSMISSIBLE INFECTIONS AT NAKASERO BLOOD BANK UGANDA

K swaib and M Ezra

Laboratory, Uganda Blood Transfusion Services, Kampala, Uganda

Background: Blood transfusions have not been ever associated with zero risk, patients need safe transfusions and risk reduction through improvement in infectious disease screening. The implementation of nucleic acid testing (NAT) technology in relation to the conventional screening assay and improved screening of volunteer non remunerated donors will assist screening safer units, confirmation as well as introduction of Malaria among Transfusion Transmissible Infections (TTIs) for routine screening in endemic Uganda. Many counties in the world have implemented NAT for the purpose of blood safety but not yet implemented as a routine in screening donor blood. UBTS currently uses enzyme linked immunosorbent assay (ELISA), chemiluminescent microparticle immunoassay (CMIA) technology for screening all donor blood but may increase risk of disease transmission depending on viraemic window period of analyzed TTIs.

Aims: This study aimed at determining the prevalence of undetected TTIs using NAT and unscreened malaria using malaria rapid diagnostic test.

Methods: This was a prospective cross-sectional study carried out at UBTS. Over the period of six months from September to February 2018, a total of 660 nonremunerated blood donors were selected from collection sites in the central region. All negative donations screened from architect were used, A total of 132 minipools of five units aliquot each were analyzed using BCIM screening kit for Ribonucleic acid and Deoxyribonucleic acid of Human immunodeficiency virus (HIV), Hepatitis C (HCV) and Hepatitis B (HBV). Also malaria rapid diagnostic Tests (RDTs) were used to screen for Malaria. The data was analysed using Microsoft Excel.

Results: A total of 660 donor blood were analyzed of which, 132 mini-pools analysed with NAT gave 08 (6.1%) mini-pool (MP NAT) detection for HBV, and 124 (93.9%) undetected for HIV, HCV and HBV. The true positive tests for TTIs after individual donor nucleic acid testing (ID-NAT) re-run was 12 (1.82%) HBV detected, and none undetected for HIV, HCV. A total of 49 units, accounting for an estimated prevalence of 7.4% tested positive on malaria RDT.

Summary/Conclusions: The estimated figures of undetected TTIs at Nakasero Blood Bank of HBV and malaria was at 1.82% and 7.4% respectively are much higher than those of Donors in developed countries. This is because of the screening algorithm at Nakasero Blood Bank does not capture all significant TTIs. In addition, the sensitivity of both ELISA and CMIA is lower compared to NAT which detects even at lower viraemic diagnostic window period for HBV, HIV and HCV. The use of Mini-pools to confirm the true negatives by NAT might be economical as it saves on reagents, and small turnover. Adoption of NAT as a routine procedure and screening for malaria will help to improve on blood safety and cost for all Ugandans.

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PERFORMANCE COMPARISON OF TWO AUTOMATED CHEMILUMINESCENT IMMUNOASSAY FOR HUMAN IMMUNODEFICIENCY VIRUS, HEPATITIS C VIRUS, HEPATITIS B VIRUS AND TREPONEMA PALLIDUM IN BLOOD DONORS

P Kitpoka[1], S Chanthet[1], S Chiawchan[1], P Suksomboonvong[1], S Onseedaeng[1], P Chaisuwirat[2] and P Kreyasa[2]

[1]Pathology, Ramathibodi Hospital [2]Army Institute of Pathology, Phramongkutklao Medical Center, BKK, Thailand

Background: The prevention of transfusion transmitted infections have been performed through serological test and nucleic acid test (NAT). Automated chemiluminescent immunoassays (CLIA) have been replaced enzyme immunoassays (EIA) and widely used due to their increased sensitivity and specificity.

Aims: The goal of this study was to compare the performance of more recent Electro Chemiluminescent Immunoassays (ECLIA) with the former Chemiluminescent Microparticle Immunoassays (CMIA) for the detection of HBsAg and antibodies against HIV, HCV and Treponema pallidum (TP) in blood donors.

Methods: Serum samples of 2609 voluntary, random blood donors from the blood banks of Ramathibodi Hospital and Army Institute of Pathology were screened in parallel with CMIA (Architect i2000SR, Abbott, Wiesbaden, Germany) and ECLIA (cobas e 601, Roche, Mannheim, Germany) for the detection of anti-HIV, anti-HCV, HBsAg and antibodies to TP. Initial reactive samples were repeated in duplicate and repeatedly reactive (RR) and discordant samples between the two systems were

investigated by confirmatory assays. The Biorad Geenius HIV 1/2 confirmatory, INNO-LIA HCV Score Line Immunoassay and EUROIMMUN Fluorescent Treponemal Ab-Absorption IgG (FTA-ABS IgG) and multiplex NAT by the cobas® TaqScreen MPX v2.0 test (Roche Molecular Systems, US) were used. Follow up samples were available for two thirds of the discordant samples which were also tested with the above tests.

Results: The concordance between the two systems was high (99.69% for HIV 1/2 Ag/Ab, 99.85% for HBsAg, 99.85% for anti-HCV and 99.39% for antibody to TP). The specificity of Elecsys HIV combi PT II and Abbott HIV Ag/Ab Combo were 99.92 and 99.77% respectively (P = 0.15). The specificity of anti-HCV was identical for Elecsys Anti-HCV II and Abbott Anti-HCV (99.92%). For HBsAg, the specificity of Elecsys HBsAg II was 100% while the specificity of Abbott HBsAg Qualitative II was 99.84% (P = 0.15).

Summary/Conclusions: The performance of the cobas e 601 and Architect i2000SR were similar with high concordance. The specificities of HBsAg and HIV 1/2 Ag/Ab were slightly higher for the cobas e 601, but no statistical significance was observed. Only concordance, but not specificity, was calculated for the Syphilis tests as the donors for the discordant samples were lost to follow up. The balance of sensitivity and specificity of donor screening assays must be considered for donor counselling and blood product management.

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PERFORMANCE VALIDATION OF FORTRESS ELISA KIT AT NAKASERO BLOOD BANK

S Ssenyonga

Laboratory, Uganda Blood Transfusion Service, Kampala, Uganda

Background: The laboratory diagnosis of HCV, HBsAg, syphilis and HIV infection, is usually made on the basis of serology. Serological assays for detection of antibodies or detection of antibodies and antigens are generally classified as either first-line assays (screening assays) or second line assays (supplemental assays). First-line assays can provide the presumptive identification of reactive specimens and thus should have superior sensitivity, and second-line and third-line assays are used to confirm whether specimens found reactive with a particular first-line assay contain antibodies specific to antigen. These assays should have a superior specificity.

Aims: The objective was to document the process results and process parameters obtained during the testing of HCV, HBsAg, SYPHILIS antibodies and HIV1/2 antibodies plus P24 antigens using fortress ELISA reagent kit in the laboratory at Nakasero Blood Bank.

Methods: Each sample was tested first with Abbott Architect immunochemistry analyzer which uses CMIA technique to identify status. Positives were then duplicated to rule out any errors that might have occurred in the first step. The negatives were then tested in duplicate form to assess specificity of the assay under validation. The strongly positive samples with OD of 400S/CO and above for HIV, HBsAg and HCV were also duplicated to asses for Sensitivity of the assay. Sixty-eight (68) chronic positive HIV samples obtained from patients attending ART-Clinic from one of the referral hospitals in Uganda were also included in the validation to serve as reference samples. For syphilis all those that turned positive on CMIA were considered in the test run for ELISA.

Results: The overall specificity of the fortress diagnostic ELISA kit is 97.85%, its sensitivity is 99.6%, reproducibility is 99.65%, Positive predictive value is 72.09%, Negative predictive value is 99.53% and its imprecision is 0.35% for the three assays.

Summary/Conclusions: An onsite validation of the test system and materials in the laboratory will be required prior to its use in routine testing and processing of blood. The recommendations put forth in this document address only the establishment of performance specifications for analytical methods and the validation of method performance characteristics.

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PERFORMANCE EVALUATION OF VITROS® SYPHILIS TPA ASSAY IN DONOR SAMPLES BASED ON CDC –REVERSE ALGORITHM PROTOCOL: PROSPECTIVE STUDY IN TERTIARY CARE CANCER HOSPITAL

A Pathak

Transfusion Medicine, Rajiv Gandhi Cancer Institute & Research Center, New Delhi, New Delhi, India

Background: Syphilis is a sexually transmitted (major route) and a transfusion transmissible (other route) bacterial infection caused by the spirochete Treponema pallidum (T. pallidum). It is mandatory to do serological test for syphilis on all donor blood samples. Serological test for syphilis is usually based on detection of antibodies against the cardiolipin-lecithin antigen (Non-treponemal) or against the Treponemal specific antigen. The large number of false results and the low sensitivity of these tests have led to the introduction of T. pallidum specific tests for syphilis screening e.g. TP haemagglutination (TPHA) test & the fluorescent treponemal antibody absorption (FTA-ABS) test.

Aims: To evaluate the performance of VITROS® syphilis TPA assay in terms of its sensitivity and specificity in comparison with current non treponemal syphilis assay followed by treponemal FTA-ABS test for the healthy donor samples, as per the CDC guidelines for screening syphilis infection based on reverse algorithm protocol

Methods: In this prospective study (from Jan 2017 to Dec 2017) a total of 6831 blood donors were screened for syphilis infection using VITROS® Syphilis TPA (VSTPA) assay. All syphilis reactive samples by VSTPA assay were again tested by ASPEN® syphilis rapid test (ASRT) strip, which is a rapid chromatographic immunoassay for qualitative detection of antibodies (IgG & IgM) to T. pallidum in serum or plasma. All syphilis blood samples reactive by VSTPA assay and non reactive by ASRT were sent for treponemal FTA-ABS test to International reference laboratory.

Results: Out of 6831 samples screened, 73 (1.06%) samples were found reactive by using VSTPA assay. 37/73 (50.68%) VSTPA assay reactive samples were showing discordant results when tested with ASRT. 15 out of 37 (40%) discordant samples, tested in international reference laboratory for FTA-ABS, showed concordant (high concordance, 40%) results with VITROS® Syphilis TPA assay.

Summary/Conclusions: VITROS® syphilis TPA assay based on enhanced chemiluminescence technology has excellent sensitivity in screening for syphilis infection and helps in minimizing false negative results thereby enhancing the safety of blood for transfusion. Assays with low sensitivity like RPR and syphilis rapid card test may lead to false negative results and may impact the blood safety. Introduction of VITROS® Syphilis TPA assay in VITROS®ECiQ/3600 system helps in consolidation of the assay with other transfusion transmittable infections viz., aHIV, HBsAg and aHCV screening assay on chemiluminescence platform which is highly valuable for optimizing workflow and efficiency.

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INVESTIGATION ON PSYCHOLOGICAL REACTIONS OF VOLUNTEER BLOOD DONORS TO DEFERRAL AND REENTRY FOLLOWING POSITIVE SCREENING TEST RESULTS

D Xie, G Zhou, L Zheng, Y Meng, J Sun and Y Cai

Shanghai Blood Center, Shanghai, China

Background: False-positive transfusion transmitted infection (TTI) screening test results remain a challenge with continued loss of both donors and blood products. In addition, being notified of a positive TTI test result can cause psychological distress in blood donors.

Aims: Establish a donor reentry procedure and investigate psychological reactions of volunteer blood donors to deferral and reentry following positive TTI screening test results.

Methods: From September 15, 2015 to February 15, 2018, a total of 112 volunteer blood donors from Shanghai Blood Center were enrolled into this study. Enrollment criteria include donors who were screened reactive by enzyme-linked immunosorbent assay (EIA) and no nucleic acid test (NAT) reactive for human immunodeficiency virus (HIV, 22 donors), hepatitis B virus (HBV, 42 donors) and hepatitis C virus (HCV, 48 donors). All the donors took the reentry procedure in accordance with a guideline of Chinese Society of Blood Transfusion. In addition, the donors were asked to fill in a questionnaire form about their opinions toward false blood test results and the impact of which on them.

Results: There were respectively 19 of 22 donors with HIV antibody positivity, 32 of 41 donors with HBsAg positivity and 41 of 48 donors with HCV antibody

positivity whose reentry testing result were qualified to be able to continue to donate blood. Among the 92 qualified reentry donors, there were 47 donors who had a total of 192 blood donations after reentry. We got 87 answer forms from the questionnaire. For the question "how about the impact of the testing result on you?", 55 (about 63 percent) respondents said that there was negative impact on them, in which 40 percent were severe. For the question "what's the meaning of blood donor reentry for you?", 45 (about 52 percent) respondents said that it is to relieve the mind burden of themselves and their family and friends, and 65 (about 75 percent) respondents said that it is for being able to donate blood again.

Summary/Conclusions: The results imply that blood donor reentry is a necessary for minimizing the number of false-positive donors and maintaining a positive predisposition towards future blood donation. The results also emphasize the importance of appropriate information and support to deferred donors.

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Abstract has been withdrawn

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NATIONAL DONOR SELECTION SURVEILLANCE SYSTEM, AN EXPERIENCE TO IMPROVE THE SAFETY OF BLOOD SUPPLIES IN IRAN

A Pourfathollah, A Sedaghat, S Aminikafiabadi, M Maghsoodlu, B Daneshvar and K Shamsasenjan

High Institute for Research and Education in Transfusion Medicine, Iranian Blood Transfusion Organization, Tehran, Iran

Background: There are many factors for increasing the risk of donor selection process. Counseling skills of qualified physicians, confidentiality of counseling room, reliability of blood donors, risky of the area of located blood collection centers are the main factors for increasing the risk of donor selection process. A national policy for "Donor Selection Surveillance System" could reduce the risk of Transfusion Transmitted Infections in blood supplies towards zero risks strategies.

Aims: 1. Improving the safety of blood and blood products. 2. Increasing the quality of blood donor selection process. 3. Decreasing the load of risky donated bloods for screening labs

Methods: "National Donor Selection Surveillance System" has been introduced in 2016 in IRAN. Based on the national protocol, each donated bloods in all blood collection centers, which have a confirmed positive results for HIV, HCV, and HBV in screening tests, should be monitored retrospectively. A technical committee evaluates all the process of the selection processes in provincial level. In this evaluation process, 3 main issues must be evaluated as follows; the level of reliability of donors, the counseling skills of qualified physicians, and the safety level of location and community of blood collection center. In this program, all donors who have a positive confirmed result for HIV,HCV,HBs, are called back for confidential counseling, then qualified physicians are evaluated for the counseling skills, and the analytic situation of positive cases are triangulated with the data of Exemption Rates, and the rate of Confidential Unit Exclusions. Based on the results of these evaluations, and under supervision of national headquarter, decisions are made quarterly. Interventions could be community awareness rising about the importance of safe blood donations, conducting training courses for qualified physicians, standardizing the confidentiality counseling room, and stop the activities or switch the location of blood collection centers to safer areas.

Results: 12 months after launching the National Donor Selection Surveillance System, the slope of prevalence trend of each HIV,HBV,HCV markers among blood donors shows a significant decreasing in 2016 Vs the past 4 years. In the past decade and based on the IBTO's common strategic vision rooted "Zero Risk", the slope of the prevalence of TTIs among blood donors had a reducing trend, but the change of degree of linear regression curve for HBV shows Arc tan(−0.032) for 2015–2016, while this Arc tan for 2012–2015 was (−0.0144). for HIV and HCV we found the same results as well, change of degree of linear regression curve for HCV in 2015–2016 is Arc tan(−0.0081) Vs in 2012–2015 it was Arc tan(−0.004), and change of degree of linear regression curve for HIV in 2016–2017 is Arc tan(−0.0011) Vs the reduction rate of Arc tan(−0.0005) for 2015–2016.

Summary/Conclusions: An active national surveillance system for donor selection process, was an important experience in Iran. Based on this program national blood transfusion service could be able to monitor all the blood collection services continuously, for better counseling, better donor selection, and better locating for blood collection, to improve the safety assurances of blood supplies towards Zero Risk.

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CONSTRUCTION AND EVALUATION OF COMPETITIVE AND NONCOMPETITIVE INTERNAL CONTROL IN THE IN-HOUSE PCR FOR THE DETECTION OF HUMAN T-CELL LYMPHOTROPIC VIRUS IN BLOOD DONORS

J Kang[1], J Kang[1], S Shin[1], Y Seo[1], H Min[1] and K Huh[2]

[1]Blood Transfusion Research Institute, Korean Red Cross, Wonju-si, Gangwon-do
[2]Nambu Blood laboratory center, Korean Red Cross, busan, Korea

Background: We are performing nucleic acid amplification test (NAT) of human T-cell lymphotropic virus (HTLV) for the donor samples showing reactive results in the HTLV antibody assay with indeterminate results in the Western blot assay. Because there was not commercial kit for the HTLV NAT which was approved by FDA, we adopted in-house PCR. However, there has not been an adequate internal control (IC) to identify false negative results owing to the inhibition of PCR in the HTLV in-house PCR.

Aims: To assure the results of HTLV in-house PCR, We established competitive and noncompetitive IC and compared efficiencies of them.

Methods: As a competitive IC to be added to the samples, we constructed plasmid DNA including the same primer recognition sequence of pX region of HTLV gene and flanking a heterologous DNA fragment of larger size. As a noncompetitive IC, we constructed additional primer for the amplification of glyceraldehyde 3-phosphate dehydrogenase (GAPDH) gene as a housekeeping gene.

Results: When we added plasmid DNA as an IC to 10 HTLV positive samples and 10 negative samples, 400 bp of amplified product of IC and 230 bp of HTLV gene were detected together in all positive samples and only 400 bp of IC was detected in all negative samples. However, when we added primer for the amplification of GAPDH gene with the primer for the amplification of HTLV gene in 10 HTLV positive samples and 10 negative samples, only 350 bp of GAPDH gene was detected in one positive samples and only 230 bp of HTLV gene was detected in one positive samples, although 350 bp of amplified product of GAPDH gene was detected together in all negative samples.

Summary/Conclusions: According to the guidelines of international standard organization, the presence of IC is recommended to monitor the false negative results of PCR. We developed two kind of IC and compared the efficiencies. In the case of noncompetitive IC application, two target genes may be amplified incompletely because of interference of primers in the reaction or formation of different primer dimers in the reaction. Therefore we considered that the adoption of plasmid DNA as an IC may be more efficient. And the construction of plasmid DNA as an IC may be a good way to apply internal quality control for the in-house PCR.

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RESIDUAL RISK OF TRANSFUSION TRANSMITTED INFECTION WITH HEPATITIS B VIRUS, HUMAN IMMUNODEFICIENCY VIRUS, HEPATITIS C VIRUS SINCE THE INTRODUCTION OF NUCLEIC ACID TEST

E Oh

Blood Laboratory center/Jungbu, Daejeon, Korea

Background: In 2005, the Korean Red cross introduced nucleic acid testing for hepatitis C virus (HCV) and human immunodeficiency virus (HIV). It upgraded to individual donation NAT including hepatitis B virus (HBV) 20 2012. This study, analyzed the residual risk of transfusion transmitted infection with hepatitis B virus, Human immunodeficiency virus, hepatitis C virus since the introduction of nucleic acid test.

Aims: The purpose of this study was to investigate the residual risk (RR) of transfusion – transmitted infection (TTI) in patients with different types of transfusion – transmitted viral diseases. It has been reported variously. The HCV and HIV NAT tests were first introduced in 2005 and the HBV NAT test was introduced in 2012 to prevent transfusion-transmitted infection. The aim of this study was to evaluate the efficacy of HBV chemiluminescence enzyme immunoassay (CLEIA) HCV, HIV-1 enzyme-linked immunosorbent assay (ELISA) and HCV immunoblot assay, RIBA), and HBV, HIV, and HCV screening test data. The prevalence and incidence of the first and multiple blood donors were calculated and compared with the residual risk of transfusion infection.

Methods: HBS Ag, anti-HIV, anti-HIV, HCV RIBA, HBV, HIV, HCV, and HIV/AIDS for blood donation accumulated in the database of Korean Red Cross Blood Information Management System Using the results of the NAT test, the prevalence, IR, TTI, and RR are divided into the period between 2003 and 2004 before NAT, and the period between 2005 and 2017 after NAT, and the total person years of each interval are calculated by the Kaplan-Meier method. IR is calculated by dividing the number of positive cases in the interval by total person years. The number of positive blood donations in the donor blood donors who had had a blood donation within a year was important, and the RR was calculated by incidence rate (IR)/window (WP) method

Results: During 2005~2017 period, a total of 29,28,670 donations. It screened with HCV NAT yield donations. Calculated RR per million donations for HBV was significantly reduced from 0.32 in the (2011) to 0.12 in (2017). HCV (3.2(2005)->0.61 (2017)) is decreased RR. HIV (0.027->0.02) is also declining trends, but not so special. Most recently, RR for HBV, HCV, HIV with TTI was estimated by 18, 2.2, 0.066 per million donations.

Summary/Conclusions: Blood donation blood screening has been carried out with various methods and reagents to minimize infection of HIV, HCV, and HBV transmitted by blood transfusion and to assure the safety of blood. This will improve the sensitivity and specificity of the screening reagent, To minimize transfusion infection and blood discontinuation due to false positives. In addition, the Korean Red Cross has lowered the residual risk of HBV, HCV, and HIV transfusion infections significantly by introducing nucleic acid amplification tests in 2005. However, in order to ensure the safety of blood, it is necessary to establish sensitive and accurate screening methods, Monitoring of blood product quality control should be strengthened so as to prevent the occurrence of as much as possible.

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FLOW CYTOMETRIC AND INDIRECT IMMUNOFLOUROCENCE IDENTIFICATION OF HSV INFECTED VERO CELLS (AS A MODEL OF HBV) USING QDS AND FITC, INTRODUCING RED AND GREEN IMMUNOFLOUROCENCE AS DEFINITIVE DETECTION

S Mousavi, Z Sharifi and R Golestani

Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: For further reduction of transfusion transmitted infections (TTIs), viral inactivation is a strategy. Viral cytopathic effect on cultured cells (CPEs) used for evaluation of viral inactivation. Evaluation of 5–7 days CPE is gold standard for viral load but it is time consuming, low throughput and tedious. Thus the need of sensitive, fast and automatable techniques is a field of research. Quantum dot nanoparticles with higher intensity and stability of emitted light comparing to organic fluorophores are promising in medical sciences.

Aims: The aim was identification and comparison of HSV-1 infected Vero cells (as a model of hepatitis B virus) using quantum dot nano-particles and FITC as antibody conjugates in flow cytometry and fluorescent microscopy using detection of viral glycoprotein D and CPEs in light invert microscope.

Methods: Vero cells cultured on DMEM, 10% fetal bovine serum with antibiotics. HSV-1 CPEs titrated on 80–90% confluency cultured Vero cells at 5–7 days as gold standard and expressed in TCID50% using invert microscope. Ten fold serial dilutions of 10^8 titrated HSV-1 sample infected 80–90% confluency cultured Vero cells at 16–20 h used as specimen for evaluation of CPEs in flow cytometry, indirect immunofluorescence and light invert microscope. Quantum dot655 and FITC used as antibody conjugates in detection of glycoprotein D.

Results: Quantum dot655 used in indirect immunofluorescent microscopy and flow cytometry with specificity and sensitivity up to 7 log (MOI = $0.5*10^{-6}$) or 1 infectious particle per ml. FITC conjugated antibody showed sensitivity of 6 log (MOI = $0.5*10^{-5}$) or 10 infectious particles per ml. while CPEs of infected cell that evaluated on invert microscope showed sensitivity of 4 log or 1000 infectious particle ((MOI = $0.5*10^{-3}$).

Summary/Conclusions: Our study showed quantum dot was at least 1 log more sensitive than FITC in flow cytometry and indirect immunofluorescence for detection of 16–20 h HSV-1 infected VERO cells. Interestingly Qdot655 conjugates under UV excitation showed emission of red light and green light for HSV-1 infected and non-infected Vero cells in indirect immunofluorescent microscopy respectively that means higher specificity to FITC conjugates.

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EVALUATION OF SENSITIVITY AND SPECIFICITY OF DIFFERENT SCREENING TECHNIQUES FOR DETECTION OF VIRAL HEPATITIS IN BLOOD DONORS AT TERTIARY CARE HOSPITALS OF RAWALPINDI PAKISTAN

F Shafiq[1] and U Waheed[2]

[1]Biosciences, Molecular Virology lab, COMSATS University, Islamabad, Pakistan
[2]Safe Blood transfusion Programme, Ministry of National Health services, Government of Pakistan, Islamabad, Pakistan

Background: Health care systems of developing nations are continuously facing the challenges of inadequate supply of safe blood and an increase in the prevalence of transfusion associated infections. One of the major challenges throughout is the access to safe blood and blood products. Blood donors are considered as the healthiest pool of population. Blood is screened for different diseases including Syphilis, HBV, HCV and HIV before transfusion, in order to make blood transfusion safe but their access still remains a major challenge throughout the world. Transmission of HBV and HCV infections via blood and blood products will lead to acute and chronic Hepatitis.

Aims: The objective of this study was to figure out which technique was more sensitive and specific for detection of HBV and HCV and best suited for tertiary care hospitals and also helpful for Blood banks to decide upon an effective screening technique for Hepatitis virus.

Methods: It was a cross-sectional prospective study conducted to evaluate the technical performance of rapid kits used for screening blood donors in tertiary care hospitals of Rawalpindi, Pakistan. Blood samples of 1200 blood donors selected who visited the blood bank from September 2015 to December 2017 were taken under aseptic conditions samples were initially tested by using Immunochromatographic technique (ICT) at the respective blood banks and confirmed by using 3rd generation ELISA at Microbiology laboratory, Holy family hospital. Chemiluminescence Micro particle Immunoassay (CMIA) of all the samples was performed at Blood Bank, Pakistan Institute of Medical Sciences, Islamabad and it was used as comparator. The results of ICT, ELISA and Chemiluminescence were then compared and statistical evaluation was done.

Results: Out of 1200 donors, 100 (8.33%) were positive for Hepatitis B virus, 30 (2.5%) were positive for Hepatitis C virus and 1070 (89.16%) were found negative. Sensitivity analysis of these tests has shown that ICT has a low detection rate of positive cases in comparison with the ELISA and Chemiluminescence as sensitivity for HBV and HCV was 10% and 40% respectively. Specificity of ICT kits was 100% for both HBV and HCV. Prevalence of HBV was 8.33% and HCV was 2.5%.

Summary/Conclusions: ICT showed inferior results compared to ELISA and Chemiluminescence and hence should not be recommended in transfusion centres for screening blood donors. Results of this study also demonstrate that CMIA is highly sensitive and specific screening assay. Each laboratory and blood bank should have a road map for interpretation and confirmation of discrepant test results to serve patients with the most accurate and standardized test results and for a safe transfusion to occur.

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COMPARATIVE STUDY OF ENZYME LINKED IMMUNOSORBENT ASSAY (ELISA) AND RAPID TEST SCREENING METHODS ON HIV, HGSAG, HCV AND SYPHILIS AMONG VOLUNTARY DONORS IN OWERRI, NIGERIA

HM Okorie[1], H Nwanjo[1], J Dike-Ndudim[1] and E Onyeneke[2]
[1]Medical Laboratory Science [2]Imo State University, Owerri, Owerri, Nigeria

Background: Blood transfusion and component therapies are well established and essential medical practice. These therapies however are not without risk and may lead to the transmission of infectious agent from donor to recipient. The common infectious agents include Human Immuno-Deficiency Virus (1 and 2), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and Syphilis. In pursue of global blood safety, the World Health Organization (WHO) recommends that all blood donation should be screened for evidence of infection prior to the release of blood and blood products for clinical use.

Aims: To compare the effectiveness of Enzyme Linked Immunosorbent Assay (ELISA) and Rapid Test Screening Method in screening of transfusion transmissible infection in blood donors.

Methods: A comparative study involving 350 blood samples were collected (250 males and 100 females) between the ages of 21–50 years. They were all voluntary

donors in Owerri. Enzyme linked Immunosorbent Assay and Rapid Test Screening method were used for the screening. All data were evaluated with SPSS (Statistical Package for Social Sciences) version 20.0

Results: The result shows that there is a difference between the two test methods, hence indicated that 30 (8.57%) infected units of blood would have been transfused due to false negative results with rapid test method.

Summary/Conclusions: The study demonstrated the prevalence of transfusion transmissible infections are the major problem associated with blood transfusion. The incidence is found to be higher in females than the males.

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PERFORMANCE OF TWO SEROLOGICAL ASSAYS AND NAT PCR COMBINATION FOR SCREENING OF TTI

T Chandra[1], D Agarwal[2] and M Agarwal[3]
[1]Department of Transfusion Medicine, King George Medical University, Lucknow
[2]GSVM Medical College, Kanpur [3]ERA Medical College, Lucknow, India

Background: Safety and cost effectiveness remain the central goal of blood screening in India. India, the second most populous country in the world (1.2 billion) has about 2.5 million HIV, 43 million Hepatitis B (HBV) and 15 million Hepatitis C (HCV) infected persons. Majority of blood banks in India employ screening by 3rd generation ELISA (70%) and only few have Chemiluminescence testing and still fewer have Nucleic Acid Testing (NAT). Cost plays a major role in selection of technology.

Aims: To compare the detection of HIV, Hepatitis B and Hepatitis C in Indian population by comparing different technologies of semi-automated ELISA, Chemiluminescence and NAT

Methods: Single centre study of 271,485 blood donor samples conducted over a period of 6 years 208,435 blood units screened by 3rd Combination of technologies were used to assess the reactive status Reactive donors were evaluated, counselled. The reactive donors were recalled and assessed for true positivity by ICTC followed by ART centres.

Results: 3rd generation ELISA reactivity was 1.555%; HIV 0.047%, HBV 1.416% and HCV 0.093%. ELISA non-reactive units showed NAT reactivity [% (yield)] of 0.827% with a NAT yield of 1:121; 0.006% (1:15783) for HIV, 0.642% (1:156) for HBV and 0.178% (1:561) for HCV. Total reactive units after ELISA and NAT were 2.369% (yield 1:42); 0.053% for HIV, 2.048% for HBV and 0.268% for HCV. Chemiluminescence reactive units were total 2.106%; 0.143% for HIV, 1.166% for HBV and 0.798% for HCV. NAT yield [% (yield)] after chemiluminescence was 0.557% (1:179); 0.019% (1:5143) for HIV, 0.42% (1:238) for HBV and 0.118% (1:845) for HCV. Total reactivity of chemiluminescence with NAT was 2.652% (yield 1:38); 0.162% for HIV, 1.577% for HBV and 0.914% for HCV. All HIV reactive donors were recalled and found to be true positive while in HBV and HCV only 75% could be recalled and 60% were found to be true positive. All NAT reactive donors were true positive. The prevalence of seroreactivity observed in the study was similar to blood donor seroreactivity observed in the state where the study site is located viz. HIV 0.11%, HBV 1.21% and HCV 0.5%.

Summary/Conclusions: NAT added to the safety of donated blood irrespective of the serology test used. In a resource constrained setting, addition of NAT to ELISA could be a first step where upgradation to the more sensitive chemiluminescence and NAT combination is not possible immediately.

Hepatitis B (HBV)

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HEPATITIS B VIRUS GENOTYPES IN BLOOD DONORS FROM KENYA AND A PILOT STUDY ON OCCULT HBV INFECTION

B Langat[1], E Songok[2], J Borlang[3], J Day[3], C Osiowy[3], A Githiomi[4], G Midigo[4], A Andonov[3] and E Muge[5]
[1]Centre for Virus Research, Kenya Medical Research Institute [2]Kenya Medical Research Institute, Nairobi, Kenya [3]Public Health Agency of Canada, Winnipeg, Canada [4]Kenya National Blood Transfusion Services [5]University of Nairobi, Nairobi, Kenya

Background: Hepatitis B virus (HBV) infection is endemic in Kenya with estimates varying from 2% to 9% in different geographic regions of the country. The HBV prevalence among blood donors is estimated between 2–3%, although a recent national baseline data is yet to be reported. Similarly there is no data on occult HBV

infection (OBI), which given the intermediate HBV prevalence in the country should be considered as a potential threat to blood safety.

Aims: To investigate the distribution of HBV genotypes from a nationally representative sample of blood donors from six Regional Blood Transfusion Centres (RBTC), determine the prevalence of anti-HBc and provide preliminary data for the residual risk of HBV transmission due to OBI.

Methods: HBsAg positive specimens were investigated for HBV DNA positivity following DNA extraction and PCR amplification using primers specific for the HBsAg coding region. Amplicons (either 330 bp or 560 bp in length) were sequenced and the sequence subjected to Maximum Likelihood phylogenetic analysis together with GenBank reference sequences to determine the HBV genotype. Elecsys Anti-HBc II was used for qualitative determination of IgG and IgM antibodies to the hepatitis B core antigen. Anti-HBc positive samples were analysed for HBV DNA by Real-time PCR detecting three different genomics regions.

Results: A cross-sectional study conducted from August to December of 2014 collected samples of HBsAg positive blood donors from the five administrative regions of Kenya; Western-Rift Valley, Eastern, Central, North-Eastern and Coastal. Two hundred and thirty-seven were HBV DNA positive and could be sequenced. The age of the donors ranged from 16 to 58 years, with a median of 25 years. Male to female ratio was 4.5: The HBV genotype distribution was 87.8% A1, 0.4% C, 11.4% D and 0.4% genotype E. Genotype D was more often found in Western Kenya (44%). Sub genotype A1 sequences clustered with both African and Asian A1 reference sequences. For the pilot OBI study 1006 samples from HBsAg negative donors were randomly selected and screened for anti-HBc. Of these 127 were found to be positive for anti-HBc (12.6%). No HBV DNA was detected among these anti-HBc (+) donors. Therefore the data in the present study, although preliminary, is welcome news for blood safety in Kenya compared to other African countries where the frequency of OBI in African blood donors is estimated to be high; for instance in neighbouring Sudan the prevalence of OBI in blood donors was 4.6%. A possible reason for this finding is the young age of the voluntary blood donor population in Kenya (approximately 80% between the age of 16–20 years of age).

Summary/Conclusions: HBV genotype A1 is predominant in blood donors in Kenya; in the Western part of the country which is geographically closer to the other two main African HBV genotypes E and D, the distribution of A1 and D is similar. Occult HBV infection in blood donors from Kenya is not of high prevalence compared to other African countries.

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EFFICACY OF TESTING SCENARIOS IN REMOVING HEPATITIS B VIRUS (HBV) TRANSMISSION RISK MODELED WITH SCREENING DATA OF A MULTI-REGIONAL STUDY

N Lelie[1], M Vermeulen[2], R Bruhn[3], M Busch[3] and S Kleinman[4]

[1]Lelier Research, Alkmaar, Netherlands [2]South African National Blood Service, Johannesburg, South Africa [3]Blood Systems Research Institute, San Francisco, United States of America [4]University of British Colombia, Victoria, Canada

Background: In previous publications we modeled the efficacy of different testing scenarios in eliminating HIV and HCV transmission risk using individual donation nucleic acid amplification technology (ID-NAT) screening results on 10,981,776 donations from 22 blood centers. Since calculating efficacy for HBV is more complex, we first published the rates of different stages of HBV infection in first time, lapsed and repeat donors in six geographic regions (Lelie, Transfusion 2017). In the current analysis we used data from 3,571,315 South African donations to estimate the efficacy of different testing scenarios in reducing HBV transmission risk compared to the baseline of no screening.

Aims: We estimated the residual HBV window period (WP) and occult HBV infection (OBI) transmission risk for ID-NAT screened RBC transfusions (20 ml plasma) in six geographic regions and calculated the efficacy of different testing strategies in eliminating HBV transmission risk in South Africa.

Methods: WP transmission risk was estimated by a combination of the risk day equivalent model (Weusten, Transfusion, 2011) and the WP NAT yield ratio model (Busch, Transfusion 2005)) using a 50% minimum infectious dose (MID_{50}) of 3.16 virions. The OBI (and the post-HBsAg WP) transmission risk was calculated by a recently published model (Weusten, Transfusion 2017) using a MID_{50} of 316 virions and 50% non-infectivity by anti-HBs-neutralisation. After correction for an observed 1.7 fold higher WP and OBI NAT yield rate after introduction of Ultrio Plus assay in South Africa, the base line transmission risk was estimated for each infection stage, i.e. 100% transmission risk when RBCs of WP NAT-yield or HBsAg and HBV-DNA concordantly positive donations would be transfused, 15% for HBsAg (and anti-HBc) positive/NAT nonreactive units and 30% for OBI (and post-HBsAg WP) donations.

The OBI transmission risk estimates reduced to 5.2% by ID-NAT and to 18.2% by MP6-NAT screening. For the risk analyses we used available analytical sensitivity data on South African (HBV genotype A1) yield samples for ID-NAT (Ultrio Plus, 50% LOD 4.1 cp/ml) and minipool (MP)-6 NAT (TaqScreen 1.0, 50% LOD 3.4 cp/ml) testing (Vermeulen, Transfusion 2013).

Results: After correction for 1.7 fold higher ID-NAT-yield by Ultrio Plus, the residual HBV WP transmission risk in all donations was estimated between 2.2 per million (North and Central Europe) and 31.0 per million (South Africa), while OBI transmission risk in these regions varied between 3.6 and 17.1 per million. For all South African donations the overall residual HBV transmission risk per million and percent efficacy in eliminating risk was modeled at 124.9 and 87.1% respectively for HBsAg testing alone, 85.8 and 91.2% for HBsAg + anti-HBc, 67.7 and 93.0% for HBsAg + MP6-NAT, 56.2 and 94.2% for HBsAg + anti-HBc + MP16-NAT, 47.5 and 95.1% for HBsAg + anti-HBc + MP6-NAT, 38.7 and 96.0% for ID-NAT only, 36.6 and 96.2% for HBsAg + ID-NAT, and 31.0 and 96.8% for HBsAg + anti-HBc + ID-NAT.

Summary/Conclusions: Infectivity based risk models are instrumental for comparing the efficacy of different screening strategies in removing transmission risk.

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TRENDS IN THE PREVALENCE OF HEPATITIS B VIRUS (HBV) INFECTION AND OCCULT HBV INFECTION AMONG TAIWANESE BLOOD DONORS AFTER UNIVERSAL HBV VACCINATION

L Li[1], C Chang[1], Y Hung[2], S Wei[1] and S Hou[1]

[1]Head Office [2]Taipei Blood Center, Taiwan Blood Services Foundation, Taipei, Taiwan, China

Background: Taiwan implemented the world's first national HBV vaccination program in July, 1984. For the first two years, the program only covered neonates whose mothers were HBsAg carriers. This program ultimately reduced the rate of HBsAg seropositivity in children from 10% to less than 1%. However, HBV seroprevalence among blood donors has not been well addressed.

Aims: The objective of this study was to assess trends in the prevalence of HBsAg, anti-HBc, anti-HBs and occult HBV infection (OBI) after HBV vaccination. The second objective was to compare the individual-donation NAT (ID-NAT) used in this study with routine minipool NAT screening (MP8-NAT), to inform future strategies for HBV screening in Taiwanese donors.

Methods: We collected 16,016 donors for ID-NAT testing, consisting of 3,642 first-time donors and 12,374 repeat donors. To evaluate the prevalence of HBV infection, first-time donors were tested for anti-HBs and anti-HBc. HBV yield cases were further examined HBV antibody serology and HBV DNA quantification using the Abbott RealTime HBV assay and digital PCR (the Clarity™ dPCR system).

Results: The overall prevalence of HBsAg among first-time donors was 2.75%, and 85% of these HBsAg carriers were HBV DNA positive. Seropositivity rates for HBsAg, anti-HBc were significantly lower in those born after the start of universal vaccination. Seropositivity rates were as follows: In those born before vaccination, 5.43% for HBsAg, 50% for anti-HBc and 60.65% for anti-HBs; In those born between July, 1984 and June, 1986, 1.99% for HBsAg, 9.30% for anti-HBc and 64.45% for anti-HBs; and in those born after widespread vaccination, 0.8% for HBsAg, 3.34% for anti-HBc and 37.82% for anti-HBs. No HBV yield cases were observed in donors born after the vaccination program. Yield rates in donors born before HBV vaccination were higher, at 0.36% and 0.21% for first-time and repeat donors, respectively. The yield rate for ID-NAT (0.17%) was more than triple the rate for the routine MP8-NAT (0.048%) in repeat donors during the same period. According to test results, all HBV yield cases were identified as OBI. Among ID-NAT yield cases, only 14.3% were MP8-NAT positive, while 71.4% were MP8-NAT negative and anti-HBc positive. The viral loads in MP8-NAT negative but ID-NAT/anti-HBc positive samples (2/3 of them undetected, 1/3 of them between 25 IU/ml and 42 IU/ml) were lower than MP8-NAT positive samples (between 32 IU/ml and 139 IU/ml).

Summary/Conclusions: The prevalence of HBsAg, anti-HBc, and OBI dramatically decreased after HBV vaccination. The yield rate in ID-NAT was significantly higher than in MP8-NAT. All HBV yield cases were determined as OBI and the majority of these OBI samples had very low viral loads, necessitating the use of ID-NAT for detection. The risk of HBV transmission from anti-HBc/ID-NAT positive but MP8-NAT negative OBI cases will be further investigated.

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ANALYSIS OF THE GRAY ZONE RANGE OF TWO KINDS OF HBSAG ELISA KITS FOR BLOOD SCREENING

L Zhao[1,2], T Xu[1], J Xu[3] and M Yuan[3]

[1]Department of Laboratory, Wuhan Blood Center [2]Department of Laboratory Medicine, Medical School, Wuhan University [3]Administration Office, Wuhan Blood Center, Wuhan, China

Background: Screening for hepatitis B virus (HBV) in blood donors is mandatory in China. Currently, enzyme linked immunosorbent assay (ELISA) is practically the serologic test mandatorily used for HBsAg (hepatitis B surface antigen) screening in China. In order to avoid the problem of failing to detect weakly positive samples and to make an utmost effort to guarantee the blood safety, most of the laboratories set up gray zone range for ELISA tests. But there is no unitary objective standard, and there is dispute among laboratories on how to set up and verify the gray zone range of ELISA tests.

Aims: To evaluate and verify the rationality of the gray zone range set up in our laboratory of HBsAg screening by two kinds of HBsAg ELISA kits.

Methods: HBsAg serum panels (791 samples) established and distributed by Blood Safety and Immunohematology Reference Laboratory, National Center for Clinical Laboratories of China were screened for HBsAg by domestic ELISA reagents and imported ELISA reagents on FAME platform (Hamilton) in parallel. The experimental data were compared with the confirmation data provided by Blood Safety and Immunohematology Reference Laboratory with chemiluminescence microparticle immunoassay (CMIA, Abbott) and neutralization test (NT, DiaSorin). The SPSS software was used to analyze the data and the receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off level.

Results: Among 28 HBsAg ELISA gray area samples (S/CO values were 0.80–0.99) from screening by imported reagent kit, 3 samples were confirmed negative, 18 samples were uncertain and 7 samples were positive by CMIA and NT. Among 31 HBsAg ELISA gray area samples (S/CO values were 0.70–0.99) from screening by domestic reagent kit, 5 samples were confirmed positive, 26 samples were uncertain and none was negative by CMIA and NT. According to Chi-square test, there was no statistically difference between the two groups of data ($X^2 = 4.246$, P > 0. 05). Data from 611 samples of serum panels (419 samples were confirmed positive and 192 samples were confirmed negative) were utilized to calculate the ROC curve of HBsAg S/CO values for the two kinds of HBsAg ELISA kits respectively. In terms of the imported reagent kit, area under the curve (AUC) was 0.996, the Youden index obtained a maximal peak when the S/CO value was 0.775; in terms of the domestic reagent kit, the AUC was 0.998, the Youden index obtained a maximal peak when the S/CO value was 0.686.

Summary/Conclusions: In different laboratories, the screening results were influenced by factors of environment, reagents, equipment, and operating procedures. The laboratory should select appropriate methods to set up the gray zone range of their own. According to this study, the optimal cut-off level for the imported kit are 0.75 to 0.8, while for the domestic ELISA kit are 0.65–0.7. It is necessary to set up the gray zone range for two kinds of evaluated HBsAg ELISA kits in our laboratory to reduce the false negative and ensure the blood safety.

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Abstract has been withdrawn

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OCCULT HEPATITIS B INFECTION AMONG BLOOD DONORS FROM YAOUNDE, CAMEROON

D Fopa[1], D Candotti[2], C Doux[2], E Murphy[3], D Mbanya[4], C Tagny[1,4] and S Laperche[2]

[1]Hematology & Transfusion Service, University Teaching Hospital, Yaounde, Cameroon [2]DATS, INTS, Paris, France [3]Blood Systems Research Institute, San Francisco, United States of America [4]Hematology, Faculty of Medicine & Biomedical Sciences University of Yaounde I, Yaounde, Cameroon

Background: In Cameroon, which is highly endemic for HBV infection, the prevention of HBV transmission by transfusion is still based on HBsAg screening alone. However, occult HBV infection (OBI) characterized by the absence of detectable HBsAg and low level of viral DNA remains a potential threat in blood safety. OBI prevalence tends to be higher where prevalence of overt HBV infection is high.

Nevertheless, there is limited data on the prevalence of OBI in Cameroonian blood donors.

Aims: The prevalence of OBI was investigated in blood donors from Yaounde to provide evidence-based recommendations to improve HBV blood safety.

Methods: 1,167 blood donors were screened initially for HBV, HIV and HCV infections (Murex HBsAg Version 3, Murex HIV Ag/Ab Combination, and Murex HCV Ag/Ab Combination [DiaSorin]). Additional HBV testing included anti-HBc (Monolisa Anti-HBc PLUS; BIO-RAD). HBV DNA was tested in minipools of two samples using the quantitative Cobas Taqman HBV assay (Roche; LOD of <6 IU/ml).

Results: Initial screening showed 85 (7.3%) donations reactive for HBsAg, 13 (1.1%) for HIV, 11 (0.92%) for HCV, and 1 (0.08%) for HBsAg and HIV. Among 1,057 donors negative for these markers, 545 (51.6%) were anti-HBc reactive: 35 (6.4%) showed low reactivity (12. When 30 of the anti-HBc low reactive samples were retested, 13 were non-reactive, 8 remained low reactive, and 9 showed S/CO values >2. Ongoing molecular testing showed that 4/134 (3%) anti-HBc positive/HBsAg negative samples carried detectable levels of HBV DNA with viral loads ranging between <6 IU/ml and 927 IU/ml. Of the 13 HIV reactive samples, 4 were confirmed positive by WB and PCR and 2 of them had anti-HBc and 1 of 3/10 HCV confirmed samples was anti-HBc positive.

Summary/Conclusions: HBV is confirmed highly endemic in Cameroon with a HBsAg positive rate of 7% and an overall anti-HBc prevalence of 53% (593/1119) in blood donors. Preliminary data suggest that approximately 1.6% % of Cameroonian blood donors screened HBsAg negative carry occult HBV infection. Further serological and molecular testing is currently ongoing to confirm these data. HBsAg alone for screening prospective donors is not sufficient to eliminate the risk of HBV transfusion-transmission in Cameroon and because anti-HBc screening appears not feasible without compromising blood supply, implementation of HBV nucleic acid testing might be considered when possible.

P-397

THE EFFECT OF 4°C STORAGE OR MINUS 20°C STORAGE AND FREEZE–THAW CYCLES ON HBV DNA TEST RESULTS

Y Yin[1], Y Sun[2], L Li[1], H Xu[1], Z Liu[1] and R He[1]

[1]Chinese Academy of Medical Sciences and Peking Union Medical College, Institute of Blood Transfusion, Chengdu [2]Haidong central blood station, Qinghai, China

Background: It is well known that HBV is a serious hazard to blood safety. Blood screening is the main means to ensure blood safety. After the serological testing, negative samples are tested by Chinese Blood collection and supply agencies with nucleic acid testing. Due to the stability of nucleic acid is easily affected by the external environment, storage temperature and freeze-thaw cycles may have impact on the detection results of nucleic acids. few articles reported the stability of HBV DNA in 4°C storage and freeze-thaw cycles with high load HBV-DNA, not can assess the different storage conditions' effect on low-load HBV-DNA test results. With the development of technology, the detection limit of HBV-DNA is getting lower and lower. At present, Roche cobas s 201 nucleic acid automatic detection system, which used widely and the detection limit of HBV-DNA is 20 IU/ml, has high sensitivity, specificity and accuracy. In this study, samples with HBV-RNA loadings near the detection limit (<102 IU/ml) were chosen, on behalf of the HBV positive samples with high risks of false negative results, to assess the effect of 4°C storage and −20°C freeze-thaw cycles on low-load HBV-DNA samples' test results by Roche cobas s 201.

Aims: To evaluate the effect of freeze-thaw cycles or 4°C preservation on nucleic acid quantitative detection results of low-load HBV-DNA positive plasma samples.

Methods: Selected two packages of unpaid plasma with low load HBV (HBV DNA load <10^2 IU/ml), and aliquot each bag of samples into two tubes, one tube stored at 4°C for 4 h, 24 h, 48 h, 7 D, 14 D, and another stored at −20°C and freeze-thaw cycle once at the same time. Repeated test HBV DNA by Roche cobas s 201 with quantitative detection two times for one sample at each time.

Results: All the test results were positive; The sample with lower load HBV has the testing results below the detection limit both stored at 4°C and freeze-thaw cycles; The sample with slightly higher nucleic acid titers did not have the result below the detection limit.;The results of samples stored in 4°C descended gradually with time, and samples with freeze-thaw cycle were stable, but the difference was not statistically significant.

Summary/Conclusions: HBV positive samples stored at 4°C less than 14 d or freeze-thaw cycles less than 5 times have little effect of HBV DNA quantitative detection results.

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COMPARSION OF THE CHARACTERIZATION OF INDIVIDUALS WITH HBVDNA+ HBSAG+ AND OCCULT HEPATITIS B INFECTION IN BLOOD DONORS, CHINA

G Xu[1,2], B Dai[1,2], Y Wu[1,2], H Zhu[1,2], J He[1,2], F Zhu[1,2] and W Hu[1,2]

[1]Zhejiang provincial Key Laboratory of Blood Safety Research [2]Blood Center of Zhejiang Province, Hangzhou, China

Background: he prevalence rate of hepatitis B virus (HBV) infection is high in the Chinese population, which is threaten to the blood safety. Currently, the nucleic acid testing (NAT) has been performed for blood donations in China and occult hepatitis B virus infection (OBI) cases were found. However, the characteristic of hepatitis B virus infection individuals with HBV DNA+HBsAg+ and OBI individuals (HBV DNA+HBsAg-) was rare reported in Chinese blood donors.

Aims: To explore the HBV infection rate in blood donors in the high prevalence country and compared the serological and molecular characteristic of individuals with HBVDNA+HBsAg+ and individuals with OBI. which is threaten to the blood safety. Currently, the nucleic acid testing (NAT) has been performed for blood donations in China and occult hepatitis B virus infection (OBI) cases were found. However, the characteristic of hepatitis B virus infection individuals with HBV DNA+HBsAg+ and OBI individuals (HBV DNA+HBsAg-) was rare reported in Chinese blood donors.

Methods: The donors were preformed a physical examination according to the regulation of China. Then, rapid screen tests for HBsAg and ALT were done and precluded the donors with HBsAg preliminary test positive and ALT level abnormal (>50 IU/ml) before donation. After donation, the samples of the donors were detected for HBsAg twice using different ELISA reagents and HBV DNA using TMA or QT-PCR techniques according to manufacture's instruction. The other serological markers (anti-HBs, anti-HBc, anti-HBe, HBeAg) of HBV infection were tested using the chemiluminescence assay. HBV load level was measured using TaqMan technique and the HBV genotype was analyzed using the PCR-SBT method.

Results: 1041 individuals were found with HBV DNA positive from the blood donations in this study, including 847 individuals with HBVDNA+HBsAg+ and 194 individuals with OBI. In the HBVDNA+HBsAg+ group, 87.25% individuals were found with anti-HBc and anti-HBe positive. However, In the HBV OBI group, 30.41% individuals were found with anti-HBc and anti-HBe positive, 23.71% individuals were found with anti-HBs and anti-HBc positive, 22.68% individuals were found with only anti-HBc positive. The distribution of these serological markers was different between these two groups. Totally, 902 individuals were analyzed the viral load level. 57.62% of the OBI individuals and 29.16 % of HBVDNA+HBsAg+ individuals were viral load level <20 IU/ml, while 58 individuals of HBVDNA+HBsAg+ and 3 OBI individuals had viral load level >10000 IU/ml. HBV B and C genotype were 82.4% and 17.6% in the HBVDNA+HBsAg+ group, while HBV B and C genotype were 71.0% and 29.0% in the OBI group. chemiluminescence assay. HBV load level was measured using TaqMan technique and the HBV genotype was analyzed using the PCR-SBT method.

Summary/Conclusions: The difference was showed in the serological characteristic and viral load level of individuals with HBVDNA+HBsAg+ or OBI in Chinese blood donors. These data will help to improve blood safety. This research was supported by the Science Foundation of Zhejiang Health Bureau (No. 2017KY316 and 2016KYA070).

P-399

INCREASING THE SAFETY OF BLOOD TRANSFUSIONS IN THE AREA OF ACTIVITY OF BLOOD CENTRE IN POZNAŃ IN THE CONTEXT OF INTRODUCTION OF OBLIGATORY VACCINATIONS FOR HEPATITIS B IN POLAND

A Zawadzka and K Olbromski

Blood Center in Poznan, Poznan, Poland

Background: Hepatitis B is an infectious disease caused by the hepatitis B virus (HBV) which is transmitted by contact with blood and body fluids of infected people. Risk factors involve medical procedures such as blood transfusions or treatment with blood derived products. In the area of blood donation there are dedicated hemovigilance procedures that aim to minimise the risk of acute post-transfusion reactions in recipients of blood.

Aims: The aim of the analysis was to compare two populations of first time and repeat donors in the age group 18*-20 (*18 is the legal age to allowed for donation

n Poland). The first population did not undergo obligatory vaccination, the second population underwent vaccination according to the vaccination schedule.

Methods: Poland is the country in which until 1993 the highest number of HBV infections in Europe was recorded. From 1994 obligatory vaccinations of infants were introduced first in 13 out of existing then 49 voivodeships (provinces) which noted the highest number of HBV infections. In the Greater Poland Province (i.e. the area of activity of Blood Centre in Poznań) obligatory vaccinations of infants were introduced in 1995, in 1996 in the rest of Poland. Infants undergo vaccination in the first 24 h of their life according to the basic schedule 0-1-6 months. According to the official reports 99.3%>99.8% of infants underwent vaccination. It was necessary to wait 18 years to evaluate the effect it brought. The analysis involved 2 groups of donors in the area of activity of Blood Centre in Poznan: the first time donors in the years 2015–2017 aged 18–20 that underwent vaccination according to the vaccination schedule; and donors in the years 2010–2012 aged 18–20 that did not undergo the obligatory vaccination. Donors in the years 2013 and 2014 were not included in the analysis due to the fact that the group 18–20 consists of 3 age groups 18, 19 and 20 and group of donors in the years 2013–2014 includes both vaccinated and non-vaccinated donors. The analysis showed that male donors dominated among the non-vaccinated donors which is consistent with the statistical data for Poland. In the group of vaccinated donors no differences according to the sex of donors were recorded. In the years 2010, 2011 and 2012 there were in total 70 donors with confirmed HBV positive test results whereas in years 2015, 2016 and 2017 there were in total only 3 donors.

Results: The analysis showed a big change in favour of the group of vaccinated donors (Chart 1) – 23-time less HBV infections in this group of donors were observed (in absolute value). Although over 99% of infants were vaccinated, several HBV infections among donors were noted. Unfortunately a small percentage of population shows no response to the vaccinations and does not acquire resistance against HBV – for Poland it is about 5%.

Summary/Conclusions: Vaccination of potential donors against HBV is an effective method to minimise the risk of HBV infection by means of transfusion of blood and its components.

P-400

DEMOGRAPHIC CHARACTERISTICS OF HBV AND HCV SEROPOSITIVE BLOOD DONORS – 10 YEARS STUDY

S Bogdanovic, N Bujandric and R Jovanovic

Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia

Background: The risk of acquiring a transfusion-transmissible infection (TTI) from a blood component today is lower than ever. Continuous improvement in donor selection, screening tests and inactivation procedures are the key tool in reducing the risk of TTI. For screening of the donated blood, the World Health Organization has recommended tests for markers of hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and syphilis. In our country obligatory screening marker for the HBV is hepatitis B virus surface antigen (HBsAg) and for the HCV is antibody to HCV (anti-HCV).

Aims: This paper is aimed to present demographic characteristic of HBV and HCV seropositive blood donors in the South Backa District of Vojvodina.

Methods: A retrospective descriptive study was carried out from January 2008 to December 2017 in the Blood Transfusion Institute of Vojvodina. The data from the screening and the confirmation tests for HBV and HCV in the study were used from the records of the TTI laboratory. Sex, age and the number of blood donation were reviewed for all blood donors who were confirmed positive.

Results: A total of 297440 blood donations were collected during ten years. The age distribution of the donors ranged from 18 to 65 years. The percent of repeat blood donors decreased over time, while the percent of the first time donors had a stable trend (about 10%). The overall seroprevalence of HBV infection was 0.027% (ranged from 0.011 to 0.047%) and of HCV infection was 0.019% (ranged from 0.004 to 0.031%). The HBV infection was more prevalent in male, first time blood donors and among donors aged 18 to 65 years. The highest HCV seroprevalence was observed among male donors, first time blood donors and donors aged 18 to 49 years.

Summary/Conclusions: The results of present study show that the overall seroprevalence of HBV and HCV infection has been low and that the risk of HBV and HCV infection was decreased over time. Still, blood transfusion remains a risk factor for the spread of blood-borne infections. Therefore, the collaboration of all parties involved in transfusion chain, including national haemovigilance system, is crucial to increase the blood safety in our District.

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INCIDENCE OF HEPATITIS-B AND HEPATITIS-C VIRUS IN WHOLE BLOOD TRANSFUSED HEMODIALYSIS DEPENDENT CKD PATIENT IN A TERTIARY LEVEL HOSPITAL

M Alam[1] and M Islam[2]

[1]Transfusion Medicine [2]Nephrology, Rajshahi Medical College, Rajshahi, Bangladesh

Background: Transfusion-transmitted virus is a single-stranded DNA virus that was identified in patients with post-transfusion hepatitis of non-A to G type. Patients with chronic renal failure on maintenance hemodialysis have a higher risk of viral infections, and the prevalence of Transfusion-transmitted virus infection is common.
Aims: Study the predictors of occurrence of infection in Blood transfusion dependent Hemodialysis (HD) patients and to determine the most frequency of transfusion-transmitted virus (TTV), Hepatitis-B & Hepatitis-C virus.
Methods: A case-control study compromising of 63 patients on maintenance Hemodialysis therapy at the Nephrology unit of Rajshahi Medical College Hospital (Group-I) and 100 healthy individuals, non-remunerated voluntary blood donor (Group-II) who were tested for Transfusion-transmitted virus by EIA (enzyme immunoassay).
Statistical analysis: The collected data were tabulated and analyzed using SPSS version 20 software. Quantitative data were expressed as mean and standard deviation; qualitative data were expressed as frequencies and percentages. student's t-test was used to compare the between mean of two groups, the Chi square "χ^2" test was used to compare between categorical data and regression analysis was used to detect predictors of occurrence of Transfusion-transmitted virus infection. $P < 0.05$ was considered to be significant.
Results: The mean age of the hemodialysis (HD) group was 42.2 ± 11.7 and that of the control group was 39.2 ± 9.7 and the male/female ratios were 63.5%/36.5% and 53%/47% in Group-I and Group-II respectively. The difference in both variables was statistically non-significant.
The prevalence of TTV infection in Group-I was 27.98% while that in Group-II was 09%, and the difference between the two study groups was statistically significant.
History of blood transfusion was the only significant predictor of occurrence of TTV infection in HD patients ($P < 0.01$), while age, duration of HD, HBV and HCV infection, elevated ALT and AST were not significant predictors for TTV infection.
Summary/Conclusions: History of blood transfusion was the only significant predictor, and we found that age of patients, duration of Hemodialysis, hepatitis B and C infection, aspartate aminotransferase and alanine aminotransferase levels were not significant predictors of Transfusion-transmitted virus positivity in Hemodialysis patients. The prevalence of Transfusion-transmitted virus among Hemodialysis patients was significantly higher than that in healthy individuals. History of blood transfusion was the only significant predictor of Transfusion-transmitted virus positivity among them.
Further studies on Transfusion-transmitted virus in peritoneal dialysis patients and transplant patients are needed.

P-402

Abstract has been withdrawn

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Abstract has been withdrawn

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HEPATITIS CORE ANTIBODY SCREEING IN BLOOD DONORS IN SAUDI ARABIA

OS Alsaweed[1], A Alomari[1], Q Haddad[2], K Aldosari[3] and F Alseraye[1]

[1]Department of Pathology and Laboratory Medicine [2]Infection Control, Security Forces Hospital [3]Regional Lab, Ministry of Health Saudi Arabia, Riyadh, Saudi Arabia

Background: In blood donors screening, hepatitis B core antibody (HBc-Ab) testing is controversial, particularly, when used in addition to hepatitis B surface antigen (HBs-Ag) and Nucleic Acid Testing (NAT). The majority of reactivity in HBc-Ab is nonspecific. World Health Organization (WHO) currently does not recommend using

HBc-Ab as a routine testing in screening blood donors, especially in high seropositive countries such as Saudi Arabia. Nevertheless, the majority of blood banks in Saudi Arabia discard blood donations from donors due HBc-Ab reactivity.
Aims: To estimate the seroprevalence and demographics of HBc-Ab among blood donors who are negative for both HBs-Ag and NAT. Also, to measure the increase in blood donors if a re-entry strategy is implemented when following WHO criteria.
Methods: A total of 22678, voluntary and replacement donors were included between 2014–2017 in a donor center in Riyadh, Saudi Arabia. Demographic data were collected for all donors. Donors were classified into three age groups: younger than 20, between 20–40 and older than 40. All donors were screened for infectious markers including testing for hepatitis B (HBc-Ab, HBs-Ag, NAT). Donors with reactive HBc-Ab and negative for both HBs-Ag and NAT testing were additionally screened by HBs-Ab.
Results: Out of 22678 blood donors, 21868 (96.4%) were males and 810 (3.57%) were females. The incidence of HBc-Ab positive cases was 15.8% (%16.2 in males and 4.56% in females). HBs-Ab was positive in 1158 (32.3%) out of HBc-Ab reactive donors. (810) 70% of positive HBs Ab donors had titer of 100 mIU/ml or more. The prevalence of HBc-Ab reactive donors as following: 0% and 0.1% for female and male donors less than 20 years, 2.0% and 13% for females and males in donors between 20 and 40 years, 14.2% and 27.6% for females and males in the group of donors more than 40 years old, respectively.
Summary/Conclusions: The prevalence of HBc-Ab among donations in Saudi Arabia was 15.8%, with younger age group having lower prevalence. In addition, females had significantly lower prevalence of HBc-Ab. Continuing using the current approach by excluding HBc-Ab leads to discarding approximately 896 donations yearly .
Applying the current WHO criteria in regards to not performing HBc-Ab routinely will result in a significant reduction in our discard rate to nil. The data presented in this study indicates the need to initiate a national policy in Saudi Arabia to allow re-entry mechanism.

Hepatitis C (HCV)

P-405

POLYMORPHISM OF HUMAN PLATELET ANTIGENS (HPA)-1 TO 18 IN CHINESE HAN BLOOD DONORS INFECTED WITH HEPATITIS C VIRUS

L Shao, H Lin and Y Liu

Jiangsu Province Blood Center, Nanjing, China

Background: Hepatitis C is a liver disease caused by the hepatitis C virus, Globally, between 130–150 million people have chronic hepatitis C infection, a significant number of those who are chronically infected will develop liver cirrhosis or liver cancer. The main part of HCV replication and infection is the liver, there are a lot of researches suggested that HCV also infected T cells, B cells and dendritic cells. Similarly, platelets have been reported to carry the HCV.
Aims: To study the relationship between the HPA1–18 gene polymorphism of HPA and susceptibility to HCV in Chinese Han population.
Methods: A case-control study was conducted among 154 HCV infected blood donors and 300 eligible blood donors, genomic DNA was extracted from 454 blood donors using commercial Genomic DNA Kit and amplified for genotype of HPA-1–18 using PCR Sequence Specific Primers (PCR-SSP) kits. Comparing the HPA genotype of HCV-infected donors and eligible donors, to analyze the association between HPA polymorphism and HCV infection.
Results: The distributions of HPA-1, 2, 3, 4, 5, 6, and 15 genes were polymorphic in HCV-infected donors, in addition to the HPA - 3 ($P < 0.05$), all the other six system antigen distribution consistent with Hardy Weinberg equilibrium. Among the eligible donors, only HPA-2, 3, 5, 6, and 15 had polymorphism and the HPA -15 not accorded with the Hardy - Weinberg equilibrium. There were statistically significant differences in HCV blood donors among HPA-1、3、4、5、15 systems compared with eligible donors.4 and 5 haplotypes with a frequency of over 0.03 were found in HCV-infected and eligible blood donors respectively. The most common type of haplotype is UTR-1 in Han population and UTR-2 in Uygur. The most common type of haplotype in the two populations both were AAAAAAA ($f = 0.308;0.259$) and AAAAAAB($f = 0.192;0.305$). But the frequencies of AAAAAAA and AAAAAAB differ significantly between the two populations.
Summary/Conclusions: In this research, HPA polymorphism of HCV-infected and eligible blood donors was analyzed, distribution data of allele and haplotype of HPA in this two populations were obtained. These results showed that HPA genotypes were statistically different between the two populations, suggesting that the HPA gene polymorphism was associated with HCV infection.

P-406

STABILITY OF NATIVE, LYOPHILISED AND INACTIVATED HBV, HCV AND HIV-1 PLASMA STANDARDS

N Lelie and H van Drimmelen

Bio Quality Control, Heiloo, The Netherlands

Background: Since the first proficiency study for HCV NAT methods in the early 1990s (Zaaijer, Lancet 1993) we have established native and inactivated viral plasma standards that for two decades were stored at −80°C and used for preparation of reference panels and run controls. These liquid frozen standards have been extensively calibrated in copies/ml and IU/ml and are directly traceable to the first established WHO standards in the late 1990s. Stability of reference samples is a pre-requisite for standardization of NAT.

Aims: We examined the stability of native, inactivated and lyophilized standards and run controls for HBV-DNA, HCV-RNA and HIV-1 RNA

Methods: The same standard dilutions (and run controls) were stored at both −80°C and −30°C for different time periods up to 8 years before testing by replicate tests in different quantitative NAT methods. Recovery of virus after inactivation was determined at 90% for HCV, 84% for HBV and 56% for HIV (and 24% after lyophilization of HIV). Stability of standards in the liquid phase was investigated in accelerated degradation studies at 4°C, 21°C and 37°C during 48–120 h. The degradation slope (and 95% confidence limits) at different temperatures was examined by regression analysis assuming first order kinetics.

Results: Long term stability of native and inactivated viral standards stored at −80°C has been firmly established. HBV-DNA standards and the native (antibody positive) HCV standard were also stable for at least 4–5 years when stored at −30°C. However at −30°C a significant annual degradation was measured of 9 (7–11)% for the (antibody negative) chemically inactivated HCV standard, 8 (5–9)% for the (antibody negative) WHO HCV 06/100 standard, 7 (5–10)% for the native (tissue culture derived) HIV standard and 9 (7–11)% for the heat-inactivated HIV standard. The native (antibody positive) HCV standard was stable for 120 h at 4°C, but a significant degradation of 6 (5–8)% in 8 h was calculated at 21°C. The 8 h decay at 4°C was estimated at 6 (2–10)% for the inactivated HCV standard, 7 (2–13)% for the WHO HCV 06/100 standard, 6 (2–10)% for the native HIV standard and 5 (1–9)% for the inactivated HIV standard. During 13 years comparable LODs were found on the same HCV and HIV standard dilution panels in Ultrio versions, but the third batch of reference panels prepared from the WHO 06/100 standard had a significantly lower potency of 69 (50–94)%. In a meta-analysis comparing analytical sensitivity on dilution panels of WHO replacement standards the WHO HCV 06/100 standard was the first one with a significantly lower potency of 78 (67–89)% (n = 750).

Summary/Conclusions: Lyophilization destroys viral particles and does not guarantee stability of viral standards. Our standards stored at −80°C proved to be an alternative to lyophilized WHO standards for validation of NAT methods. Run control batches have been consistently manufactured for 20 years and can be stored for a maximum of 2 years at −30°C to guarantee less than 20% degradation of viral RNA.

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HEPATITIS C VIRUS PREVALENCE AMONG PATIENTS WITH THALASSEMIA AND INHERITED BLEEDING DISORDERS IN IRANA SYSTEMATIC REVIEW AND META-ANALYSIS

A Khosravi[1], M Karimzadeh[2], A Jalili[3], M Abdollahi[1] and M Jalalifar[1]

[1]Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine [2]Medicine Faculty, Shahid Beheshti University of Medical Sciences [3]Department of Stem Cells and Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Islamic Republic of Iran

Background: Hepatitis C Virus (HCV), a most common causes of post transfusion infections, is a major global health problem that results liver cirrhosis and hepatocarcinoma. Its prevalence is vary in different part of the world. Also, it has been shown that HCV is more prevalent in patients who received multiple transfusions. Hence, Patients with thalassemia and inherited bleeding disorders are at high risk of HCV infection. Some reports showed that HCV prevalence is high among Iranian patients underwent multiple transfusions.

Aims: This systematic review and meta-analysis study aimed to determine hepatitis C virus prevalence among patients with thalassemia and inherited bleeding disorders in Iran.

Methods: Comprehensive searches have carried out in different databases such as PubMed, Embases, the Scientific Information Database (SID) of Iran and the World Health Organization Index Medicus for the Eastern Mediterranean Region (IMEMR

WHO) up to January 2017. The findings were reported following PRISMA guidelines. The pooled proportion rates was calculated using Metaprop program on Stata version 14.1 for Mac. Also, the confidence intervals of each study was calculated using the exact method.

Results: Forty-seven studies, composed of 12449 patients; 8673 thalassemia and 3776 patients with inherited bleeding disorders (mainly hemophilia), fulfilled our criteria and included in this meta-analysis. The year of data collection in the evaluated studies were between 1998 and 2015. The pooled HCV prevalence was estimated 28% (95% confidence intervals [CI] = 22%>33%). The prevalence in patients with thalassemia and inherited bleeding disorders were 19% ([CI] 95%= 16%>23%) and 42% ([CI] 95%= 33% >52%), respectively. There was a considerable heterogeneity between studies.

Summary/Conclusions: Our findings indicated the high prevalence of HCV among patients with thalassemia and inherited bleeding disorders in Iran. Moreover, it is significantly higher in patients with inherited bleeding disorders than those with thalassemia. The results also showed that transfusion related transmission of HCV in Iran is higher than other developing countries.

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PREVALENCE OF TRANSFUSION TRANSMISSIBLE INFECTIONS AMONG BLOOD DONORS IN NIGERIA DURING 2006–2016: A SYSTEMATIC REVIEW AND META-ANALYSIS

OA Ukwedeh[1] and B Ebruke[2]

[1]Clinical Services, Prime Care Hospital Gwarinpa, Abuja [2]International Foundation Against Infectious Diseases in Nigeria, Abuja FCT, Nigeria

Background: Unsafe blood is a well-documented pathway for transmitting infections. The prevalence of Transfusion Transmissible Infections (TTIs) in donated blood, is an indication of how safe a country's blood supply is. It is also used to appraise the system of donor selection and is a cost-effective approach for monitoring the distribution and trends of infection among healthy individuals and the general population. Paucity of data and poor monitoring and evaluation, make it difficult to estimate the residual risk of TTI in Nigeria. To date, there has been no effort to systematically review and consolidate data on the prevalence of TTIs in donated blood in Nigeria

Aims: The aim of this study was to synthesize from existing literature the prevalence of major TTIs (HIV, Hepatitis B (HBV), Hepatitis C (HCV) and Syphilis) in donated blood in Nigeria.

Methods: A systematic review and meta-analysis was conducted on published data assessing the prevalence of TTIs amongst blood donors in Nigeria over the period 2006–2016. The sources of data were PubMed, Google Scholar and African Journals Online. The search strategy combined terms related to TTIs such as "transfusion transmissible infections, blood borne infections, viral infections, hepatitis, HCV, HBV, HIV and syphilis." All potentially relevant papers were reviewed and a random effects model was used to implement the meta-analysis with MetaXL version 5.1.

Results: Fifty- eight articles met the inclusion criteria and were included in the final review and meta- analysis. Of 5 published articles with available data on the 4 major TTIs reported, pooled prevalence of at least one TTI was 17.3%(95% CI: 11.3- 23.7). The most prevalent TTI was HBV with a prevalence of 10.4%(95% CI: 7.9–13.2). Prevalence of the other major TTIs were as follows HCV 2.8%(95% CI: 2.1–3.7), HIV 3.8%(95% CI: 2.2–5.6) and syphilis 1.2%(95% CI; 0.8–1.8%).

Prevalence of the major TTIs was variable across the classes of blood donors.

The prevalence of HBV, HCV, HIV and Syphilis among commercial donors was 12.4% (95%CI: 7.2–18.4), 3.0% (95% CI: 1.4–5.1), 2.5% (95%CI: 0.5–5.6) and 2.8% (95% CI: 1.0–5.3) respectively; among family replacement donors it was 8.8% (95% CI;1.7–19.9), 2.0% (95%CI:0.6–4.1), 2.7% (95%CI:1.2–4.7) and 1.8% (95% CI:0.5–3.7) and among voluntary non-remunerable donors it was 9.9% (95%CI: 5.0–16.1), 4.2% (95%CI:2.4–6.4), 1.8% (95%CI:0.3–4.3) and 1.6% (95%CI: 0.4–3.6) respectively.

Prevalence of the major TTIs were consistently higher in women (HBV11.4%, HCV 4.2%, HIV 6.5%, Syphilis 1.5% in women versus Hepatitis B 11.2%, Hepatitis C 3.0%, HIV 3.7%, Syphilis 0.9% in men). This higher prevalence in women was in spite of a higher proportion of blood donors being men. (84.7% men Vs 15.3% women).

Summary/Conclusions: Our findings indicate that prevalence of TTIs amongst blood donors in Nigeria is high and varies across different donor groups. There is an urgent need for appropriate control measures in order to make blood donation safer in Nigeria

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DETERMINATION OF THE OPTIMAL SIGNAL-TO-CUTOFF RATIO OF ANTI-HCV ASSAYS AND SUGGESTION OF A LABORATORY ALGORITHM: EXCLUSION STRATEGY FOR FALSE-POSITIVE RESULTS

D Shin[1], M Choi[2], K Lee[1,3], Y Hong[1,3], E Song[1], D Kim[2], J Song[1,3] and K Han[1]

[1]Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul [2]Department of Laboratory Medicine, Chonbuk National University College of Medicine, Jeonju [3]Department of Laboratory Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

Background: Following discontinuation of the recombinant immunoblot assay (RIBA), the only available supplementary test for detection of Hepatitis C virus (HCV) infection is the nucleic acid amplification (NAA) test. However, the NAA test does not adequately detect past, resolved HCV. Consequently, it is hard to distinguish between past resolved HCV infection and biological false positivity.
Aims: The present study was aimed to assess the diagnostic performance of each immunoassay (IA) based on the signal to cut-off (S/CO) ratio, and to explore an algorithm with optimal efficiency that assesses the anti-HCV results of one or two IAs.
Methods: In the present study, both RIBA and NAA tests for anti-HCV positive samples were performed using two immune assays: 1) Architect anti-HCV chemiluminescent microparticle immunoassay (CMIA), 2) Access HCV Ab PLUS chemiluminescent immunoassay (CIA). We assessed the diagnostic performance and utilized an optimized algorithm to determine the true positive anti-HCV results.
Results: In total, 1,035 samples were evaluated. RIBA was positive in 512 of the 1,035 anti-HCV positive samples, indeterminate in 160, and negative in 363. The 165 samples were NAA test positive. Diagnostic sensitivity, specificity, the false positive rate, and positive predictive values of CMIA were 96.7, 18.1, 81.9, and 52.1, respectively, followed by CIA, which was 94.7, 67.2, 32.8, and 72.3, respectively. We also assessed the optimal S/CO value, which were 5.2 in CMIA and 2.6 in CIA at 95% PPV. In a single immunoassay (IA), we determined the positive as 286 (30.1%) in CMIA and 444 (66.2%) in CIA. However, using two IAs, 443 samples were determined to be positive (CMIA to CIA: 46.6%), (CIA to CMIA: 75.5%).
Summary/Conclusions: It is hard to determine the positivity of anti-HCV with S/CO ratio alone. Therefore, this study sought to elucidate the fundamental role of the S/CO ratio by referring to the NAA test and RIBA, as well as to determine as many true positives as possible from anti-HCV positive results using one or two IAs.

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LABORATORY SIGNS OF OCCULT HCV INFECTION IN BLOOD DONORS AND RECIPIENTS

N Yaroslavtseva[1], T Tupoleva[1], D Tikhomirov[1], T Gaponova[2], A Dedova[3] and L Nikolaeva[3]

[1]Department of Virology [2]National Research Center for Hematology [3]Laboratory of genetically engineered substances, N.F. Gamaleia National Center for Epidemiology and Microbiology, Moscow, Russian Federation

Background: Occult HCV infection (OCI) is presented in two types: seronegative and seropositive with low titers and/or incomplete pattern of antibodies to individual viral antigens. Low viremia (under 10 IU/ml) during OCI can lead to false negative results of viral markers detection if insufficiently sensitive test is used. HCV RNA accommodation in liver tissue and within peripheral blood leucocytes is another distinctive feature of OCI. Uncertain results of anti-HCV detection such as "grey zone" results point out to new challenges for transfusion services and blood banks.
Aims: Search and close analysis of serologically weakly expressed forms of HCV infection in blood donors and recipients.
Methods: 33 blood donors with uncertain results of anti-HCV detection and 42 blood recipients (19 with severe hemophilia A, 3 - severe hemophilia B, 6 – different types of lymphoma, 3 – acute leukemia, 2 – myeloproliferation and 9 – other blood disorders) with incomplete pattern of antibodies to individual HCV antigens were followed up for HCV markers close investigation. Mean age of donors was 27.9 years (18–43), m/f ratio – 25/8. Mean age of recipients was 34.5 years (21–70), m/f ratio – 29/13. Follow-up examination period was 1–24 months for blood donors and 2 months for recipients. Investigation included routine (sensitivity 100 IU/ml) and ultra-sensitive (sensitivity 15 IU/ml) HCV RNA detection, anti-HCV detection by ELISA and CMIA and HCV immunoblot. All included samples were HIV and HBV negative.
Results: ELISA and CMIA anti-HCV detection results provided poor match. 25 donors' samples were positive or "grey zone" in CMIA but negative in ELISA and

immunoblot. The rest 8 samples gave 4 positive and 4 "grey zone" results in ELISA and 2 uncertain result in immunoblot. 15.2% of discordant results contained HCV RNA in concentration under 100 IU/ml.
Recipients of donor's blood showed HCV RNA in 40.5% of cases (both low and high viremia). Samples with low HCV RNA concentration showed low titers of antibodies to single HCV antigen or anti-core HCV in combination with anti-NS3, -NS4. In contrary, samples with levels of HCV genome exceeding 10^5 IU/ml contained high titers of anti-core HCV.
Summary/Conclusions: OCI may be revealed by discordant results of anti-HCV detection. Such samples demand close investigation. Low levels of HCV RNA in plasma or blood cells in samples with discordant results of anti-HCV detection proves this point. Low viremia in blood recipients correlated with low titers of antibodies to individual HCV antigens.

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BLOOD TRANSFUSION SAFETY AND ELIMINATION OF HEPATITIS C IN GEORGIA

E Bloch[1], E Kipiani[1], L Gvinjilia[2], M Alkhazashvili[2], N Chitadze[2], I skhomelidze[2], A Turdziladze[2], V Getia[2] and S Keating[3]

[1]Pathology, Johns Hopkins University School of Medicine, Baltimore, United States [2]National Centers for Disease Control and Public Health, Tbilisi, Georgia [3]Blood Systems Research Institute, San Francisco, United States

Background: In response to a national Hepatitis C (HCV) epidemic, the Government of Georgia has initiated a public health program to eliminate HCV by 2020. The program combines screening and treatment with a goal of identifying 90% of HCV-infected individuals, treatment of 95% of those with chronic HCV infection, and attainment of cure in 95% of those treated for HCV infection. Blood transfusion has been identified a significant mode of transmission for HCV in Georgia.
Aims: To assess blood transfusion operations in Georgia to inform development of a strategic plan and targeted intervention for HCV prevention under the broader goal of improved blood transfusion safety.
Methods: Twenty-two blood banks hold a license to produce blood in Georgia and all are required to use a donor-donation database. Unique donor identification numbers are assigned to the donor and donation, providing access to the donation information, donor demographics and testing records. Data from 2015 to 2017 were extracted from the blood donor database and summarized according to operational indices (e.g. numbers of donations), donor demographics (sex; remunerated, voluntary or replacement; first time or repeat) and infectious marker status (the prevalence of transfusion transmitted infection). Information on the blood banks that participated in the State Safe Blood Program were also available for evaluation.
Results: During this time period, 227,725 donations were recorded. Sixty percent of donations were collected from male donors and 59% of donations were from paid donors. HCV and HIV prevalence results were based on screening with an ELISA assay as reported by the blood bank laboratories. The HCV and HIV prevalence was 0.7% and 0.1% respectively. The HCV positive donations were collected, predominantly, from first-time donors (82% of HCV positive).
Summary/Conclusions: Previous studies in Georgia have shown that HCV prevalence is highest among men and in people who inject drugs. Given that the majority of Georgian blood donors were male and constituted paid donors, this constitutes a possible high-risk population for HCV acquisition. Since the window period of HCV screening by ELISA can take 8 weeks or longer, testing approaches in use, which typically comprise serological (antibody) screening alone, lack sufficient sensitivity to detect recent infection in donors, thus failing to interdict transfusion- transmitted HCV. While the goal of the HCV elimination program is to test and treat all HCV infected Georgians, blood transfusion remains to be a risk for transmission but also an opportunity to identify and link HCV positive donors to HCV treatment programs. Work towards transition to HCV antigen screening and ultimately nucleic acid testing of blood donations will shorten the window period, reduce the risk for transfusion transmitted HCV infection and improve access to optimal HCV screening. Linkage of the donor database to an HCV treatment database will improve referral of HCV positive donors to care and treatment services.

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HEPATOCELLULAR CARCINOMA IN NON HCV MULTI TRANSFUSE PATIENT

A Oshidari[1], A azarkeivan[1], M Eslami[1] and F Zamani[2]

[1]Thalassemia Clinic, Iranian Blood Transfusion Organization [2]Gastroentrology Clinic, Iran Medical University, Tehran, Islamic Republic of Iran

Background: Thalassemia is a hereditary anemia with chronic transfusion. This treatment may have some side effects. One of these consequences is transfusion transmitted infections (TTI). Hepatitis C (HCV) is one of them. HCC may develop in the consequence of HCV infection.

Aims: we report a Case of HCC in thalassemia major patient with no HCV infection and as a consequence of iron overload and hepatic fibrosis.

Methods: A 54 year old Thalassemia Major patient who was on chronic blood transfusion since first year of life, and had some complication of thalassemia such as sever skeletal problem, osteoporosis, vertebral compression fracture, and necrosis of head of his left femur. The patient had history of splenectomy and cholecystectomy. Also the patient had some degree of iron over load; relatively high Ferritin level; and moderate iron siderosis on his liver in T2*MRI. In the course of his regular treatment he developed severe abdominal pain and in abdominal sonography he had coarse parenchymal liver with two masses in porta hepatis suggestive lymph node or extramedullary hematopoiesis and was advised to be confirmed with MRI with contrast. In few days later the patient had Abdominal and Pelvic MRI with IV gadolinium which shows ill defined mass in segment VII of liver which suggestive an invasive mass such as metastatic malignancy or cholangiocarcinoma and also had some metastatic para aortic lymph nodes .

Results: The patient was admitted in hospital and liver biopsy was done for him and hepatocellular carcinoma was diagnosed with pathologic report. Also the patient developed rising level of alphafetoprotein. The course of his disease was progressive and the patient was very ill and asthenic. Unfortunately the patient died before starting the chemotherapy.

Summary/Conclusions: HCC is usually is a consequences of HCV infection in thalassemic patients, but nowadays with increasing the quality of treatment, we have longer life expectancy and with patients growing into middle age and beyond and with this increased survival, we have other complications of thalassaemia which we didn't have not before because of short life time. Risk of HCC is increased in cirrhotic liver damage from Iron overload as a result of chronic transfusion. Regular follow up and good treatment of iron overload may prevent such high risk malignancy in thalassemic patients.

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HIV

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RISK FACTORS REPORTED BY DONORS IN THE 12 MONTHS BEFORE DONATION DISCLOSED AFTER TESTING HIV POSITIVE

TT Goncalez[1], E Sabino[2], L Amorim Filho[3], A Carneiro Proietti[4], L Capuani[5], C Miranda[4], M Mundim[3], C de Almeida Neto[6], P Loureiro[7,8], A Mendrone[6] and B Custer[9,10]

[1]Epidemiology, Blood Systems Research Institute, San Francisco, United States [2]Tropical Medicine, Medical School University of São Paulo, São Paulo [3]Fundação Hemorio/Hemocentro do Rio de Janeiro, Rio de Janeiro [4]Fundação Hemominas/Hemocentro de Minas Gerais, Belo Horizonte [5]Medical School University of São Paulo [6]Fundação Pro-Sangue/ Hemocentro de São Paulo, São Paulo [7]Departamento de Medicina, Universidade de Pernambuco [8]Fundação Hemope/Hemocentro de Pernambuco, Recife [9]Epidemiology, Blood Systems Research Institute, San Francisco, Brazil [10]Laboratory Medicine, University of California San Francisco, San Francisco, United States

Background: Donor eligibility assessment is conducted using in-person interviews in Brazil. HIV infections in blood donors in Brazil are about 10-fold higher in donors compared to countries with high human development indices. Monitoring risk factors among blood donors is an important tool to help reduce the risk to recipients.

Aims: Determine recent behavioral factors that are putatively associated with HIV infection among accepted blood donors in Brazil who tested confirmed positive.

Methods: HIV+ donors who return for standard counseling and referral were invited to participate in the study. From November 2012 to March 2017, donors were enrolled at the four REDS-III blood centers, located in the cities of Recife, Rio de Janeiro, Sao Paulo, and Belo Horizonte. Study participants completed a confidential audio computer assisted structured interview (ACASI) on motivations and risk factors for blood donation and also provided a blood sample for molecular surveillance. In this analysis, we primarily focused on risk behaviors reported by the donors in the 12-month period before donation.

Results: Out of 375 HIV positive donors enrolled, 154 (41%) were from Recife, 92 (24.5%) from Rio de Janeiro, 80 (21.3%) from Sao Paulo, and 49 (13%) from Belo Horizonte; 72.2% were male, 70.8% were 18–39 years old; 56% were single, never married, and overall 56% self-defined as straight/heterosexual (88.8% of females vs 46.2% of males). Participants in the study were similar to HIV+ non-participants by sex, age, race, being a community or replacement donor, and blood center where they donated. However, participants were significantly more likely to be repeat donors. HIV risk factors disclosed on the ACASI varied according to sex. As expected, sex with a man who had sex with another man in the last 12 months was more common in males than females (43.0% vs. 4.5%). Females were more likely than males to report having sex with an inmate in the last 12 months (13.5% vs 3.1%), and sex with a HIV+ partner in the last 12 months (9.0% vs 5.2%). An equal proportion of males and females reported having sex with a HIV+ partner who was taking antiretroviral therapy in the last 12 months (4.2% vs 4.5%). In addition, 17.5% of males and 6.7% of females reported ever being persons who injected drugs (PWID), and 5.9% males and 13.5% females reported ever needle exposure in their professional work. All of these behaviors if disclosed at the time would have made the donors ineligible.

Summary/Conclusions: Blood donors with important undisclosed behavioral risk factors continue to donate at blood centers in Brazil. The results indicate an vital need to understand reasons and motivations for nondisclosure of deferrable risk during the donor selection process. Approaches to self-interview such as ACASI should be evaluated as alternatives to enhance disclosure in Brazil.

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DEMOGRAPHIC CHARACTERISTICS OF CONFIRMED HIV POSITIVE BLOOD DONORS OF TURKISH RED CRESCENT IN 2017

C Keskin[1], K Demirel[1], E Koşan[1], C Beker[2], I Mıstıkı[3], I Birinci[1], M Günçıkan[4], I Karahacıoğlu[4], A Aksoy[4] and F Yılmaz[5]

[1]Northern Marmara Regional Blood Center, Turkish Red Crescent, İstanbul [2]Aegean Regional Blood Center, Turkish Red Crescent, İzmir [3]Middle Anatolia Regional Blood Center [4]Blood Services General Directorate, Turkish Red Crescent [5]Biochemistry Department, Yıldırım Beyazıt University, Ankara, Turkey

Background: HIV/AIDS (Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome) has become one of the most studied infectious diseases since it was defined. HIV/AIDS is still an important health problem worldwide and the

number of people living with HIV worldwide continued to grow in the last years. The first HIV/AIDS cases had been reported in 1985 from Turkey and with an increasing trend during the following years, the number of cases reached to 13158 with 2470 new cases in 2016.

Aims: This study was performed to determine retrospectively the demographic characteristics of 229 confirmed HIV positive blood donors of Turkish Red Crescent in 2017, including gender, blood donation number, age, education and occupation status.

Methods: Among the 2 018 222 blood donors who attended Turkish Red Crescent blood donation centers between the dates 01.01.2017 and 31.12.2017, 229 confirmed HIV positive donors have been included in the study. The demographic characteristics of these blood donors have been reviewed from the records of the related blood centers. HIV ½ Ab-Ag tests have been performed by enzyme immunoassay method (ELISA); (DIASORIN, Murex HIV Ag/Ab Combination, UK), Nucleic Acid Amplification tests by Real Time PCR; (ROCHE, Cobas TaqScreen MPX v.2.0, Germany) and Anti HIV confirmation tests by Line Immunoassay (LIA); (FUJIREBIO Inno-LIA HIV1/2,Belgium).

Results: In this study, among the donated blood samples of 2.018.222 donors accepted by Turkish Red Crescent in 2017, reactivity has been found in 5.417 samples by HIV ½ Ag-Ab and/or Real Time PCR tests. Among the 5417 reactive samples, HIV positivity has been confirmed in 229 (0.0113%) by LIA testing. Of the confirmed HIV positive cases, 97.38% is male and 49.35% is a first time donor; 161 (70.30%) have completed high school and the occupational status does not show a specific characteristic.

Of the HIV positive cases, 223 (97.38%) are male, 6 (2,62%) are female. Among the male cases, 116 (52%) have made two or more blood donations. Among the HIV positive female cases, the percentage of first time donors (5/6; 83.33%) is higher than the percentage of first time donors in HIV positive male cases (108/223; 48%). The majority of HIV cases (178, 77.23%) have been found to have an age between 18 and 34 years. A majority of the HIV positive cases (161, 70.30%) have completed High School. HIV confirmed positive cases are distributed in all different occupational groups.

Summary/Conclusions: The primary target of all blood centers is a safe blood transfusion. The obligatory screening tests applied and the other measures taken (donor inquiry and physical examination processes) are means of preventing transfusion transmitted infections. In our country, there is an increasing trend of infection by years. The number of annual new HIV positive cases were 661 in 2011, whereas in 2016, this number has increased by (273.6%) and has reached 2470 annual new HIV positive cases. There is a similar increase for Turkish Red Crescent blood donors; the number of annual confirmed HIV positive cases was 79 in 2013 and has reached 229 annual cases in 2017 with an increase of (189.8%). The results found in our study are similar to our nationwide data. In order to prevent HIV infection, an important public health problem in the World and nationwide as well, it is essential to create a continuous flow of correct information to the whole community, especially through school curricula and through media channels, regarding the etiologic agent of HIV/AIDS as well as the prevention methods and safe behaviours.

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USE OF A LIMITING ANTIGEN AVIDITY ASSAY TO DETERMINE HIV INCIDENCE IN SOUTH AFRICAN FIRST-TIME BLOOD DONORS

M Vermeulen[1], D Chowdhury[2], D Brambilla[2], G Beck[1], M Busch[3], B Custer[3], U Jentsch[4] and E Murphy[3,5]

[1]Operations: Donation Testing, South African National Blood Service, Roodepoort, South Africa [2]RTI, Bethesda [3]Blood Systems Research Institute, San Francisco, United States [4]South African National Blood Service, Roodepoort, South Africa [5]REDS III, NHLBI, United States

Background: In the South African general population, 2016 HIV prevalence was 19% among adults and 2012–2015 HIV incidence has been estimated at 12–13 per 1,000 person-years (PY) (UNAIDS and Statistics South Africa). Incident infections pose the greatest risk to blood safety. Although first time (FT) donor incidence has been estimated using parallel HIV antibody and nucleic acid testing (NAT) with a 15.4 day RNA to antibody window, a limitation of this method is that relatively few NAT yield (RNA+, Antibody -) donors are detected per year.

Aims: We applied a new antibody recency assay to detect the much larger number of recent (within 4 months) incident infections, allowing more precise time trend and subgroup analyses for FT donors.

Methods: Plasma samples from HIV seropositive FT donors during calendar years 2012 through 2016 were tested with a limiting antigen avidity (LAg) assay (Sedia

Biosciences, Portland OR). We used a cutoff of 1.50 normalized optical density units corresponding to an incidence "window" of 129 days. Incidence was calculated as cases/1,000 PY of which numerator cases were recent infections as classified by the LAg assay. Each uninfected donor contributed the full 129-day person-time to the denominator while recently infected donors contributed half that. We used multiple imputation to adjust incidence for missing LAg results for 414 (7%) confirmed HIV-positive donors. Donors classified as longstanding HIV were excluded from both the numerator and denominator. 95% confidence intervals were calculated using the Poisson method.

Results: Among 513,896 donations by FT donors in 2012–2016, 5763 (1.12%) tested HIV seropositive. Of these and after imputation, a total of 857 were classified as recent incident infections and the denominator consisted of approximately 179,738 PY. Overall incidence per 1,000 PY was 4.77 (95% CI 4.66–4.89) and declined from 4.88 in 2012 to 4.35 in 2016 (P trend < 0.0001). By age, HIV incidence was 8.03 in those aged 20–25 years, 5.28 in those 26 and older and 3.2 in those aged 16–19. By sex, HIV incidence was 6.36 in females and 2.78 in males. By race/ethnicity, incidence was 8.44 among Black, 2.00 among Colored, 0.27 among White and 0.20 among Asian donors. By province, incidence ranged from a high of 8.27 in Mpumalanga, 6.47 in Free State and 6.23 in Kwa-Zulu Natal to a low of 2.33 in the Northwest.

Summary/Conclusions: In South Africa, HIV incidence among FT donors was high but two- to threefold lower than general population estimates and is declining over time. Incidence is highest in the 20–25 year age group, twice as high in females compared to males and highest in Mpumalanga province followed by Kwa-Zulu Natal and Free State provinces, consistent with public health data. Because we could not control for undisclosed antiretroviral therapy among HIV positive donors, resultant false recency on the LAg assay may have caused a small over-estimation of incidence. The use of antibody recency assays is an important new tool and future research will compare these results to those obtained using other incidence methods

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SITUATION OF SYPHILIS AND TRANSFUSION TRANSMITTED VIRUSES CO-INFECTIONS, AMONG BLOOD DONORS IN TIRANA

I Seferi[1], Z Abazaj[1], A Metka[1], M Xhetani[2] and V Spahiu[1]

[1]NBTC [2]University of Tirana, Faculty of Natural Sciences, Tirana, Albania

Background: Syphilis, HIV, HBV and HCV share common modes of transmission. Syphilis has a high prevalence among our family replacement blood donors and being a sexually transmitted infection, the presence of syphilis is since years considered as an indicator towards "high risk" behavior and as a consequence towards higher risk of exposure to infections like HIV and hepatitis. Actually we have about 70% of our donations coming from family replacement donors (FRD) and 30% from voluntary non remunerated blood donors (VNRBD).

Aims: The aim of the study was to determine the co-infection rate of Syphilis with other transfusion transmitted viruses, and the donor population with the highest rate of this co-infection.

Methods: This is a retrospective analysis of our donation data, extracted from the registers of testing blood for infectious agents in NBTC Tirana for the years 2016–2017. Testing has been performed with ABBOTT ARCHITECT ci8200. All donations taken into consideration were first time donations.

Results: Total number of first time donations was 42745. Total number of confirmed syphilis positive donations was 58 with an overall prevalence of syphilis 0.13%. The overall seroprevalence of HBV, and Co-infection with Syphilis in our donor population was respectively 4.8%, 0.01%. The overall prevalence of HCV and co-infection with Syphilis was respectively 0.84%, 0.002%. The overall prevalence of HIV and co-infection with syphilis was 0.04%, 0.002%. One of the cases with co-infection of HBsAg and Syphilis presented also high level of transaminase. HIV was the infection mostly accompanied by syphilis. Among HIV infected donors 5,8% presented with a co-infection with syphilis. This rate of association with syphilis is significantly higher for HIV compared to HBV and HCV infected donors, where we found a rate of co-infection with syphilis respectively 0.29% and 0.27% .

All donors with co-infections were family replacement donors. Among FRD the rate of co-infection was 0.02% whereas there are no co-infections among VNRBD.

Summary/Conclusions: The high overall co-infection rate of syphilis in our FRD and the high co-infection rate of HIV with syphilis demonstrate once more the highest risk of exposure towards transfusion transmitted infections with family replacement donations. Efforts towards 100% VNRBD should be intensified as the safest way for sufficiency.

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ASSESSMENT OF SOCIO DEMOGRAPHIC PROFILE AND RISK FACTORS IN HIV SERO REACTIVE BLOOD DONORS IN A TERTIARY CARE CENTRE OF NORTHERN INDIA

R Kaur, K Mittal, R Kaur, G Kaur, P Kaur and T Sood

Department of Transfusion Medicine, Government Medical College and Hospital, Chandigarh, Chandigarh, India

Background: The rate of transfusion transmitted Human immunodeficiency virus infection (HIV) has shown a declining trend in the recent years in India because of increased sensitivity of screening tests and increased awareness in the general public, but it still remains a major public health issue. This study examined socio-demographic characteristics and risk factors of HIV seroreactive blood donor.

Aims: The study was done to evaluate the response rate of blood donors to the disclosure of HIV seroreactive status. This study also examined the socio-demographic characteristics and risk factors of HIV sero reactive blood donors.

Methods: This retrospective study was conducted in the department of Transfusion Medicine of a tertiary care hospital over a period of 18 months (from June 2016 to December 2017). Blood donor samples were screened for HIV using fourth generation ELISA (enzyme linked immunosorbent assay) kits as per manufacturer's instructions. These kits were approved for use in blood banks by Drug controller General of India. The seroreactive donors were notified telephonically and letters were also sent at their respective address. Responders to calls or letters were counseled by taking proper history and confidentiality was maintained; and then referred to ICTC for further testing and treatment. Reactive donors not responding to three telephonic calls and letter were labeled as defaulters. Data regarding socio-demographic characteristics, age, sex, donor status (voluntary/replacement), donation status (first time/ repeat), history of high risk behavior, history of prolonged hospitalization and blood transfusion, history of tattooing and ear piercing was obtained from donor record form and post donation counseling register.

Results: Out of total 32852 blood donations, twenty (0.061%) donations were seroreactive for HIV. Of these twenty seroreactive donors, nineteen were male and one was female. Eleven of these twenty donors donated first time while nine were repeat donors. Nineteen were voluntary and one was a replacement donor. Of these twenty donors, written correspondence could be sent to nineteen donors (95%) whereas one donor (5%) could not be informed as his address was incomplete on donor record card. Telephonic calls could be made to seventeen donors (85%) while two donors (10%) did not respond to calls and one donor (5%) could not be informed as his phone was switched off. Of the fourteen donors who reverted to department and referred to Integrated Counseling and Testing Centre (ICTC), nine male donors (47%) revealed history of high risk behavior and one donor (5.2%) was aware of his reactive status on post donation counseling. Three donors (15.7%) gave history of prolonged hospitalization following which blood transfusion was given in one case. Four donors (21%) had history of tattooing and ear piercing.

Summary/Conclusions: The present study emphasizes the importance of creating awareness about various modes of Transfusion transmitted infections (TTI's) among blood donors. It also stresses the need to strengthen pre donation screening, counselling and confidentiality in outdoor voluntary blood donation camps and to repeatedly track these seroreactive donors so as to eliminate them from the safe donor pool.

Bacteria

P-421

PREVALENCE OF SYPHILIS INFECTION IN BLOOD DONORS AT THE NATIONAL BLOOD CENTER, THAI RED CROSS SOCIETY

P Thunnok, D Intharasongkroh, R Kimilar, N Yuttayoth and K Chaiwong

Blood Testing Section, National Blood centre, Thai red cross Society, Bangkok, Thailand

Background: Syphilis is a chronic infectious disease caused by Treponema pallidum. The main route of transmission is sexual-transmission. Otherwise, it can be transmitted by blood transfusion from asymptomatic donors as well. For the blood donation, Syphilis is the one of pathogen that is important for testing before give the blood to the patients. So, the Treponema pallidum testing in blood donor has been included in the blood donor screening algorithm that must be tested. Generally, the serological testing is the most common to use for blood donor screening both Treponemal and non-treponemal tests. In Thailand, we have screened for syphilis infection by using a combination of both method to decrease the risk of infection in patients.

Aims: To study the prevalence of syphilis antibodies in blood donors at the National Blood Center, Thai Red Cross Society.

Methods: The study was performed between 2016–2017 at the National Blood Center, Thai Red Cross Society. The Treponemal test was used for antibody detection by using chemiluminescent microparticle immunoassay (CMIA) in the first screening step. Then, the positive result was repeated by using Immuno Chromatographic Strip (ICS) and the Rapid Plasma Reagin (RPR) for supplementary testing.

Results: 762,031 blood donors were screened for syphilis infection. We found 1,046 samples were positive for syphilis infection (0.14%). The prevalence of syphilis infection in male blood donors was higher than female blood donors significantly different (0.20% and 0.09%, P value <0.001) and the first-time donors also had a positive result more than repeated donors (0.44% and 0.07%, P value <0.001). Moreover, we found the co-infected with HIV (3.25%), HBV (1.63%) and HCV (0.86%) as well.

Summary/Conclusions: Our study shows that the syphilis infection has been identified in Thai blood donors and the sero-prevalence was not different from the past. In addition, it was similar to neighboring countries but lower than African countries. Male blood donors and the first-time donors were at higher risk for syphilis infection in Thai blood donors. Moreover, syphilis infection was associated with the HIV infection, Hepatitis B infection and Hepatitis C infection, respectively. However, blood donation in the risk groups may require additional screening procedures to ensure the highest quality of blood product.

P-422

AMOTOSALEN–UVA INACTIVATES HIGH LEVELS OF TREPONEMA PALLIDUM IN PLATELET CONCENTRATES SUSPENDED IN 100% PLASMA

A Laughhunn[1], S Lukehart[2], B Molini[2], M Lanteri[3], P Bringmann[1] and A Stassinopoulos[4]

[1]*Microbiology and Bioanalytical R & D, Cerus Corporation, Concord, CA* [2]*Department of Medicine, Harborview Medical Center, University of Washington, Seattle, WA* [3]*Global Scientific Affairs, Cerus Corporation, Concord, CA, United States* [4]*Global Scientific Affairs and Research, Cerus Corporation, Concord, CA, United States*

Background: Treponema pallidum (Tp) is the spirochete bacterium responsible for syphilis. Symptomatic infection can result in development of chancre and rash, but the organism disseminates via the blood and lymphatic systems producing systemic infection. Without treatment, infection persists for decades, though usually asymptomatic, with bacteria detected in blood. The World Health Organization reports >11 million new syphilis cases a year and >36 million are infected worldwide. The Centers for Disease Control and prevention estimates infectious syphilis cases have tripled since 2000 in the US.

Silent, long-term bacteremia in infected donors poses a risk to the blood supply with several reported cases of syphilis transfusion-transmission (TT). High prevalence in the early 20th century led to mandatory serological testing of blood donations in the US and throughout the world. The last time a documented case of TT syphilis was in 1966. AT least part of the protection is offered by the high cold sensitivity of the spirochetes to cold storage. That is not applicable to PC that must be stored at 22C, as well as components that are transfused within 7 days of donation. In the US alone, 11 million blood donations are screened each year, at a cost of ~$16 million. A recent study of US blood donors revealed a 0.16% seroprevalence in first-time blood donors, while up to 2.8% of blood donors in South America are positive for Tp. This is a higher prevalence than HIV, HBV, and HCV, and as prevalent as Trypanosoma cruzi (Schmunis et al. 1998). Pathogen reduction can offer additional protection against TT syphilis.

Aims: The objective of this study was to evaluate the inactivation of Tp in platelets suspended in 100% plasma (PC-100) to mitigate syphilis TT. For treatment of PC-100, photochemical treatment utilizing amotosalen and low energy ultraviolet A (UVA) light (INTERCEPT™ Blood System) was used to prevent nucleic acid replication, transcription, and translation through the formation of covalent adducts and crosslinking of nucleic acids in leukocytes and contaminating pathogens.

Methods: For each experiment, components were spiked with Tp harvested from previously infected New Zealand white (NZW) rabbit testes. A pre-treatment sample

was removed prior to addition of amotosalen to determine the input titer. Post-treatment samples were removed immediately after amotosalen/UVA treatment. NZW rabbits were inoculated with diluted pre-treatment and undiluted post-treatment samples via intratesticular inoculation and monitored for orchitis. Log reduction was calculated as the difference between the mean titer in pre- and post-treatment samples.

Results: Robust inactivation of Tp was achieved to the limit of detection, at >7.0 $\log_{10}$ for PC-100. This corroborates data from previous studies in Plasma (PL) and platelets suspended in PAS (PC-PAS), with inactivation of >5.9 $\log_{10}$ for PL, >6.8 $\log_{10}$ for PC-PAS.

Summary/Conclusions: Tp was inactivated to the limit of detection in PC-100 after treatment with amotosalen/UVA. This data, combined with previous findings, illustrate that the INTERCEPT Blood System may mitigate the risk for syphilis TT in endemic and non-endemic areas.

P-423

PREVALENCE OF SYPHILIS AMONG TURKISH RED CRESCENT BLOOD DONORS, 2013–2017

CM Beker[1], L Hayat[1], E Koşan[2], I Mıstıkı[3], I Karahacıoğlu[4], A Aksoy[4] and F Yılmaz[5]

[1]Aegean Regional Blood Center, Turkish Red Crescent, Izmir [2]Northern Marmara Regional Blood Center, Turkish Red Crescent, Istanbul [3]Middle Anatolian Regional Blood Center [4]General Directorate of Blood Services, Turkish Red Crescent [5]Department of Biochemistry, Yıldırım Beyazıt University, Ankara, Turkey

Background: Laboratory testing of donated blood prior to transfusion is intended to ensure that recipients receive the safest possible blood products. It is mandatory to test donated blood for transfusion-transmitted infections (TTIs) such as hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis in Turkey.

Aims: This study was performed to review the screening and confirmatory test results and examine the seroprevalence rate of syphilis in Turkish Red Crescent (TRC) blood donors from 2013 to 2017. Also, we aimed to contribute the epidemiological data of Turkey with TRC's relatively higher numbers of blood collections.

Methods: From 2013 to 2017, a total of 9,651,637 blood donors at TRC Blood Donation Centers were enrolled in the study. Screening for syphilis was done by using enzyme immunoassay (EIA) Treponema pallidum Total Ab kits. (Enzygnost Syphilis, Siemens, Germany between 2013 and 2015; Diasorin Murex ICE Syphilis, Diasorin, UK between 2015 and 2017). Initially reactive samples were tested in duplicate and repeatedly reactive samples were tested by confirmatory assay: Fluorescent Treponemal Antibody-Absorption IgG (FTA-Abs IgG, Euroimmun, Germany). The statistical data of the five years between 2013 and 2017 was reviewed, retrospectively. Seroprevalence rate was defined as the percentage of seropositive donors.

Results: Between 2013 and 2017, the number of test positives and the seroprevalence rate of syphilis by year was 2,447 (0.155%), 2,394 (0.131%), 3,390 (0.177%), 5,228 (0.251%) and 4,626 (0.205%) respectively. The overall seroprevalence rate was 0.187%, and there was a significant increase in seroprevalence rates, from 0.155% in 2013 to 0.205% in 2017 (P < 0.0001; 95% CI, 0.149–0.162). The number of blood donors found to have confirmed seropositivity by year was 1,165 (0.074%), 985 (0.054%), 1,203 (0.063%), 1,533 (0.073%) and 1,603 (0.071%) respectively. The overall confirmed seropositivity rate was 0.067%, and there was a slight but statistically significant decrease in confirmed seropositivity rates from 0.074% in 2013 to 0.067% in 2017 (P < 0.0001; 95% CI, 0.068–0.075).

Summary/Conclusions: The seroprevalence of syphilis demonstrated an increasing trend by year. There was a slight fluctuation in the seroprevalence rate of syphilis by year, now it tends to increase. According to Department of Communicable Diseases Statistical Data by Turkish Ministry of Health (MoH), the reported number of syphilis cases and incidence rate of syphilis in general population also have been increasing in recent years. So, we thought that increased seroprevalence in blood donors were consistent with the increasing syphilis prevalence and incidence in general population. Although the increasing trend in seroprevalence rates, confirmed seropositivity rates showed a decreasing trend. We evaluated that the discordance between seroprevalence and confirmed seropositivity rates were consistent with higher sensitivity and relatively lower specificity of EIA test we used for syphilis screening. Also, we concluded that continued syphilis screening was still important to maintain blood safety, but a confirmatory test using globally accepted assays to perform further testing on the syphilis-reactive and inconclusive donations was essential to prevent unnecessary waste of blood units and loss of donors.

P-424

TRANSFUSION TRANSMISSIBLE INFECTIOUS DISEASES TRENDS: RESURGENCE OF SYPHILIS, AN OLD FOE

S Butt[1], M Ahmad[2], M Saeed[3], U Waheed[4] and N Rasheed[5]

[1]Blood Bank, District Headquarter Hospital, Mandi Bahauddin, Mandi Bahauddin [2]Blood Bank, Punjab Institute of cardiology, Lahore [3]Microbiology, Government College University, Faisalabad [4]Safe Blood Transfusion Program of Pakistan, Safe Blood Transfusion Program of Pakistan, Islamabad [5]Chemical Pathology, University of Health Sciences, Lahore, Pakistan

Background: Syphilis has plagued humankind for over 500 years, After first reported outbreaks struck Europe in 1495, disease spread quickly to further continents and resulted in a global pandemic. In mid-twentieth century penicillin based treatment became available and infection rates started to decline dramatically. However Strikingly, in last few decades infection with Treponema pallidum is re-emerging. globally >10 million cases are being reported per annum, adults 15–49 years are more prone, almost 90% of this burden is from developing regions. Furthermore, in last eras, syphilis has acquired a new potential for morbidity and mortality through its association with Human Immune deficiency virus (HIV).

Aims: This study was planned to evaluate trends of Transfusion-Transmissible Infectious diseases (TTID) among blood donor community attending blood bank (BB), District Headquarter Hospital, Mandi Bahauddin, Pakistan. So preventive measure may be arranged accordingly.

Methods: This retrospective cross-sectional study was conducted at blood bank, District Headquarter Hospital, Mandi Bahauddin, Pakistan, from 1st January 2012 to 31st December 2016. 79,774 blood donors were enrolled. 04 ml blood (Yellow top - 3 ml & Lavender top 01 ml) was collected from each subject. All samples were tested for Hepatitis B Surface Antigen (HBs Ag), Anti Hepatitis C Virus (Anti-HCV), Anti Human Immunodeficiency Virus (Anti-HIV), malarial parasite and Syphilis by rapid Immunochromatographic (ICT) technique.

Results: Out of 79,774 blood donors, 91% were male and remaining 09% were female with mean age 44 ± 10 years. Only 4.0% of study population was detected positive for any of TTID. A decreasing trend for TTID positivity was seen from 2012 to 2016. Only 0.36% of total TTID positive cases were found co-infected with TTID. Most prevalent co-infection was HBs Ag and Anti-HCV followed by HBs Ag + Syphilis, Anti HCV + Syphilis, Anti HCV + Malarial parasite and HBs Ag + Malarial parasite. Seroprevalence of HBs Ag, Anti HCV, syphilis, Malarial parasite, HIV was 0.9%,1.7%, 1.1%, 0.1% and 0% respectively. The prevalence of HBs Ag and Anti HCV was noticed going downward while increasing trend was seen for malarial parasite and syphilis. Not any case of Anti HIV was found (0%) during this period of study.

Summary/Conclusions: The resurgence of syphilis is an alarming situation. The graph of other TTID is going down which is attributed to hepatitis, malaria, AIDS control and safe blood transfusion programs of the state. But still, sexual education, common public awareness programs, national and international level approaches are hardly needed to stop this emerging threat on initial phases.

P-425

THE ADVANTAGES OF THE VERSATREK® BACTERIAL CULTURE SYSTEM FOR THE DETECTION OF BACTERIAL CONTAMINATION OF PLATELET CONCENTRATES

Y Chetouane[1], P Gallian[2], J Chiaroni[2] and L Camoin[1]

[1]Air-Marseille University, IHU Mediterranean infection, Research Unit on Emerging Infectious and Tropical Diseases [2]Air-Marseille University, French blood establishment, Marseille, France

Background: The risk of bacterial contamination by transfusion of platelet concentrates (PCs) remains the leading cause of transfusion incidents.

Various diagnostic methods to screen for bacterial contamination in PCs exist. These methods must be implemented at as early a stage as possible within the PC production sites, i.e., before the PCs are transferred to the hospitalization units.

No techniques are currently available which satisfactorily meet the requirements of early, sensitive and specific detection.

Aims: The aim of this study is to evaluate the performance of two bacterial culture systems: the TREK Diagnostic Systems (VersaTREK®) and Bactec FX (BD Microbiology).

Methods: Seven bacterial species were tested. Each strain was inoculated into five different PCs at an initial concentration of 100 CFU per bag in aerobic bottles. Two volumes of inoculation, 5 and 10 ml, were systematically tested, in duplicate. Time-to-detection and detection rate between the two methods were compared.

Results: For an inoculation volume of 5 ml, the VersaTREK method has a higher sensitivity than the BACTEC FX method (99% versus 82% of bottles detected, P < 0.05).

In contrast, the detection is 100% for both culture methods when used for an inoculation volume of 10 ml.

The average time-to-detection is significantly different between the two methods, whatever the volume tested.

Summary/Conclusions: The VersaTREK bacterial culture method is more sensitive for detecting PC contamination with low inoculation volumes. It could, therefore, be proposed for the detection of PC contamination.

P-426

Abstract has been withdrawn

P-427

INVESTIGATION OF SEPTIC REACTIONS IN TWO PEDIATRIC PATIENTS INVOLVING A DOUBLE APHERESIS PLATELET UNIT CONTAMINATED WITH STAPHYLOCOCCUS AUREUS

S Ramirez-Arcos[1], M Zeller[2], M Fearon[3], J Karlowsky[4], D Alexander[5] and D Lane[6]

[1]Canadian Blood Services, Ottawa [2]Canadian Blood Services, Vancouver [3]Canadian Blood Services, Toronto [4]Diagnostic Services Manitoba [5]Cadham Provincial Laboratory [6]Canadian Blood Services, Manitoba, Canada

Background: Contamination of platelet concentrates (PCs) with Staphylococcus aureus is one of the most significant ongoing transfusion safety risks in developed countries. In the present case, two pediatric patients were transfused each with one of the splits of a 4-day-old double apheresis platelet unit. The transfusions were stopped when the patients developed septic symptoms and both patients were successfully treated with antimicrobial therapy. The hospital clinical microbiology laboratory isolated Staphylococcus aureus from the patients' blood cultures and from both platelet split units. Skin and nasal swabs were obtained from the donor and S. aureus was isolated from the nasal sample. Microbiological and molecular characterizations of the S. aureus isolates were carried out at the microbiology laboratory of Canadian Blood Services, at the Winnipeg Health Sciences Centre clinical microbiology laboratory (Diagnostic Services Manitoba), and at the Cadham Provincial Laboratory, with results presented in this report. The implicated platelet unit had been screened for bacterial contamination with the BacT/ALERT culture system yielding a negative result.

Aims: Characterize S. aureus isolate implicated in a septic transfusion reaction.

Methods: Bacterial concentrations were determined using 10-fold serial dilutions of residual platelets remaining in both split units and plating onto blood agar. The identity and relatedness of the S. aureus isolates cultured from both platelet split units and the blood of the two patients were confirmed using microbiological methods including Gram stain, biochemical identification with API Staph strips, and antimicrobial susceptibility testing of six antibiotics using Etest strips. Molecular relatedness of the isolates cultured from platelet units and patients' blood samples were assessed by PCR fingerprinting of the S. aureus Protein A gene and pulsed-field-gel-electrophoresis (PFGE). Whole genome sequencing was also performed on the isolates from the platelet units, the patients' blood samples, and on the donor's nasal isolate.

Results: Bacterial concentrations in the platelet units were estimated to be between 10^7 and 10^8 colony forming units (CFU)/ml. The four isolates cultured from the platelet units (two isolates) and the patients' blood (two isolates) were identified as S. aureus by biochemical testing and demonstrated identical antimicrobial susceptibility profiles. PCR fingerprinting of the four isolates showed identical band patterns for repeats of the Protein A gene and molecular relatedness was confirmed by PFGE. Whole genome sequencing analyses demonstrated that the isolates from the platelet units and the patients were identical while the donor isolate had only 7 high-quality single nucleotide variants and is therefore considered to be a match with the other isolates. Genome analyses also revealed that this strain of S. aureus is spa type t012 and belongs to the MLST Clonal Cluster 30.

Summary/Conclusions: The results presented herein confirm that the transfused platelet units were the cause of the septic transfusion events described in this case and that platelet screening for bacterial contamination yielded false-negative results. This report also highlights the importance of donor follow up to identify the source of platelet contamination.

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Abstract has been withdrawn

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COMPARISON OF INITIAL POSITIVE RATES OF BACTERIAL SURVEILLANCE TEST OF PLATELET CONCENTRATES CULTURED FOR 48 HOURS AND EXTENDED HOURS UNTIL EXPIRY

L Tang, N Chan, R Lo, C Chan and W Tsoi

Laboratory Department, Hong Kong Red Cross Blood Transfusion Service, Hong Kong, China

Background: The Hong Kong Red Cross Blood Transfusion Service has implemented short-term culture of pre-release platelet concentrates (PCs) for bacterial surveillance test (BST) to minimize the risk of platelet transfusion-associated sepsis since 1998. PCs with negative results after 24 h of bacterial culture were released for transfusion while the culture bottles are continuously monitored for another further 24 h. If a positive signal was detected, the PCs and the associated components would be recalled for further investigation. Since the end of 2016, there has been a BST protocol change in that the total bacterial culture time was extended till expiry of PCs (i.e. 5 days).

Aims: To conduct a retrospective analysis to compare the initial BST positive rates of PCs found in bacterial culture for 48 h and extended time until expiry of PCs.

Methods: Routine pre-release bacterial surveillance of PCs by BacT/ALERT 3D automated blood culture system (bioMérieux, Durham, NC, USA) has been implemented since 1998 (Liu HW, et al. Vox Sang 1999;77:1–5). Sampling of individual PC was undertaken at 36–48 h after donation and pooled from a maximum of 5 platelet samples for bacterial culture. Initial positivity in the pooled sample would be subject to resolution by repeat bacterial culture of samples taken from individual PC and/or other blood components of the implicated initial positive donations. Bacteria isolated from confirmed positive samples would be subject to bacterial identification. For the purpose of this study, bacterial culture results of PCs during the period from 23 December 2016 to 31 December 2017 were retrieved from database. The initial positive rates of BST cultured for 48 h and until expiry of PCs were computed and statistically compared by z-test. A p-value <0.05 was considered as statistically significant.

Results: Of 173,335 units of PCs cultured, the initial BST positive rates cultured for 48 h and until PC expiry were 0.033% (57 pooled samples) and 0.036% (63 pooled samples) respectively (P = 0.58). The 6 initial positivities detected after cultured for 48 h could not be confirmed and were considered as false positive results. The PCs associated with these 6 initial positive results had been transfused and the attending physicians were informed of the results. No transfusion transmitted sepsis was reported. Of 57 initial reactive pooled samples, 11 were confirmed positive. The average time to the initial positive signals was 15.4 h (Median: 16.3; SD = 7.94, Range: 4.6–27.4).

Summary/Conclusions: There were no statistical differences between the BST initial positive rates of PCs cultured for 48 h and extended time until PC expiry. Our study provided evidence that the majority of initial positivity (90.5%) and all confirmed positive cases were detected within 48 h of bacterial culture and no true positive cases were found after 48 h. Extension of bacterial culture did not pick up additional true positive PCs and based on these data, it was then not cost-effective to perform pre-release BST for >48 h. More data will be collected to confirm such findings in due time.

P-431

ANTIMICROBIAL PEPTIDES: AN EFFECTIVE APPROACH TO PREVENT BIOFILM FORMATION BY STAPHYLOCOCCUS EPIDERMIDIS IN PLATELET CONCENTRATES

M Alabdullatif[1], C Atreya[2] and S Ramirez-Arcos[1]

[1]Canadian Blood Services, Ottawa, Canada [2]Food and Drug Administration, Silver Spring, United States

Background: The safety of platelet concentrates (PCs) is a major concern in transfusion medicine due to contamination mainly with skin Gram-positive bacteria. The predominant contaminant Staphylococcus epidermidis forms cell aggregates (biofilms) in PCs, posing a high safety risk for transfusion recipients. Bacterial biofilms display higher resistance to immune clearance and antimicrobial susceptibility than its non-biofilm (free-floating cell) counterparts. Combinations of synthetic antimicrobial peptides (AMPs) have demonstrated bactericidal activity against free-floating bacterial cells in PCs. It is therefore important to investigate whether AMPs also display bactericidal activity against biofilm-embedded cells.

Aims: This study aimed to evaluate the ability of a combination of synthetic AMPs to inhibit biofilm formation and/or eliminate mature S. epidermidis biofilms.

Methods: Three synthetic AMPs, the platelet-derived peptide (PD4) and two Arginine-Tryptophan repeats (RW3 and RW4) were used for bactericidal and anti-biofilm experiments in glucose-supplemented trypticase soy broth (TSBg) and PCs spiked with three different strains of S. epidermidis. Time-killing assays were performed to evaluate the bactericidal capability of the peptides against free-floating cells. Inhibition of biofilm formation was assayed by seeding the wells of 6-well plates with approximately 10^4 colony forming units (CFU)/ml of S. epidermidis into cultures containing TSBg or PCs supplemented with 10 μM of the AMP combination or PBS (negative control). Biofilm eradication assays were performed following treatment of pre-formed (mature) S. epidermidis biofilms with 10 μM of AMPs, with or without mechanical dislodging. For mechanical dislodging, AMP-treated biofilms were subjected to either scrapping alone or to scrapping followed by pipetting and vortexing. Inhibition of biofilm formation and eradication of pre-formed biofilms were measured using a semi-quantitative crystal violet assay and viable cell enumeration. All assays were performed three independent times with two replicates per repetition. Statistical analyses were performed to determine differences in bacterial viable counts. P values less than 0.05 were considered statistically significant.

Results: Viability of AMP-treated free-floating S. epidermidis cells was gradually decreased reaching a 4-$\log_{10}$ reduction after 120 min of treatment with complete elimination after 24 h, while negative controls grew to concentrations >10^7 CFU/ml. AMP treatment of preformed un-dislodged S. epidermidis biofilms did not have a bactericidal effect. However, when mature biofilms were dislodged by scrapping, their viability decreased by approximately 1 $\log_{10}$ in TSBg with no effect on PCs. When scrapped biofilms were homogenized by pipetting and vortexing, AMP treatment was significantly efficient (p < 0.05) in reducing bacterial concentrations by approximately 2.5 $\log_{10}$ in biofilm cells grown in TSBg and by approximately 1.5 $\log_{10}$ in biofilm cells grown in PCs.

Summary/Conclusions: The results presented herein provide promising evidence for the use of synthetic AMPs to prevent S. epidermidis biofilm formation in PCs, which would enhance the safety of transfusion recipients. Further investigation is warranted to overcome AMP resistance of mature biofilms, which is likely due to the barrier posed by the biofilm matrix and biochemical modifications of the cell wall of biofilm-embedded cells.

P-432

EFFECT OF AIR ENTRY DURING INOCULATION OF ANAEROBIC CULTURE BOTTLES USED FOR BACTERIAL TESTING OF PLATELET CONCENTRATES

D Kumaran[1] and S Ramirez-Arcos[1]

[1]Canadian Blood Services, Ottawa, Canada

Background: Since 2004, Canadian Blood Services have used aerobic culture bottles exclusively with the BacT/ALERT 3D system to screen platelet concentrates (PCs) for bacterial contamination. Screening procedures were modified to include anaerobic culture bottles with the extension of platelet shelf-life from 5 to 7 days in August of 2017. The tubing of platelet sampling devices contains approximately 0.5 ml (apheresis PC units) and 1 ml (buffy coat PC pools) of trapped air which precedes PC flow during sampling. The effect of potential air entry into anaerobic culture bottles during PC sampling on bacterial detection is unknown.

Aims: Determine the effect of air entry during inoculation of PC samples into culture bottles on detection of anaerobic bacteria by the BacT/ALERT system.

Methods: Suspensions of Pseudomonas aeruginosa (aerobe) and Bacteroides fragilis (anaerobe) were prepared in trypticase soy broth (TSB) or PCs with a target concentration of approximately 120 colony forming units (CFU)/bottle (N = 3). The assay was repeated with the anaerobes B. fragilis and Propionibacterium acnes in PCs only at a target concentration of approximately 8 CFU/bottle (N = 3). Eight ml of the bacterial suspensions prepared in TSB or PCs were inoculated into aerobic (BPA) and anaerobic (BPN) BacT/ALERT culture bottles to which no air (control), 1 ml, or 3 ml of air was added during sample inoculation. Culture bottles were incubated in the BacT/ALERT system as per standard procedures at Canadian Blood Services.

Results: B. fragilis prepared in TSB or PCs, inoculated at ~120 CFU/ bottle, were detected only in BPN bottles in all three air conditions tested. Inoculation of 0, 1, or 3 ml of air into the bottles resulted in detection times of 38 ± 14, 71 ± 14 and 104 ± 6 h (TSB), and 44 ± 7, 45 ± 4 and 59 ± 10 h (PCs), respectively. A similar trend was observed at lower concentrations (~8 CFU/bottle) of B. fragilis prepared in PCs, with detection only in BPN bottles at times of 52 ± 8, 65 ± 14, and 69 ± 8 h when 0, 1, or 3 ml of air was added into the bottles, respectively. P. acnes PC suspensions inoculated at ~8 CFU/bottle were detected at similar times when either 1 ml (102 ± 9 h) or 3 ml (101 ± 4 h) of air was present in BPN bottles, which was slightly longer compared to the detection time of 97 ± 9 hobserved when no air was added. No difference in detection of P. aeruginosa was observed with the presence of air in BPA bottles. While TSB suspensions of P. aeruginosa were detected in BPN bottles when air was added, P. aeruginosa was not detected in BPN bottles inoculated with PC suspensions even with addition or air.

Summary/Conclusions: This study demonstrated that air entry in BPN bottles does not impair growth of the anaerobes B. fragilis and P. acnes. However, air entry during anaerobic bottle inoculation should be avoided since it could result in delayed detection of anaerobic bacteria, resulting in the inadvertent release of contaminated products for transfusion. Differences in times of bacterial detection between TSB and PCs suggest competition for air consumption between platelets and bacteria, an interesting observation that merits further investigation.

P-433

RED BLOOD CELL TRANSFUSION RELEVANT BACTERIAL REFERENCE STRAINS – PRESELECTION OF DIFFERENT CANDIDATE STRAINS

M Prax[1], A Schneider, M Anders-Maurer, I Bekeredjian-Ding and O Krut

Paul-Ehrlich-Institut, Langen, Germany

Background: Bacterial transmission by Red Blood Cell (RBC) concentrates still remains a persistent problem corroborated by anecdotal reports on fatal transfusion reactions. A general application of Blood Bacteria Reference Strains (BBRS) could help to reduce the risk in the future. BBRS allow an objective validation and assessment of various microbiological methods and the development of new techniques in a standardized manner. However, already existing reference strains for platelets fail due to the mandatory cold storage conditions of RBC. As a result, the ISBT Working Party on Transfusion-Transmitted Infectious Diseases Subgroup Bacteria is conducting a collaborative study on the establishment of RBC Transfusion Relevant Bacteria Reference strains.

Aims: Identification and characterization of promising bacterial candidate strains to assess their eligibility for the subsequent study with international partners.

Methods: 32 bacterial isolates, the majority of these from actual transfusion incidents involving RBC concentrates, were collected worldwide. The identity of the strains was verified and bacterial suspensions with a known concentration were produced. Low-count spiking experiments (10–25 colony forming units (CFU)/bag) of RBC concentrates from three different donors were performed for each strain. The growth was monitored under routine storage conditions at 4°C without agitation by determination of CFUs over time. Bags showing no growth at the end of the testing period were incubated at 37°C subsequently. In addition, long-term viability of the strains was measured by CFU counting to ensure storage stability.

Results: Six of the strains tested demonstrated consistent growth in RBC. Few strains did not proliferate but survived within RBC which was detected after incubation of the bags at 37°C. The remaining candidates did not show growth at all. The successful candidates Listeria monocytogenes, Serratia marcescens, Serratia liquefaciens, Pseudomonas fluorescens, Yersinia enterocolitica (I) and Yersinia enterocolitica (II) represent bacteria with mainly facultative meso- and psychrophilic growth properties. The individual growth kinetics revealed a growth to counts in excess of 1×10^7 CFU/ml (P. fluorescens) by day 14 of storage starting from an initial inoculum of approximately 0.03 CFU/ml. After the initial selection process, stability studies have been performed. The candidate strains have been shown to date to be very stable under storage conditions of −80°C.

Summary/Conclusions: Reliable growth at cold storage conditions independent of donor variability was observed only for small proportion of the tested candidate strains. The outcome of this study clearly demonstrates the necessity for well characterized bacterial reference strains providing robust and consistent results. In a next step, these strains will be challenged in an international study to prove their validity.

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Abstract has been withdrawn

Parasites

P-435

INACTIVATION OF TRYPANOSOMA CRUZI WITH AMOTOSALEN/UVA IN PLATELET COMPONENTS AND APHERESIS PLASMA

A Laughhunn[1], F Buckner[2], R Gillespie[2], P Bringmann[1] and A Stassinopoulos[3]

[1]Microbiology and Bioanalytical R & D, Cerus Corporation, Concord [2]Division of Allergy and Infectious Diseases, University of Washington, Seattle, WA [3]Global Scientific Affairs and Research, Cerus Corporation, Concord, United States

Background: Trypanosoma cruzi (Tc), the causative agent of Chagas disease, is a hemoflagellate parasite that can be transmitted to people by triatomine insect vectors. While "kissing bugs" are found throughout the Americas, they are most prevalent in Latin America. The WHO estimates that roughly 8 million people have Chagas disease, with 70–80% experiencing lifelong asymptomatic chronic indeterminate infection. The potential for transfusion transmission (TT) through blood components from parasitemic donors is a threat to the blood supply. The transmission of Tc by blood transfusion occurs frequently in endemic areas with estimates of roughly 10,000–20,000 TT in Brazil alone in the late 1990s and up to 800 TT cases documented in the past decade. While endemic in Latin America, Tc-TT by platelets has also been documented in the United States, Canada & Spain (Benjamin et al. 2012); A bone marrow transplant recipient contracted Chagas disease in Los Angeles leading to his death. Tc has the capability of surviving at room temperature in platelets, as well as in freeze/thawed plasma and cryoprecipitate, highlighting the need for mitigation strategies. A photochemical treatment process utilizing amotosalen and low energy ultraviolet A (UVA) light, developed to inactivate pathogens and residual leukocytes is in routine use globally for the preparation of Plasma (PLS), and PC manufactured either in 65% platelets additive solution (PAS-PC) or in 100% plasma (PC-100).

Aims: The objective of this study was to evaluate the inactivation of Trypanosoma cruzi (T. cruzi) in plasma and platelet components to mitigate transfusion transmission.

Methods: Tc was propagated to high titer in NIH-3T3 cells, harvested, quantified and spiked into either PLS, PAS-PC or PC-100 components to a final concentration of $\sim 10^7$ trypomastigotes/ml. Tc-contaminated PCs and PLS were dosed with amotosalen and a control sample (pre-illumination) was removed to determine the pre-UVA treatment parasite titer. The control sample was serially diluted to 10^{-7} and appropriate dilutions were inoculated in quintuplicate onto NIH-3T3 cell monolayers to determine pre-illumination 50% Tissue Culture Infective Dose ($TCID_{50}$). Each unit was then illuminated and a post-treatment sample was withdrawn. Test samples were diluted 1:3 for PLS and 1:5 for PC and inoculated onto NIH-3T3 cells. Cultures were monitored for trypomastigote viability, indicated by motility, and scored positive or negative for survival and replication over a 3–4 week period. For the post-treatment samples, no viable trypomastigotes were observed in any treated component. Tc inactivation was calculated as the difference between the log_{10} values of mean $TCID_{50}$ in pre-UVA samples and post-UVA samples. The limit of detection (LOD) was defined for the total volume plated, resulting in a LOD of <0.0 and <0.1 for PLS and PC, respectively.

Results: Robust inactivation of Tc in all components was achieved to the LOD, at >6.6 log_{10} for PLS (n = 8), >7.8 log_{10} for PAS-PC (n = 8), and >8.4 log_{10} for PC-100 (n = 8).

Summary/Conclusions: Photochemical treatment with amotosalen and UVA of PAS-PC, PC100 and PLS resulted in inactivation of Tc to the LOD in all components, indicating this approach could successfully mitigate Tc-TT in transfusable PC and plasma components.

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NUCLEIC ACID TARGETED TECHNOLOGIES INACTIVATE HIGH LEVELS OF PLASMODIUM FALCIPARUM IN ALL BLOOD COMPONENTS

A Laughhunn[1], C Sow[2], P Grellier[2], C Lobo[3], M Lanteri[4], P Bringmann[1] and A Stassinopoulos[5]

[1]Microbiology and Bioanalytical R & D, Cerus Corporation, Concord, CA, United States [2]Muséum National d'Histoire Naturelle, Paris, France [3]New York Blood Center, New York [4]Scientific Affairs, Cerus Corporation, Concord, CA, United States [5]Global Scientific Affairs and Research, Cerus Corporation, Concord, CA, United States

Background: The intra-erythrocytic protozoan parasite, Plasmodium falciparum (Pf), is accountable for nearly all malaria mortality in Africa and in 87 endemic tropical countries. In 2015, WHO reported ~212 million new malaria cases worldwide, resulting in >400,000 deaths. Malaria is a major cause of morbidity and mortality globally but prevalence is the highest in sub-Saharan Africa, where 90% of all infections and 92% of the mortality occur. More than 30 species of Anopheles mosquitoes serve as vectors for the disease on all continents except in Antarctica. Due to global warming, malaria transmitting vectors have been spreading to new areas and the risk of malaria transfusion -transmission (TT) in developed countries is significant due to an increase in global travel to malaria endemic regions. With an asymptomatic period lasting 7–30 days and delayed symptom appearance for weeks to months in travelers taking antimalarial drugs, mitigation strategies based on the deferral of symptomatic donors are not optimal.

The objective of this study was to evaluate the inactivation of Pf in blood components using nucleic acid targeted technology to provide a comprehensive approach to mitigate Pf TT. For red blood cells in additive solution (AS-RBC), a chemical treatment utilizing amustaline and glutathione (GSH) was used. For treatment of plasma (PLS) and platelets resuspended in PAS (PC-PAS) or 100% plasma (PC-100), a nucleic acid targeted photochemical treatment utilizing amotosalen and low energy ultraviolet A (UVA) light was used. In both cases, the treatments result in adducts and crosslinks in the nucleic acids (NA) of pathogens and leukocytes present, that inhibit replication, transcription, and translation of the NA and result in their inactivation.

Aims: To evaluate the inactivation of Pf in blood components using nucleic acid targeted technology to provide a comprehensive approach to mitigate Pf TT.

Methods: For each experiment, blood components were spiked with ring-stage Pf-infected RBC (iRBC). A pre-treatment sample was removed prior to addition of amustaline or amotosalen to determine the input titer. Post-treatment samples were removed 3 h post-treatment for AS-RBC or immediately after amotosalen/UVA treatment for platelets/plasma. All samples were serially diluted in flasks containing medium with 5% fresh RBCs. The diluted samples were used to inoculate flasks or plates and monitored for parasitemia by counting iRBC in blood smears and/or by flow cytometry. Log reduction was calculated as the difference between the mean titer in pre- and post-treatment samples.

Results: Robust inactivation of Pf was achieved to the limit of detection, at >6.9 log_{10} for PLS (n = 4), >8.1 log_{10} for PC-PAS (n = 8) and >8.2 log_{10} for PC-plasma (n = 8), and >8.7 log_{10} for AS-RBC (n = 4).

Summary/Conclusions: Pf was inactivated to the limit of detection in all blood components after nucleic acid targeted treatment of plasma and platelets with amotosalen/UVA and treatment of RBC with amustaline/GSH, demonstrating that INTERCEPT Blood Systems provide an approach to mitigate the risk for Pf TT in endemic and non-endemic areas where components are collected and transfused.

(The amustaline/GSH system for RBC is not approved for use).

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DYNAMICS OF ANTI-T. CRUZI ANTIBODY DETECTION IN A BLOOD BANK SURROUNDED BY ENDEMIC REGIONS: A 13-YEARS ANALYSIS

DM Baquero and A Rodriguez

National Blood Bank, Colombian Red Cross, Bogota D.C, Colombia

Background: Chagas disease, an infection caused by Trypanosoma Cruzi, is endemic in several regions in Colombia. Apart from vector-borne transmission, transfusion related cases have also been documented. Since 1980, the capital city has experienced substantial migrations from the countryside, in part due to the internal social conflict. Serologic screening of blood donors for T. Cruzi antibodies is mandatory since 1993 in our country. Several strategies to prevent at-risk donors to give blood have been implemented over time, but their impact has not yet been assessed.

Aims: This study aimed to calculate and compare the detection rates of anti-T cruzi confirmed positive donors over the last 13 years, at a blood bank placed in the capital city.

Methods: Results of screening and confirmatory tests for T. cruzi were retrospectively reviewed for all blood donations from January 2005 to December 2017 and grouped by year of detection and donor age, as follows: 18–29 years, 30–39, 40–49, 50–59 and 60 - > 65 years. Despite the use of various ELISA-based assays for donor screening during the 13 years, all repeat-reactive samples from 2005 to 2012 were confirmed by Indirect Immunofluorescence. From 2012 to 2017 a supplemental two-step testing algorithm was introduced for confirmation of repeat reactive samples. This algorithm included a second screening test with a different method and a T. cruzi Immunoblot in case of a negative result. A chi square test was used to compare proportions.

Results: In total 312.222 donations were tested during the time frame analysed. There were 356 samples confirmed to be positive (0.11%). The proportion of confirmed cases significantly decreased from 0.26% in 2005 to 0.06% (P < 0.0001) in 2017, although there was not a consistent reduction year by year. However, a negative trendline was clearly detected. Rates of confirmed cases were 0.2, 0.09 and 0.1% during the following periods respectively: 2005–2007, 2008–2010 and 2011–2013. The rate during the last four year was 0.06%. The largest proportion of cases was detected in the 40–49 age group (31.8%), followed by the 50–59 age group (29.0%).

Summary/Conclusions: Despite continuous migrations to the capital city from endemic areas, we found sustained low rates of confirmed infections during the last 6 years. This could be explained by several factors: improvements in vector control in endemic areas, impact of the education materials and the introduction of specific questions in donor questionnaires. More strategies to prevent at-risk donors to give blood should be focus on the population older than 40 years of age.

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Abstract has been withdrawn

Newly Emerging Pathogens and Other Transfusion Related Pathogens

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HOST–DERIVED COAGULATION FACTORS ON THE VIRUS SURFACE

E Pryzdial[1,2,3], H Lin[2,3], M Sutherland[1,2,3] and J Morrissey[4]

[1]Centre for Innovation, Canadian Blood Services [2]Centre for Blood Research [3]Department of Pathology and Laboratory Medicine, University Of British Columbia, Vancouver, Canada [4]Departments of Biological Chemistry & Internal Medicine, University of Michigan Medical School, Ann Arbor, United States

Background: The function of plasma clotting factors is known to be modulated by numerous virus types. To explain this link, we have shown that the envelope of three herpesviruses acquire the cellular initiators of coagulation from the host, tissue factor (TF) and anionic phospholipids (aPL). Viral TF and aPL act as cofactors for clotting factor VIIa (FVIIa)-mediated factor X (FX) activation, leading to clot formation and cell signaling. Using herpes simplex virus 1 (HSV1) as a model envelope virus, virus TF was previously shown to enhance infection. HSV1 encoded glycoprotein C (gC) has also been implicated in FX activation.

Aims: The aims of the current research are to: 1) dissect the role of gC on HSV1-mediated FX activation; and 2) investigate the ubiquity of viral TF and aPL on blood-borne enveloped viruses.

Methods: TF⁺/TF⁻ HSV1 variants and dengue virus (DENV) propagated in cell culture were purified and characterized. The FX activating roles of viral TF and a soluble form of gC were assessed by chromogenic and plasma clotting assays. Protein binding experiments were performed using microscale thermophoresis and enzyme kinetic assays. Immunogold electron microscopy was used to simultaneously visualize TF, aPL, and a virus-encoded marker on the virus surface.

Results: In plasma, HSV1 and DENV induced TF-mediated clotting. Viral TF was required for optimal FX activation by HSV1. The presence of gC on viruses could further enhance FX activation and plasma clotting. Furthermore, the virus-derived

gC can replace TF cofactor function in purified chromogenic systems with preliminary evidence suggesting direct binding to FVIIa. Both TF and aPL were incorporated into HSV1 and DENV particles.

Summary/Conclusions: Virus surface TF function is enhanced by gC and contributes to FX activation and clot formation. In purified systems, gC mimicked TF function. Identification of TF on both HSV1 and DENV demonstrates the viral acquisition of host constituents and suggests the ubiquity of TF on enveloped viruses. Combined with the prior observation that virus TF enhances infection, the data presented here may support targeting viral TF as a broad-spectrum anti-viral agent.

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INACTIVATION OF YELLOW FEVER VIRUS IN PLASMA AND IN PLATELET CONCENTRATES FOLLOWING TREATMENT WITH THE THERAFLEX PATHOGEN INACTIVATION (PI) TECHNOLOGIES

D Marks[1], J Fryk[2], R Hall[3], P Young[3], S Reichenberg[4], F Tolksdorf[4], C Sumian[5], U Gravemann[6], A Seltsam[6] and H Faddy[2]

[1]Research and Development, Australian Red Cross Blood Service, Sydney [2]Research and Development, Australian Red Cross Blood Service [3]School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, Australia [4]MacoPharma International GmbH, Langen, Germany [5]MacoPharma, Tourcoing, France [6]German Red Cross Blood Service NSTOB, Springe, Germany

Background: Yellow fever virus (YFV) is endemic to tropical and subtropical areas in South America and Africa, and is currently a major public health threat in Brazil. Although a live, attenuated vaccine is available, for some individuals residing in endemic areas and for many travellers to countries endemic for YFV, affected areas still experience significant morbidity and mortality. Most YFV infections are asymptomatic, but when symptoms occur, they can include fever, muscle pain with prominent backache, headache, loss of appetite, and nausea or vomiting. Transfusion-transmission of the yellow fever vaccine virus has been demonstrated, indicative of potential for viral transfusion-transmission. The Australian Red Cross Blood Service (Blood Service) restricts donations from individuals who have been vaccinated against YFV for four weeks post vaccination and from individuals diagnosed with YFV infection for three months post-complete recovery. An alternative approach to manage the potential YFV transfusion-transmission risk is the use of pathogen inactivation (PI) systems, such as THERAFLEX MB-Plasma and THERAFLEX UV-Platelets.

Aims: To investigate the efficacy of the THERAFLEX MB-Plasma and THERAFLEX UV-Platelets systems to inactivate YFV spiked into plasma or buffy coat-derived platelet concentrates (PCs).

Methods: YFV was spiked into plasma or PCs units (n = 3 per blood component). Spiked plasma units were treated using THERAFLEX MB-Plasma system (visible light doses: 20, 40, 60 and 120 (standard) J/cm²) in the presence of methylene blue (MB; approximately 0.8 μmol/l). Spiked PCs were treated using THERAFLEX UV-Platelets system (UVC doses: 0.05, 0.10, 0.15 and 0.20 (standard) J/cm²). Samples were taken prior to the first and after each illumination dose and tested for residual virus using a modified plaque assay (normal and large-volume plating methods). For each PI system the level of viral reduction was determined.

Results: Treatment of plasma with THERAFLEX MB-Plasma system resulted in an average of 4.77 $\log_{10}$ reduction in YFV infectivity at the standard visible light dose. Residual viral infectivity reached the detection limit of the assay at 40 J/cm². Similarly, for PCs treated with THERAFLEX UV-Platelets system, an average of 4.8 $\log_{10}$ reduction in YFV infectivity was observed at the standard UVC dose, with residual viral infectivity at the limit of detection of the assay at 0.10 J/cm².

Summary/Conclusions: Our study suggests the THERAFLEX MB-Plasma and the THERAFLEX UV-Platelets systems can efficiently inactivate YFV in plasma or PCs. The observed reduction in viral infectivity after treatment with these PI systems was similar to that for other arboviruses, including dengue, chikungunya, Zika and West Nile viruses. Studies examining the threshold concentration to elicit disease are needed in order to determine whether the level of reduction in viral infectivity by these PI systems in plasma and PCs is sufficient to prevent transfusion-transmission. Nonetheless, given the reduction levels observed in this study, these PI systems could be an effective option for managing YFV transfusion-transmission risk in plasma and PCs.

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IS PARVOVIRUS B19 A CONCERN FOR BLOOD SAFETY IN AUSTRALIA?

C Styles[1], E Gorman[2], V Hoad[1], E Roulis[2], R Flower[2], C Seed[1] and H Faddy[2]

[1]Donor and product Safety Unit, Australian Red Cross Blood Service, Perth [2]Research and Development, Australian Red Cross Blood Service, Brisbane, Australia

Background: Parvovirus B19 (B19V) is a globally ubiquitous DNA virus. Infection results in a variety of clinical presentations including erythema infectiosum in children and arthralgia in adults. Asymptomatic infection is possible. Transmission is usually through the respiratory route, however, vertical transmission and transmission through solid organ or haematopoietic transplantation has been documented. Transmission through plasma-derived products and liable fresh components can occur. In Australia, a small number of B19V infections have been investigated and attributed to probable transfusion-transmission (TT).

Aims: To measure the current seroprevalence of B19V IgG in Australian blood donors, estimate the likelihood of collecting a B19V viraemic donation from whole blood donors in Australia, and assess whether this virus poses a current TT risk in Australia.

Methods: Age/sex/region stratified plasma samples (n = 2,241) were collected from whole blood donors in Australian states and territories, and screened for B19V IgG using indirect-based enzyme-linked immunosorbent assay. A separate cohort of samples from whole blood donors (n = 4,232), stratified by blood donation processing state, were tested for B19V DNA by PCR, with confirmatory testing performed externally. The viral load was determined in B19V DNA confirmed positive samples. Prevalence data were used to model the B19V TT risk.

Results: B19V IgG was detected in 61% (95% CI: 59–63%) of donors. Increased donor age was associated (P < 0.001) with B19V IgG seroprevalence, and there was no difference in B19V seropositivity between the sexes (P = 0.5456). Samples from 12 donors were B19V DNA initially reactive, 10 of which were confirmed (0.24%; 95% CI: 0.09–0.38%). Samples reactive for B19V DNA were distributed equally between sexes and processing centres. Viral loads ranged from 1.90 to 6.25 log IU/ml, with two samples having a viral load above the theoretical infectious dose of 10^5 IU/ml, giving a potential infectious donation rate of 1 in 2,116 (0.047%, 95% CI 0.013% to 0.172%). A risk assessment modelled the overall predicted number of TT B19V cases with significant complications at 3.1 per year, with an associated risk per component of approximately 1 in 300,000. For all transfused groups, the risk from community exposure was much higher and contributed the majority of the overall risk. Adult and paediatric recipients would have to receive in excess of 17 or 55 components, respectively, to equal the risk of infection from one year of community exposure.

Summary/Conclusions: This study demonstrates, as expected, a clear association between B19V seroprevalence and increasing age, with over half of donors tested having B19V IgG antibodies. We detected B19V DNA in blood donors at a similar rate to other developed countries. The modelled B19V TT risk for general recipients was negligible and a minor route of infection compared to community exposure. This information will inform the development of an optimal risk management strategy for managing TT B19V in Australia based on stakeholder feedback.

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WEST NILE VIRUS DONOR SURVEILLANCE IN HUNGARY – A PILOT STUDY

É Barabás[1], T Szöllősi[1], M Takács[2] and A Nagy[2]

[1]Confirmatory Laboratory, Hungarian National Blood Transfusion Service (HNBTS) [2]Division of Virology, National Public Health Institute (NPHI), Budapest, Hungary

Background: West Nile virus (WNV), a worldwide distributed member of the genus flavivirus is responsible for numerous human and animal infections in Europe. The severity of its clinical manifestations varies widely from the milder form of West Nile fever to West Nile neuroinvasive disease. The main transmission route is via the bite of infected mosquitoes, however, infections related to blood transfusion and organ transplantation have been also described. The WNV is one of the most important viral zoonotic infections in Hungary, as the biggest part of the country is affected and the figures of clinical cases have been increasing since 2004. However, similarly to the most European countries, the seasonal WNV screening of whole blood donors has not been implemented yet.

Aims: The aim of our study was to assess the WNV RNA reactivity and the seroprevalence of anti-WNV IgG antibodies in the samples of whole blood donors collected from the territories with active virus circulation in Hungary.

Methods: Based on the confirmed clinical WNV cases reported by the NPHI in 2016, EDTA samples of 2112 donors were collected from the affected areas. We performed cobas TaqScreen WNV test (WNV PCR, Roche Diagnostics) and determined anti-WNV IgG antibodies with an in-house developed indirect-immunofluorescence assay (WNV IIF). After the IIF screening, positive and indeterminate samples were tested with an in-house TBEV assay to exclude the cross-reactivity with the tick-borne encephalitis virus (TBEV), another human pathogenic flavivirus endemic in Hungary. IIF results were confirmed by haemagglutination-inhibition (HI) assay. HI tests were conducted using anti-WNV and anti-TBEV antibodies parallelly. The confirmed WNV seropositive samples were also tested for the presence of anti-WNV IgM antibodies using the WNV IIF assay and a commercial WNV IgM Capture ELISA of Focus Diagnostics.

Results: None of the samples showed reactivity in the WNV PCR. The WNV IgG IIF screening resulted in 522 reactive samples. In the HI tests, 55 donors (2.6% CI: 1.9% – 3.3%) were found to be positive for anti-WNV IgG antibodies. In additional 13 samples, the anti-WNV and anti-TBEV IgG IIF showed similar titers. In the anti-WNV IgM antibody determination 3 samples showed reactivity in both in-house IIF and ELISA tests suggesting acute or recent WNV infections. 276 donors indicated reactivity to anti-TBEV IgG from the 522 reactive sera.

Summary/Conclusions: The WNV donor screening is not mandatory at the HNBTS and no transfusion transmitted WNV infections have been confirmed so far. The most of the WNV clinical cases (44) were reported in the year of 2016. As a result, both 30-day deferral of whole blood donors spent at least 24 h in the WNV exposed areas and the exclusion of the WNV affected Hungarian territories from blood donation were enforced by the HNBTS. However, these regulations should be reconsidered to ensure both recipient safety and the stable blood stock level in Hungary.

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AN EMERGING VIRUS IN A NEW GEOGRAPHIC AREA – SEROLOGICAL EVIDENCE OF THE CRIMEAN–CONGO HAEMORRHAGIC FEVER VIRUS AMONG HUNGARIAN BLOOD DONORS

É Barabás[1], N Magyar[2,3], B Pályi[2,3], A Nagy[3], J Henczkó[2,4], M Takács[3] and Z Kis[2,3]

[1]Confirmatory Laboratory, Hungarian National Blood Transfusion Service (HNBTS) [2]National Biosafety Laboratory [3]Division of Virology [4]Division of Bacteriology, National Public Health Institute (NPHI), Budapest, Hungary

Background: The Crimean-Congo Haemorrhagic Fever (CCHF) is a tick-borne infection that fatality rate is up to 40% among hospitalized people. The CCHF virus is endemic in Africa, in the Middle East and in western and south-central Asia. In Europe, the Balkan region is the most affected, but the CCHF appeared in Spain in 2016. The principal vector (Hyalomma marginatum) of the virus was first reported in Hungary in 2012. Despite the vector presence, no clinical cases have been confirmed in Hungary so far. Disease control authorities consider CCHF a potential transfusion transmittable infection, however, its spread via blood products has not been strengthened yet.

Aims: The aims of our study were to set up a pilot serosurvey and assess whether Hungary could be considered a new area in the distribution of the CCHF virus and the virus poses a factor for the risk assessment of haemovigilance.

Methods: In total 1885 serum samples were obtained from healthy blood donors and tested for anti-CCHF antibody presence. Randomly selected blood donors aged between 18–65 years were enrolled in the study. The proportion of male donors was slightly higher (52%). The samples were screened for anti-CCHF antibodies using an in-house developed whole-virus containing indirect-immunofluorescence assay (CCHF IFA). To exclude the potential cross-reactions, IFA slides were tested for specific viruses and bacteria. To support the results obtained with the in-house IFA assay, commercially available immunofluorescence- and ELISA tests containing recombinant CCHF antigens were applied. The in-house CCHF IFA slides were produced at the NPHI National Biosafety Laboratory under BSL-4 conditions.

Results: Based on the first IFA screening, 10 (0.53%) samples indicated reactivity towards CCHF virus. Commercial tests gave concordant results in 7 samples (2 negative, 2 borderline, 3 positive) and discordant in 3 samples (positive/negative, negative/positive and negative/borderline). Among IFA reactive donors the average age was 36 years (22–64) and the proportion of men among the positive donors was significantly higher (90%).

Summary/Conclusions: Our results support the serological evidence of CCHF infection in Hungary. The principal vector H. marginatum is endemic in the Mediterranean region and its appearance in the continental area may indicate an important role of climate change in the expanding distribution. Haemovigilance is a complex monitoring system covering the entire way of donated blood from donor to

recipient. One of its important aspects is to monitor the possible impact of infectious agents on blood product safety. Based on the low seroprevalence and the lack of clinical cases, the 30-day deferral of whole blood donors after a tick bite is a suitable measure to prevent the virus transmission. Substantial tasks of the public health are to determine the pathogenicity of the circulating virus strains in Hungary and to increase the awareness of the groups in the community that are at risk (e. g. foresters, hunters and health care workers) about the emerging threat of the CCHF virus. E. BarabAs and N. Magyar contributed to this work equally.

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CONTRIBUTION OF ALANINE AMINOTRANSFERASE TO PREVENT DENV TRANSFUSION INFECTION AMONG ASYMPTOMATIC BLOOD DONORS IN TAIWAN DURING 2015 DENGUE EPIDEMIC

C Lu[1], Y Chen[2], M Tsai[1], C Wu[1], C Hung[1] and P Chen[3]

[1]Kaohsiung Blood Center, Kaohsiung [2]Taiwan Blood Services Foundation [3]Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan, Republic of China

Background: Dengue virus (DENV) is a transfusion-transmissible infectious agent. An outbreak of dengue fever occurred with more than 40,000 affected cases during 2015 in Taiwan, which is the most serious one in recent nearly two decades. Since DENV is not included in the routine blood screening, it is critical to evaluate the prevention effect of using alanine aminotransferase (ALT) value as a surrogate marker to detect asymptomatic dengue infection among blood donors during epidemic period.

Aims: This study estimated the proportion of DENV infection among the asymptomatic blood donors with different ALT value and epidemic area with different dengue incidence by transcription-mediated amplification (TMA) nucleic acid test during 2015 epidemic.

Methods: Donor serum samples were randomly selected by stratified groups of ALT level, including ALT<=68 IU/l (N = 3,700) and ALT>68 IU/l (N = 1,300, which judged to be ineligible for blood supply), from donations contributed by donors living at dengue epidemic area where week incidence was more than 5 per 100,000 residents during 2015. The selected samples were tested for DENV RNA by Procleix Dengue virus TMA assay on Procleix Panther System. TMA reactive samples were further sent to the national DENV reference laboratory at Centers for Disease Control Research and Diagnostic Center to conduct DENV diagnostic tests using reverse transcription polymerase chain reaction (RT-PCR), sequence for DENV typing, NS1-antigen (Ag) test, and enzyme-linked immunosorbent assay (ELISA) test for anti-DENV antibodies.

Results: Among 5,000 tested samples from dengue epidemic area, a total of 21 samples were DENV TMA reactive, including 13 samples in donations with ALT<=68 IU/l and 8 samples in donations with ALT>68 IU/l. Among donors with ALT<=68 IU/l, 0.08%, 0.33%, and 0.62% of them, from epidemic area where week incidence was 5–50, 50–200, and >200 per 100,000 residents, were detectable to DENV, respectively; while among donors with ALT>68 IU/l, 0.45%, 0.83%, and 2.0% of them were detectable to DENV, respectively. The DENV TMA detection rate was generally increased with increased dengue incidence, and no statistical significance of DENV TMA detection rate was found between donors with ALT<=68 IU/l and ALT>68 IU/l in all three different incident area. As we use the detection rate to proportionate the situation that we faced during the epidemic, only 4.5% of DENV TMA reactive samples were able to be discarded due to ALT>68 IU/l. The 21 DENV TMA reactive samples were further performed DENV tests by the national DENV reference laboratory and found 17 (81%) of them were recent DENV infections, including 8 (38%) RT-PCR positives, 9 (43%) NS1-antigen positives, and 9 (42.9%) ELISA antibody positives. Sequencing of 8 RT-PCR positive samples identified that the epidemic during 2015 was caused by DENV type 2.

Summary/Conclusions: Higher positive proportion was observed in donors with ALT>68 IU/l in different dengue epidemic area, but no statistical significance was found. Only 4.5% of DENV TMA reactive samples were preventable for the risk of transfusion-transmitted DENV infection when using ALT value as a surrogate marker.

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IMMUNOGLOBULIN-G ANTIBODY SEROPREVALENCE OF WEST NILE VIRUS AMONG BLOOD DONORS IN NAIROBI AND NAKURU REGIONAL BLOOD TRANSFUSION TESTING CENTERS IN KENYA

JC Soi[1] and P MATURI[2]

[1]Laboratory Department, University of Nairobi, Nairobi [2]Laboratory Department, Nakuru Level 5 Hospital, Molo, Kenya

Background: West Nile Virus (WNV) is an arbovirus transmitted by infected mosquitoes which causes most its incidence. It is transmitted by the culex mosquito which is prevalent in Kenya.

Aims: To Determine and compare the IgG-Antibody seroprevalence of WNV among Blood Donors In Nairobi and Nakuru Regional Blood Transfusion Testing Centres In Kenya

Methods: A cross-sectional study. It was carried out in two Regional Blood Transfusion Centers (RBTCs) which are based in Nairobi and Nakuru. These two centers are associated with possible low and high prevalence respectively. A total of 180 blood samples were randomly selected over a period of one month. These blood samples were tested for WNV IgG using ELISA.

Results: Majority of the donors were below 35 years of age and were predominantly male. WNV IgG prevalence was 15% in blood donors (95% CI 10–20.5%). Prevalence of cross infection of TTI and WNV was 8.3% (95% CI 4.4–12.2%). The prevalence of WVN IgG was highest in the 19–35 years age group (16.5%) and females (21.6%) though the results were not statistically significant. There was no difference in the IgG positivity between the different centers.

Summary/Conclusions: Infection with WNV should be of public health concern because about a fifth of those infected with WNV develop illness. About 10% of those who develop neurological symptoms succumb to the disease. Further testing is recommended for all positive samples for confirmation as this is outside the scope of this study.

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SEROPREVALENCE OF HUMAN T-CELL LYMPHOTROPIC VIRUS-1/2 AMONG BLOOD DONORS IN UGANDA

R Ayikobua[1], F Bwanga[2] and A Carneiro-Proietti[3]

[1]Quality/Laboratory, Uganda Blood Transfusion Service [2]Medical Microbiology, Makerere University, Kampala, Uganda [3]Hematology, Fundação Hemominas, Belo Horizonte, Brazil

Background: HTLV-1/2 causes serious diseases in humans and is transmittable by blood transfusion. The need to screen for these viruses in the donated blood remains a concern for blood transfusion services and to ensure the safety of the blood recipient, its prevalence in a given population must be known.

Aims: Assess the seroprevalence of HTLV-I/2 among blood donors in Uganda.

Methods: The study was a cross sectional one, which enrolled 1,294 randomly selected healthy blood donors, with age ranging from 17–54 years. These donors were from six regional blood banks in Uganda and were screened for HTLV-I/2 using a chemiluminescence micro particle immunoassay technique to test the serum samples.

Results: HTLV-I/2 antibodies were present in 13/1294 (1%) of the blood donors. The highest HTLV1/2 seropositivity was found in the Gulu regional blood bank center (7 of 146, 4.7%, P < 0.039, OR 5.31). The results also showed a slight variation in the prevalence of seropositivity between female (4/459, 0.9%) and male donors (9/835, 1.1%). The prevalence also varied among the various types of blood donors, with the highest sero positivity (7/628, 1.1%) among first-time donors. The presence of some risk factors was associated with relatively higher rates of HTLV 1/2, but these associations were not statistically significant in the population tested.

Summary/Conclusions: The HTLV-1/2 seroprevalence found in blood donors in Uganda is relatively high, when compared to other regions endemic for these viruses (South America, Japan, and Caribbean region) and points to the need of screening for HTLV-1/2 in blood donated in Uganda. More studies are necessary to understand the risk factors associated with HTLV in the country.

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SHOULD BE INCLUDED THE UNIVERSAL SCREENING FOR HEPATITIS E VIRUS INFECTION IN BLOOD DONORS? RESULTS FROM SOUTH OF THE CENTER SPAIN

M Jarilla Fernández[1], M Madrigal Sanchez[1], G Andujar Troncoso[1], P Muñoz Valbuena[1], P Lopez-Lopez[2], M Frías[2], A Rivero[2] and A Rivero-Juarez[2]

[1]Centro de Transfusión de Ciudad Real, Hospital General Universitario de Ciudad Real, Ciudad Real [2]Unidad de Enfermedades Infecciosas. Instituto Maimonides de Investigación Biomédica de Córdoba (IMIBIC), Hospital Universitario Reina Sofía de Córdoba, Córdoba, Spain

Background: Spanish Hepatitis E virus (HEV) Guidelines and European Centre for Disease Prevention and Control establish that the decision to screen blood donations for HEV should be determined by the background prevalence of transmissible infection in the donor population and the susceptibility of recipients.

Aims: To evaluate the prevalence of HEV infection in blood donors from south of the center Spain.

Methods: It was included in the study blood donations from healthy donors collected in Ciudad Real (south of the center Spain) between September 2017 and January 2018. Serum samples were analyzed for HEV using nucleacid testing methods, in pools of 8 samples. RNA was extracted using QIAcube (QIAgen, Hilden, Alemania), and tested by RT-PCR amplifying the ORF3 viral region using an in-house method (CFX Connect Real Time PCR System. Biorad, Hercules, California). Positive pools were tested and quantified individually using LightCycler 480 (Roche, Basel, Switzerland). An external in run standard curve was applied to calculate HEV viral load using the WHO HEV standard strain supplied by the Paul-Ehrlich-Institut (code 6329/10), consistent with genotype 3a. Viral load was expressed as IU/ml. It was calculated the prevalence of HEV infection.

Results: A total of 6.097 donations were included in the study. We identify 4 samples positive for HEV. This supposed a prevalence of 0.06% or one in 1.519 donations. These sample were from 4 different donors. Viral loads were, 2 million IU/ml, 43.978 IU/ml, 10.788 IU/ml, and 28.236 IU/ml, respectively. All viral isolated were consistent with genotype 3.

Summary/Conclusions: Our study show a high HEV infection prevalence among blood donors from south of the center Spain. Our data suggest that the risk for HEV transfusion-transmitted HEV could be important in our setting.

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THE FIRST DOCUMENTED CASE OF ACUTE TRANSFUSION TRANSMITTED HEPATITIS E (TT-HEV) IN THALASSAEMIA

C Politis[1], E Zervou[2], M Drosou[3], P Siourounis[4], S Ijaz[5], I Koskinas[6] and C Richardson[1]

[1]Hellenic Coordinating Haemovigilance Centre, Hellenic Centre for Disease Control and Prevention, Athens [2]Blood Bank, University Hospital, Ioannina [3]Thalassaemia Unit [4]Blood Bank, General Hospital of Piraeus, Athens, Greece [5]Public Health Reference Laboratory for Blood Born viruses, Public Health Reference Laboratory for Blood Born viruses, London, United Kingdom [6]Hepatology, Hippokrateio University Hospital, Athens, Greece

Background: HEV infection has caused epidemiological and clinical concern in the field of Public Health primarily by consumption of undercooked pork products.

As an important cause of acute viral hepatitis worldwide, HEV threatens blood safety. The increasing incidence of TT-HEV raises questions about the need to include blood screening in preventive strategies. FFP and apheresis platelets may present greater risk than red cells. Consequently, the risk of TT-HEV in groups such as thalassaemia patients with extensive exposure to donor RCCs raises new issues in their clinical management.

Aims: To present the results of haemovigilance in investigating a case of acute HEV in a thalassaemic patient and to examine comorbidities in exacerbating the inflammatory process of HEV and clinical outcome.

To contribute to Greek national strategies to prevent TT-HEV.

Methods: Reporting post-transfusion infection in the recipient to the blood establishment and subsequently to the Haemovigilance Centre.

Tracing of recipients of potentially infectious blood donation (look-back/review).

Testing of the archived and new samples of the implicated donations for HEV antibodies and HEV-RNA. In case of positive results testing of HEV genotype and sequence analysis in samples of both the donor and the recipient were performed.

Results: The patient was a 50-year-old male with thalassaemia. Transfusion with RCCs started at 4 months old; by the end of 2016 he had received 1500 units. He had no other risk factors for HEV.

The patient has a history of splenectomy and chronic HCV genotype 4. Sustained viral response was succeeded following anti-viral treatment. Effective iron chelation therapy is applied. Liver iron concentration (LIC) is currently 4.4 mg/g dry weight (liver R2 MRI analysis) and serum ferritin is 212 ng/dl.

In May 2017 he presented with symptoms of acute hepatitis. HEV was diagnosed from serological testing. Liver function tests were very high. Self limiting recovery was achieved within a month and liver biochemical tests were normalized.

Haemovigilance investigation of possible TT-HEV: Look-back showed that the patient was transfused with six units of RCCs within the relevant time period two months prior to the occurrence of HEV. Testing of all available archived samples detected that one unit was positive for HEV IgM antibody. The implicated donor was a 46-year-old male, asymptomatic at the time of donation, no relevant travel, diet or occupation. Post-donation information revealed liver steatosis diagnosed 4 years ago. The donor recalled mildly raised serum transaminases in an annual checkup one week before blood donation. The FFP from the implicated blood unit was retrieved and discarded.

HEV–RNA PCR testing was positive in both patient and donor. Phylogenetic analysis indicated that the sequences from both samples belong to the 3(G3) genotype. Sequence comparison indicated that the samples to be 100% identical across the ORF2 region. These results makes it highly likely that the sequences are linked.

Summary/Conclusions: The prevalence of this documented TT-HEV incident is 1:2873 thalassaemic patients transfused with 116,352 units of RCCs in 2017.

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HEV PREVALENCE IN FLEMISH BLOOD DONATIONS

A Vercouter[1], F Van Houtte[1], L Verhoye[1], I González Fraile[2], L Blanco[2], V Compernolle[3] and P Meuleman[1]

[1]Department of Clinical Chemistry, Microbiology and Immunology, Laboratory of Liver Infectious Diseases, Ghent, Belgium [2]Centro de Hemoterapia y Hemodonación, Valladolid, Spain [3]Red Cross Flanders, Ghent, Belgium

Background: Hepatitis E virus (HEV) is a worldwide underdiagnosed virus responsible for at least 20 million infections yearly. It is a positive-sense single-stranded RNA virus and isolates that can infect mammals are classified in the Orthohepevirus genus of the Hepeviridae family. The Orthohepevirus A species is subdivided into seven major genotypes, all belonging to a single serotype. Genotype 1 and 2 are endemic in many developing countries. The zoonotic genotypes 3 and 4 cause sporadic infections in industrialized countries and are mainly associated with foodborne infections. HEV mainly causes acute self-limiting infections. However, chronic infections may occur among immunocompromised patients (e.g., solid organ transplant recipients) and can lead to fulminant hepatitis and death. Transmission through transfusion of blood components has already been reported in several European countries such as Great Britain, Germany, Spain and France, but also in Canada and Japan. Nevertheless, no transmission via plasma-derived medicinal products (PDMPs) obtained after virus inactivation and/or removal steps has so far been documented.

Aims: We wanted to assess the HEV prevalence in Flemish blood donors. This study is of importance to determine the risk of HEV transmission through blood transfusion, especially for immunosuppressed solid organ transplant patients.

Methods: A total amount of 43,369 samples was collected at the Red Cross Flanders during the period May to June 2015. Previously frozen samples were initially pooled per 6 and screened for the presence of HEV RNA using the cobas® HEV test on the cobas® 6800 System (Roche Diagnostics, Pleasanton, CA, USA). In a second phase, RNA reactive pools were deconstructed and analyzed individually using the same methodology. Because of volume limitations, individual samples were diluted with an equal volume of PBS. The limit of detection of the assay on undiluted samples is 18.6 IU/ml. Using a specific ELISA (Wantai, Biological Pharmacy Enterprise, Beijing, China), the presence of HEV IgG was determined in all HEV RNA positive samples, as well as in a selection of 301 randomly chosen samples that scored HEV RNA negative when tested in pool format. HEV-specific IgM (Wantai) was determined in all viremic samples, as well as in the IgG-positive/RNA-negative samples.

Results: During initial HEV RNA screening, valid results were obtained for 6,434 pools, of which 11 reacted positive. After deconstruction of the RNA reactive pools, 7 blood donations (7/38,599; 0.02%) were confirmed as HEV RNA positive (range 1×10^2–7×10^3 IU/ml). Serological screening of the RNA positive samples showed that 6 out of 7 samples were HEV IgM positive, of which 3 donors were also IgG positive. Within the 301 randomly selected samples, 27 (8,97%) donations were HEV IgG positive, including 1 donation also being HEV IgM positive

Summary/Conclusions: Here we show that approximately 0.02% of blood donations in Flanders may originate from donors that are actively infected with HEV. Upon transfusion, these donations may pose a risk to immunocompromised patients, or

patients with pre-existing liver disease. Interestingly, we also identified one non-viremic blood donor being HEV IgM-positive, suggesting recent exposure. Epidemiologic analysis and genotyping experiments are ongoing.

P-449
PREVALENCE OF HEPATITIS E VIRUS AMONG HEMOCENTRO'S BLOOD DONORS

MF Bangueses[1,2], C Viera[3], J Abin[3] and J Curbelo[4]

[1]Supervisor, Hemocentro Regional Maldonado, Maldonado [2]Teacher, E.U.T.M - Universidad de la Republica [3]Diagnose Laboratory, ATGen, Montevideo [4]Hemocentro Regional Maldonado, Maldonado, Uruguay

Background: Hepatitis is a global health problem that results in injury and destruction of hepatocytes, leading to liver malfunction. Hepatitis E virus (HEV) is one of the leading causes of acute liver inflammation that is considered an important public health concern in many developing countries. According to the World Health Organization (WHO), 20 million people are infected with HEV annually.

HEV infection is usually self-limiting, however, it may develop into acute fulminant hepatitis in high risk groups such as patients with liver problems and pregnant women. Acute fulminant hepatitis could then develop into a chronic infection that may progress to cirrhosis or even death.

Hemocentro Regional Maldonado is a state-run blood bank that centralizes blood donations for the east region of Uruguay, including Maldonado, Rocha, Lavalleja, Cerro Largo y Treinta y Tres. The east region represents 7,5% of total population of Uruguay.

Annually Hemocentro collects 20.000 donations and distributes blood components among east region and Montevideo, task that is done according to high quality standards.

Aims: Investigate the prevalence of HEV among blood donors in the east region of Uruguay in 2017.

Methods: Taking into account demographic information, 401 plasma samples of blood donors were obtained from the Hemocentro's plasma library.

Samples were tested for the presence of anti-HEV IgG and IgM (HEV Ab Version ULTRA DIA.PRO). HEV Ab positive samples, were tested for the presence of anti-HEV IgM (HEV IgM DIA.PRO).

IgM positive samples were further tested for the presence of HEV RNA by RT-PCR. Finally, viral RNA samples were sequenced to determine HEV genotype.

Results: Forty of the 401 blood donors (10,0%) were HEV positive for total antibodies (IgG + IgM). Nineteen of the 40 IgG + IgM reactive samples (47,5%) were IgM reactive, and 3 of them were RNA positive.

All RNA positive samples (3) were genotype 3.

Summary/Conclusions: This is the first study of HEV among blood donors in the east region of Uruguay. The obtained result alert us about the high prevalence of the pathology and suggests that we should include the screening of HEV in blood donors.

P-450
HEPATITIS E: AN UNDERESTIMATED EMERGING DISEASE

C Sargento, C Ferreira, E Silva, P Achando and J Tomaz

Blood Department and Transfusional Medicine, Centro Hospitalar Universitário Coimbra, Coimbra, Portugal

Background: Hepatitis E virus (HEV) was discovered by Mikhail Balayan in 1983 but, its genome was only cloned and sequenced in 1991 by Smith, Bradley, Reys et al. HEV is a member of the family Hepeviridae, genus Orthohepevirus which comprises 4 species, Orthohepevirus A-D. Orthohepevirus A contains 8 genotypes (HEV 1–8). HEV1 and HEV2 infect humans only; HEV3, HEV4 and HEV7 can infect humans and other mammals, and HEV5, HEV6 and HEV8 have been detected in animals only. HEV is a leading cause of acute hepatitis in developing countries, mostly Asia and sub-Saharan Africa, and is responsible for an estimated 20 million infections. In this geographical areas the HEV involved are mostly genotypes 1 and 2 and transmitted through the faecal-oral route.

In developed countries HEV infections were considered as acquired only in travelers to endemic areas but today it has been demonstrated that the majority of this infections were autochthonous and involved in most cases genotype 3 or eventually genotype 4. The main transmission is related to consumption of uncooked pig (porcine viral reservoir) and game meat.

Transfusion is the other route of transmission who is worrying almost all European countries. Some of them already do routine research of RNA- HEV in all blood donations (England, Germany, Italy), others do selective tests for some transfusion patients (immunosuppressed patients, transplant recipients, pregnant women). In these clinical situations, HEV infection can be very dangerous or even fatal.

Aims: To assess the accuracy of RNA-HEV detection kits to screen donors and on the other hand, to determine the viral load to study patients.

Methods: Kits to be tested:
1-FTD Hepatitis E RNA (Fast Track Diagnostics-Luxembourg)
2-quanty HEV rtPCR-Clonit-Milano
- Selected samples: 100 samples of blood donations; 13 HEV RNA positive patient samples;
- 2 validation panels with known viral loads;
- 19 standards to quantify the viral load;
- 8 negative controls and 2 positive controls;
- In doubtful PCR results we used an additional test - RecomLine HEV IgG/IgM-Mikrogen, performed on Auto-LIPA–Innogenetics;
- Nucleic acids extraction–easyMAG- Biomerieux;
- RNA-HEV amplification, detection and quantification by rt PCR performed on Rotor-Gene Q-Quiagen.
- Sample handling in the laminar flow chamber.

Results: 100 samples of blood donations: 98 HEV RNA negative results on FTD and clonit; 2 HEV RNA border line results on clonit and negative on FTD
13 HEV RNA positive patient samples: 11 HEV RNA positive results on FTD and clonit; 1 HEV RNA positive result on FTD and negative on clonit; 1 HEV RNA positive result on FTD and negative on clonit.
On these 2 samples with discrepant results, one is RecomLine HEV IgG and IgM negatives and the other is RecomLine HEV IgG and IgM positives.
With the FTD kit we confirmed results with the 2 panels HEV RNA used.
The standards demonstrate a good performance in both kits.

Summary/Conclusions: We concluded that both kits have good performances for quantitative HEV-RNA but larger studies are required to make a sound and consistent assessment.

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BLOOD DONORS' PARVOVIRUS B19 INFECTION IN A SOUTHWESTERN EUROPE HOSPITAL

C Sargento, C Ferreira, E Silva, P Achando and J Tomaz

Blood Department and Transfusional Medicine, Centro Hospitalar Universitário Coimbra, Coimbra, Portugal

Background: Parvovirus B19 is a single stranded DNA virus, non-enveloped, icosahedral of the family parvoviridae and genus erythrovirus. It was discovered in 1975 by Cossart while screening normal blood bank donors' sera.

The majority of parvovirus B19 infections are clinically asymptomatic. The symptoms of an acute infection with parvovirus B19 are flu-like, but may also resemble those of rubella and, especially in adults, those of rheumatism. Later studies confirmed the close association of parvovirus and aplastic crisis in a large study of sera from sickle cell disease patients. Cases of nonimmune hydrops fetalis were then reported when infection in a woman occurred during pregnancy. There is some evidence that intrauterine parvovirus infection leads to developmental abnormalities in childhood. Transmission is primarily spread by infected respiratory droplets (household/classroom contacts) but, blood-borne transmission has been largely reported. There is no vaccine available for human parvovirus B19.

Aims: Considering the mainly asymptomatic infection, the problems that this infection can cause in sickle cell disease, pregnancy, immunocompromised patients and the role of blood transfusion on transmission parvoviruses, we made a small study on blood donors' samples to evaluate the risk and take security measures.

On the other hand, we want to validate the kit that we want to introduce in our laboratory.

Methods: - 176 Blood donor samples,
- 16 patient samples with other pathologies to show the specificity of the test
    5 with HCV Ab and HCV RNA positives
    3 with HCV Ab positive and HCV RNA negative
    5 with HBsAg and HBV DNA positives
    3 with HBsAg positive and HBV DNA negative
- 4 samples with clinical suspicion of parvovirus infection
- 10 repeated samples to show reproducibility
- 2 QCMD panels-8 samples (Quality Control Molecular Diagnostics)
- 10 Standards with known concentration.

- 8 positive controls and 8 negative controls
- DNA extraction -easyMAG-BioMerieux
- Test used-Artus Parvo B19 RG PCR-Quiagen-Sensitivity:200 UI/ml
- Amplification/detection-Rotor-Gene Q - Quiagen

Results: The QCMD sample results were as the expected.

The positive and negative controls showed a correct result.

The standards showed consistent results.

In the 10 repeated samples we obtained the same results.

The results were not affected in the 16 patient samples with other pathologies

On blood donor samples, we found 3 positive results for DNA Parvovirus B19. The samples were repeated and the results confirmed.

Summary/Conclusions: The Artus ParvoB19 RG PCR kit seems to be sensitive, specific (looking at the results of the panels samples) and have good reproducibility. Regarding blood donor samples, we found 3 positive results (1.7%) for DNA Parvovirus B19 indicating 3 active infections.

This is a small study but, the positive results suggest a more extensive crawl.

P-452

IS THE NUCLEIC ACID TEST HELPFUL IN THE CLINICAL USE OF BLOOD?

E Borici, R Skendaj, V Doci and I Dallaku
National Blood Transfusion Center, Tirana, Albania

Background: Nucleic acid testing (NAT) is a molecular technique for screening blood donations to reduce the risk of transfusion transmitted infections (TTIs) in the blood and blood products recipients. It is founded safer than other testing methods for human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) as highly sensitive and specific for viral nucleic acids. NAT detects these infective agents earlier than the other screening methods thus, narrowing the window period of HIV, HBV and HCV infections.

As a modern and useful technique, it is becoming more and more popular in many countries that are benefitting from its safety in blood transfusion medicine. In Albania the NAT screening began as a protocolled procedure on 2016. Since then all blood donations are screened by NAT procedure for HIV, HBV, HCV and syphilis.

Aims: In this study we bring our results of blood donations screening by NAT method aiming to see its efficacy and role in safety of clinical use of blood.

Methods: We undertook this retrospective study analyzing all blood donations overall the country from January 2017 to January 2018. There were 30242 blood donations that were screened for infective agents HIV, HBV, HCV and syphilis. All donations were screened before by immune-enzymatic method for the above mentioned infective agents and after in another sample tube from the donor by NAT method. As protocol, all the reactive NAT donations were tested by discrimination process to define if they were reactive for HBV, HCV, HIV or high ALT-transaminases. All the data were collected and archived electronically and each blood sample had its identification barcode. As part of functionality, the temperature and humidity in the room where the NAT machine operated were monitored.

Results: From all blood donations were excluded from transfusion 1550 blood unit because of positive result by the immune-enzymatic method. We found that by NAT method were 143 blood donations (0.5% of all donations) excluded from transfusion as resulted reactive but in immune enzymatic test were not identified as positive for the infective agents or high ALT-transaminase level. After the discrimination of these 143 reactive NAT we found 79 HBV reactive and other 64 without results for infective agents or transaminases. Although 64 reactive NAT donations did not give any result in discrimination test we excluded them from transfusion.

Summary/Conclusions: We argue that NAT method for the blood analyze to infective agents is an effective method that supports the clinical use of blood. It gives a big advantage in safety of blood used in transfusion medicine.

Immunohaematology – Red Cell Immunology: Serology

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ABH GENOTYPE AND SECRETOR STATUS IN INFERTILE COUPLES. ITS APPLICATION IN REPRODUCTIVE BIOLOGY

MS Brunori, A Marelli, E Vallejos and A Brufman
Inmunohaematology, National University of Rosario, Rosario, Argentina

Background: Fucosyltransferase locus2 (FUT 2) controls the secretion of ABH blood group antigens in organic fluids and plays an important role in infertility, recurrent abortions and fetus-mother antigenic incompatibilities. The 80% of Caucasian population inherits the secretor gene Se expressing ABH antigens in soluble state. The incidence of infertility related of both male and female factors continues to rise despite many advances in reproductive technologies. It is well known that ABO antigens are expressed on sperm membrane and in seminal fluid of secretors as well as ABO antibodies are present in cervical mucus. In previous studies we observed significant loss in progressive motility of spermatozoa of non secretors in relation to secretor ones caused by specific cervical mucus antibodies in ABO-incompatible couples. In addition, sperm cells are haploid cells, so that a heterozygous individual has two sperm subpopulations, each expressing the corresponding allele. The specific antibody of the cervical mucus will attack only the complementary sperm.

Aims: To evaluate the prevalence of secretor character in men belonging to fertile and infertile couples in order to investigate a possible association with reproductive success.

Methods: Ninety-seven samples of semen, 53 from infertile men and 44 from fertile controls were studied. Secretor phenotype was evaluated in seminal plasma by laboratory standard procedure of inhibition of haemagglutination technique. To distinguish between ABO genes, a PCR was designed with two sets of oligonucleotides that allow amplificate two different regions of the transferases without use of restriction enzymes. By comparison of bands of the PCR products, the individual genotype was determine. Cervical mucus antibodies of their female partners were titrated with the corresponding red blood cells.

Results: Results were analysed in both groups. In infertile couples with ABO incompatibility, the frequency of non-secretor phenotype of husbands (76.9%) were significantly higher than those from fertile couples (21.6%) (P < 0.03) The results obtained by PCR in sperm cells correlated 100% with red cells phenotypes.

Summary/Conclusions: The immunological implications in reproductive biology are now being studied and are being considered as a cause of failures in sperm-egg interaction even between normal gametes. Secretor phenotype of the male partner could help reproductive success blocking cervical ABO antibodies. Besides, if he is heterozygous, cervical mucus antibodies will only affect the corresponding sperm. We propose to evaluate ABH antigen expression on sperm membrane and seminal plasma to contribute to the diagnosis and treatment of human infertility.

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INVESTIGATION INTO AN ABO DISCREPANCY BETWEEN A MOTHER AND HER NEWBORN

N Baillargeon[1], C Ethier[1], C Parent[1], M St-Louis[2], A Lemay[3] and M Lamarre[3]
[1]Immunohematolgy Reference Laboratory [2]Medical Affairs and Innovation, Héma-Québec, Québec [3]CIUSSS MCQ, Trois-Rivières, Canada

Background: The ABO system was discovered in 1900 and is considered the most clinically significant blood group system in transfusion. ABO genotyping of donors and patients is not routinely performed but might be helpful and complementary to serology tests for resolving cases with discrepant result. Here is one example.

Aims: Samples from a 25 years old Caucasian female G1P1 and from her newborn were sent to the blood bank to investigate an ABO discrepancy. The laboratory who referred the cases typed the mother as AB negative and the baby as O positive in tube method using Ortho BioClone reagents

Methods: Both samples were analysed according to the manufacturers' insert in tube method. Results were recorded after immediate spin and after incubation at 22°C and 4°C to enhance antibody binding and detection of weak ABO antigens and antibodies. As ABO antigens reach detectable level around the age of 1 year, reverse typing was not performed on the baby samples. Following discrepant serological results, both samples were sent for DNA sequencing of ABO gene exons 6 and 7.

The sequencing of the reverse transcriptase-PCR was also performed on the mother samples.

Results: Mother's red blood cells (RBCs) gave weak reactivity (w-2 +) with DBL Novaclone, Ortho BioClone and Bio-Rad Seraclone anti-A reagents. Her RBCs gave 4 + reactivity with anti-B (DBL Novaclone, Ortho BioClone, Bio-Rad Seraclone, Immucor Gammaclone) and 4 + with anti-AB (DBL Novaclone, Ortho BioClone and Immucor Gammaclone) reagents. No mixed fields were observed. At reverse typing, a 4 + reaction was obtained at immediate spin with A_1 RBCs and negative reactions were obtained with A_2B and O RBCs. Tests tube were incubated at 22°C which resulted in an additional 1 + reactivity with A_2 cells. Additional positive reactivity (1–2 +) was observed at 4°C with B cells, O cells and auto control. An anti-A_1 was identified in the mother sera in gel LISS, tube LISS and in tube incubated at 22°C. Sequencing analyses identified a B allele polymorphism in addition to a heterozygous polymorphism on the A alleleABO*A3.01/ABO*B.01. The mother probable phenotype is A_3B. The newborn was typed as O with forward typing (DBL Novaclone and Bio-Rad Seraclone). Sequencing analyses showed heterozygous polymorphisms at positions c.646T>A and c.681G>A of the O allele and at position c.871G>A of the A allele (ABO*A3.01/ABO*O1.45). His probable phenotype is A_3O. Baby RBCs showed the same ABO*A3.01 genotype found in the mother. ABO*O1.45 genotype was probably inherited from the father.

Summary/Conclusions: Sequencing results confirm that the mother and the newborn shared the same A_3 phenotype although it was not detected by serology testing on the baby as expression of A and B antigens may be weakened in some cases given their young age. This highlights the clinical relevance of confirming the serology of ABO subgroups by molecular methods whenever an apparent discrepancy is observed.

P-455
CAUSES OF UNBALANCED LEVELS OF ANTI–A AND ANTI–B IN O CELL TYPE PATIENTS WITH ABO DISCREPANCY

S Choi[1], J Seo[1], S Chun[2] and D Cho[1]

[1]Department of Laboratory Medicine and Genetics, Samsung Medical Center, Seoul [2]Department of Laboratory Medicine, Chonnam National University Medical School, Gwangju, Republic of Korea

Background: Endogenous synthesis of anti-A and anti-B can develop as early as a3 to 6 months of age. After this period, anti-A and anti-B in their serum in group O individuals peaks with similar levels. However, some O blood type patients with ABO discrepancy show remarkably different reactivity with A1 and B cells, respectively, in reverse typing.

Aims: The aim of our study was to determine the incidence of ABO discrepancies and analyze the causes of unbalanced levels of anti-A and anti-B among O cell type patients.

Methods: This retrospective study involves all patients who received ABO typing between July 2016 and December 2017 in Samsung Medical Center. Records of all results were retrieved and analyzed for the cause of ABO typing discrepancies. Unbalanced level in serum typing was defined as grade two or more difference with the tube method, it was classified as anti-B > -A group and anti-A > -B group. Neonate was defined as infants less than 12 months of age. ABO genotyping was performed in patients with unresolved ABO discrepancy by serology or clinical information. Differences in proportions of causes were analyzed using Fisher's exact test.

Results: A total of 66,145 patients underwent ABO typing and the incidence of ABO discrepancy was 1.3% (846/66,145). The number of O cell type patients was 100 (11.8%) and 51 samples (anti-B > -A group, n = 26 and anti-A > -B group, n = 25) showed unbalanced levels of anti-A and anti-B in serum typing. In both group, ABO incompatible hematopoietic stem cell transplantation was the most frequent cause as 65% (17/26) and 55% (11/25), respectively. A single patient in each group was due to ABO incompatible liver transplantation. All 8 neonates were classified into the anti-A > -B group. The remaining 13 patients were due to various causes, and 10 patients underwent ABO genotyping (anti-A > -B group: 4/5, anti-B > -A group: 6/8). The frequency of O genotype was significantly higher in the anti-A > - B group (p = 0.048).

Summary/Conclusions: Except for ABO incompatible transplantation, the main cause of unbalanced low level of anti-A was A subgroup, whereas that of unbalanced low anti-B was a temporary phenomenon caused by age or underlying disease rather than B subgroup.

P-456
DETECTION OF ABO CHIMERISM IN A LONG TERM BLOOD DONOR FOLLOWING A CHANGE IN BLOOD GROUPING TECHNIQUE

J Kralova[1], M Pisacka[2], H Cechova[2], M Leinertova[3], J Storry[4], M Olsson[5] and A Hult[4]

[1]Immunohematology Department [2]Institute of Hematology and Blood Transfusion, Prague [3]Hospital Jihlava, Jihlava, Czech Republic [4]Clinical Immunology and Transfusion Medicine, Laboratory Medicine, Region Skåne [5]Department of Laboratory Medicine, Lund University, Lund, Sweden

Background: A chimera is a single organism composed of cells with distinct phenotypes and/or genotypes. This can be acquired, such as is seen following hematopoietic stem cell transplantation, or more transiently following blood transfusion, but may also be inherited most commonly through blood exchange in utero between twins. Other rare type called tetra-gametic chimerism occurs through the fertilisation of two separate ova by two sperm, followed by aggregation of the two at the blastocyst or zygote stages. This results in the development of whole body chimerism - an organism with intermingled cell lines (double set of genetics signs – mother's and father's). In transfusion medicine, chimeras are often detected when mixed field reactivity is observed in ABO/D typing or, less commonly, when phenotyping for other blood group antigens.

Aims: This investigation was prompted by finding a double population of erythrocytes in a healthy blood donor with no transfusion history. The blood donor had donated 38 times, and had typed previously as group A RhD positive without discrepancies until the method for blood grouping changed from tube agglutination to column agglutination in gel cards. The double population was found in column agglutination in tests with anti-A, and subsequently when typing for c antigen. Our aim was to investigate the chimera and determine the underlying ABO genotype of this blood donor.

Methods: Blood samples from the blood donor, his parents and 6 siblings were investigated. Routine blood grouping was performed by column agglutination. Separation of the double cell populations was performed by differential agglutination with IgM anti-A and anti-c. Flow cytometry with monoclonal anti-A and anti-H was performed to characterise the two populations. Initial ABO genotyping was performed by PCR-SSP and gel-electrophoresis (FluoGene; Inno-train Diagnostik GmbH); further resolution was performed using in-house PCR-ASP and PCR-RFLP methods. Karyotyping was performed by standard methods. Identification of reference alleles was performed by fragment analysis of Short Tandem Repeats (STR) polymorphisms.

Results: The donor's genotype was identified as ABO*O.01/O.02 by CE-certified PCR-SSP kits however these systems detect the ABO*A genotype by exclusion only. Subsequent in-depth resolution detected 3 allelesABO*A1.01/0.01.02/O.02.01, both on DNA isolated from peripheral blood and from saliva (somatic genome). The genotype of the donor's father was ABO*O.01/0.02 and that of his mother was ABO*A1.01/0.01. There were no other ABO discrepancies among the donor's 6 siblings.

Blood group typing of the RBC population after removal of RBCs agglutinated with anti-A typedO RhD-positive, Ccee. The second population was typed after agglutination of c-positive cells with anti-c: these RBCs typed A RhD-positive CCee. Flow cytometry with using anti-A and anti-H shown a double population of erythrocytes; 38% group A, 62% group O.

Cytogenetics demonstrated a normal XY karyotype. STR polymorphisms: in 8 polymorphisms are two maternal and two paternal; in one two maternal and one paternal. Same alleles in same ratio in were from peripheral blood and saliva derived DNA.

Summary/Conclusions: A rare case of a high-grade chimera was observed in a healthy blood donor with two healthy children. Such situations can cause troubles in blood grouping and discrepancies in blood group genotyping.

P-457
COMPARISON OF ABO ANTIBODY TITRES BY TUBE AND COLUMN AGGLUTINATION TECHNIQUES

S Basu[1], M Reddy[1], D Basu[1] and C Patil[2]

[1]Transfusion Medicine [2]Palliative Medicine and Psycho-oncology, Tata Medical Center, Kolkata, India

Background: Titration of ABO antibodies is important in transfusion practice. Antibody titers influence the outcome in ABO incompatible organ and hematopoietic stem cell transplantation. Antibody titrations also determine the need for

intervention in hemolytic disease of the newborn. Inter-laboratory variation in titration results and variations in titer between techniques is known to occur. Although antibody titration results affect patient management, in India there are no standard antibody titration protocols. We conducted a study with support from Ortho Clinical Diagnostics, to assess the conventional tube technique (CTT) and column agglutination technique (CAT) for antibody titration.

Aims:

1. To compare the CTT with CAT for antibody titration.
2. To assess IgM interference (if any) in IgG antibody estimation and determine the need for DTT treatment for IgG estimation.
3. Compare IgM and IgG titers amongst groups A, B and O.

Methods: Twenty voluntary blood donors, each from blood group A, B and O were assessed for anti-A and anti B titers. A total of 80 titers were assessed, each for IgM and IgG (with and without IgM inactivation) by both CTT and CAT (Ortho BioVue system). Dithiothreitol (DTT) treatment was used for IgM inactivation. Double dilutions were prepared by master dilution method, Affirmagen cells (Ortho Clinical Diagnostics) were used for both the methods, and standard validated techniques were used. The quantitative variables were expressed in terms of median and interquartile ranges. Further, Wilcoxon rank sum test was applied to test the significance of two medians.

Results: IgM titer was more than IgG titer (with DTT treatment), for groups A, B, O (P < 0.001). Higher titers were obtained by CAT as compared to the CTT method for IgM, IgG with DTT and IgG without DTT. IgG antibody titer with DTT treatment was less than IgG titer without DTT treatment, by both CAT and CTT methods (statistically very significant). The high IgG titers of non-DTT treated plasma was noted even when using monospecific IgG AHG cards. The IgM and IgG titers (with and without DTT) amongst the three blood groups by CTT and CAT were: group O > A > B. The turn-around time for IgM titer by CTT was much more than CAT method.

Summary/Conclusions: The study revealed higher titers by CAT than by CTT. An interesting observation was that DTT treatment significantly reduced IgG titers by both CTT and CAT methods. Hence it appears that IgM interferes with IgG estimation by CTT and CAT. Variation in results due to different titration methods and whether IgM inactivation is done; could lead to inter-laboratory variation in results and impact patient management. Hence there is an urgent need for uniform antibody titration practice protocols. The CAT titers must also be clinically correlated to ensure appropriate interpretation. In addition, this study provides baseline data of IgM and IgG titers amongst A, B and O group blood donors.

P-458

IMMUNE HEMOLYTIC ANEMIA WITH POSITIVE DONATH–LANDSTEINER TEST IN AN ELDERLY MAN WITH SEVERE NECROSIS OF THE EXTREMITIES ASSOCIATED WITH CRYOGLOBULINEMIA AND CRYOFIBRINOGENEMIA

TN Nguyen[1], E Maenulein[1], A Dossier[2], I Vinatier[1] and J Moh Klaren[1]

[1]Medical Biology Laboratory, French Establishment of Blood, Ile de France, Site Saint-Antoine Paris, France [2]Department of Internal Medicine, Bichat-Claude Bernard Hospital, Paris, France

Background: Paroxysmal cold hemoglobinuria (PCH) is a rare type of autoimmune hemolytic anemia (AIHA). It is more commonly observed in children than in adults following viral infections. It is characterized by the presence in the serum of a biphasic hemolysin, an IgG anti-P complement-binding autoantibody which sensitizes red blood cells (RBCs) most effectively in the cold, and causes hemolysis when the temperature is subsequently raised to 37°C. We report a case of a 60-year-old man with a history of acute P. falciparum malaria treated by Artemether+ Lumefantrine (automedication) one month prior to admission to the hospital for coldness, pain, numbness, edema and cyanosis of the extremities. Evolution of the illness was marked by the onset of a severe immune hemolytic anemia (nadir Hb= 64 g/l) with dark urine and a rapidly irreversible distal ischemia and necrosis leading to an imputation of all the fingers and the lower extremities. Cryoglobulin and cryofibrinogen were detected in patient's serum. A strongly complement positive direct anti-globulin test (DAT) was initially demonstrated. Patient's samples were sent to our laboratory for further AIHA serological investigation.

Aims: The aim of this study was to support a clinical diagnosis of AIHA.

Methods: Screening for cold reactive antibodies was performed by testing the patient's plasma against untreated and enzyme-treated allogeneic (OI /Oi) and autologous RBCs at 4°C. A hemolytic serum screen with acidified patient's serum plus acidified normal serum (as a source of complement) tested against enzyme-treated RBCs was also performed. The Donath-Landsteiner (D-L) test was realized using enzyme-treated P1-positive, P1-negative (P2) and patient's own RBCs (1 h-

incubation at 0°C in melting ice followed by a 30-min incubation at 37°C). Controls tested in parallel were maintained at 0°C and 37°C.

Results: A cold agglutinin titer of 2 and 8 was obtained in 4°C tests against untreated and papain-treated group OI RBCs, respectively. No hemolysis was observed in tests designed to demonstrate monophasic hemolysins. The D-L test was positive. The set of cells incubated first at 0°C for 1 h and then 37°C for 30 min demonstrated hemolysis with P1-negative (P2) and the patient's own RBCs, only following the 37°C phase. The set of cells maintained throughout at 0°C or 37°C showed no hemolysis. The biphasic hemolysin thus appeared to show anti-P specificity.

Summary/Conclusions: We describe here an unusual case of detecting a D-L antibody. Although AIHA with a biphasic hemolysin is not common in adults, it should be considered and investigated in any case in which there is serological or clinical evidence suggestive of PCH especially when cold agglutinin syndrome (CAS) is excluded in a patient with a complement-positive DAT.

P-459

EVALUATION OF DAT NEGATIVE AUTOIMMUNE HEMOLYTIC ANEMIA, AN INSIGHT BEYOND CONVENTIONAL TEST

SS Das

Transfusion Medicine, Apollo Gleneagles Hospitals, Kolkata, India

Background: A negative direct antiglobulin test (DAT) does not rule out AIHA. The clinical entity known as "DAT negative AIHA" is reported to be 2–4%. Although conventional tube technique (CTT) with polyspecific Coombs reagent is the gold standard method to investigate DAT however due to its low sensitivity false negative DAT may result in hemolyzing patients carrying low number of IgG molecules per RBC. Various advanced methods have been described previously for diagnosing DAT negative AIHA. Majority of blood bank in India lack these methods except for few facilities having column agglutination technique (CAT). In addition to above advanced costly methods, authors in the past have described simple techniques that yield DAT positivity in an otherwise DAT negative AIHA. Our blood bank being a part of a referral hospital we encounter clinically suspected cases of AIHA who are otherwise DAT negative with CTT. Here we share our experience of diagnosing DAT negative AIHA using CAT and other simple methods described before.

Aims: Our blood bank being a part of a referral hospital we encounter clinically suspected cases of AIHA who are otherwise DAT negative with CTT. Here we share our experience of diagnosing DAT negative AIHA using CAT and other simple methods described before.

Methods: Blood samples of 464 patients suspected of AIHA were received in the blood bank for DAT investigation. DAT was performed by both CTT and CAT using polyspecific Coombs reagent. All positive DAT results were reported immediately. For any negative result extended DAT evaluation included monospecific gel card DAT, IgG subclass DAT, cold acid elution and cold wash DAT. Hemolysis in a patient was documented when ≥ 2 of 4 laboratory parameters a) Hb (< 9 g/dl), b) reticulocyte (> 2%), c) serum bilirubin (> 2 mg/dl) and d) LDH (> 500 IU/ml), were abnormal. Hemolysis was classified into moderate and severe on the basis of whether 2–3, or all the 4 laboratory parameters respectively, were abnormal. Statistical analysis was done using SPSS statistical software (version 12).

Results: Of the 464 patients 439 (94.6%) were autoimmunized and others suffering from non immune hemolytic anemia. Eighteen (M: F = 1:2, median 37 years) of the 439 autoimmunized patients (4.1%) were clinically and serologically diagnosed as "DAT negative AIHA". Secondary AIHA was observed in 3 patients. All patients complained of fatigue on routine activity, 5 presented clinical icterus. Moderate and severe in vivo hemolysis were observed in 14 and 4 patients respectively. The median Hb, reticulocyte, serum bilirubin and LDH were 6.9 g/dl, 2.85%, 2.3 mg/dl and 528.5 IU/ml respectively. Polyspecific CAT could diagnose 8 cases of DAT negative AIHA. Other 7 were diagnosed by monospecific CAT (N = 2), subclass CAT (N = 1), cold wash DAT (N = 2) and elution (N = 2) methods. Three patients responded to AIHA therapy despite negative DAT. No free serum antibodies were detected in these 18 patients.

Summary/Conclusions: Absence of high end sensitive methods in developing countries including India makes diagnosis of DAT negative AIHA challenging. However majority of these patients can be diagnosed using simple but relatively sensitive methodologies.

Aims: To study the occurrence of RBCs autoimmunization among multiple trans-fused AIHA patients and identify blood group antibodies potentially developed and induce antigen-antibody reaction affecting patients. Study was carried out in 133 multi-transfused patients recorded with AIHA registered at Central Blood Transfusion Service Indonesian Red Cross Jakarta. This study is useful to see the percentage of AIHA species found in referral patients in CBTS IRC. This result can be used for reference of the case of incompatibility in IRC CBTS.
Methods: Study was carried out in 133 multi-transfused patients recorded with AIHA registered at CBTS IRC Jakarta. Immune hemolytic anemia is characterized by clinical and laboratory features of hemolytic anemia with direct antiglobulin test (DAT) positivity.
Results: In Central Blood Transfusion Service Indonesian Red Cross, we have 133 patients AIHA in 2 years (2016–2017). Furthermore, based on thermal amplitude of autoantibody, AIHA is classified as warm (10,52%), cold (13,53%), AIHA cold and Drug Induce (20,31%) and mixed (55,64%) type. Mixed AIHA is the most in referral patients and must be differentiated from warm AIHA with clinically insignificant cold agglutinins and cold hemagglutinin disease as their treatment is different. It may present as blood group discrepancy or cross-match incompatibility leading to delay in arranging suitable blood unit for transfusion. Therefore, a thorough immunohematology workup including monospecific DAT, indirect antiglobulin test at 4°C and 37°C, determination of thermal amplitude and titer is essential.
Summary/Conclusions: This study shows that in Indonesia most cases AIHA is AIHA Mix (cold and Warm) autoantibody. In the presence of this result, pre-transfusion management should be performed for AIHA patients. To see the success of therapy in AIHA patients can be done DAT examination before and after therapy.

P-460
CHARACTERIZATION OF THE SEROLOGY AND TRANSFUSION MANAGEMENT OF ADULT AND PEDIATRIC LIVER TRANSPLANT PATIENTS PRESENTING WITH HEMOLYTIC ANEMIA

S Sen[1], M Combs[2], N Bandarenko[1] and J Poisson[1]
[1]Pathology, Duke University [2]Transfusion Services, Duke University Hospital, Durham, United States

Background: Immune-mediated hemolysis following liver transplant treated with calcineurin inhibitor may be associated with the presence of red blood cell (RBC) antibodies. Immunohematology workups in these cases can be complex and transfusion support may require incompatible RBCs to maintain adequate hemoglobin levels.
Aims: To characterize the serologic findings and transfusion strategies developed in liver transplant patients presenting with hemolytic anemia.
Methods: Consecutive medical records for adult and pediatric (< 18 years old) liver transplant patients presenting to our tertiary care academic institution from January 2013 to January 2018 were reviewed. Serologic evaluations were characterized as complex when the following were identified: warm autoantibody/panagglutinin, cold antibody, or inconclusive (immunohematologic reactivity that could not be resolved). The date of liver transplantation, the start date of calcineurin inhibitor therapy, and the date when complex serologic findings were identified, were collected. Transfusion management and adverse reactions were included.
Results: A total of 443 liver transplants in 429 patients were reviewed. 84 of these transplants occurred in 75 pediatric patients. Thirteen patients had complex serology with significant RBC antibodies classified as warm autoantibody in 10 cases, inconclusive in 2 cases, and cold autoantibody in 1 case. This represents an overall incidence of 3% in our patient cohort; 6.7% (5 of 75) incidence in pediatric patients versus 2.2% (8 of 354) in adults. All patients received the calcineurin inhibitor, tacrolimus, for post-transplant immunosuppression. Direct antiglobulin test (DAT) was positive in 12 of the 13 cases; 8 patients showed presence of immunoglobulin IgG alone, while 4 patients showed both IgG and complement C3. The presence of a strong interfering cold antibody precluded accurate direct antiglobulin testing in one patient. Five patients developed complex serology following transplantation and tacrolimus initiation; all five were in the pediatric age group. Antibody-mediated hemolysis was confirmed in 6 patients: 2 adults and 4 pediatric patients. Hemolysis seen in the adult cases was milder; antibodies were pre-existing (pre-transplant), and only one required post-transplant transfusion support. Antibody-mediated hemolytic anemia in the 4 pediatric patients was associated with significant hemolysis evidenced by extended transfusion support post-transplant. Transfusion management included phenotype matched RBCs (provided in 3 of the 4 pediatric cases), along with least-incompatible crossmatched units (2 patients). A febrile non-hemolytic transfusion reaction in one pediatric patient prompted preventative management including washed pRBCs to minimize cytokine content and slow infusion of small aliquots.
Summary/Conclusions: Immune mediated hemolysis post solid organ transplant has been reported in patients on immunosuppression with calcineurin inhibitors. Calcineurin inhibitor-mediated T cell suppression and dysregulated B cell proliferation have been postulated as mechanisms causing the hemolytic anemia. Pediatric patients seem to be more susceptible to the development of significant hemolytic anemia and may require extended transfusion support. Serologically compatible blood for transfusion may not always be possible, and limited information is available regarding transfusion guidance and outcomes in these patients. Transfusion service should be aware of the challenging scenario in such cases, and direct transfusion regimens accordingly after careful evaluation of the clinical and laboratory findings.

P-462
AUTOIMMUNE HEMOLYTIC ANEMIA WITH RETICULOCYTOPENIA

S Mahjoub[1], M Bel Hadj[2], A Chakroun[2], H Baccouche[2] and N Ben Romdhane[2]
[1]Hematology, La RABTA [2]11 rue jebel lakhdar, Hopital La rabta, Tunis, Tunisia

Background: Autoimmune hemolytic anemia (AIHA) is a relatively uncommon disorder. The diagnosis is made by demonstrating an anemia combined with reticulocytosis, hyperbilirubinemia, elevated lactate dehydrogenase (LDH) and demonstrating a positive direct antiglobulin test (DAT). A significant subset of patients may present atypical features, as in the following case.
Aims: Case report.
Methods: Case report.
Results: A 57 year men with diabetes and hypertension was evaluated for anemia. He has been admitted 5 months prior for cardiac surgery with cardiopulmonary bypass and requires 4 units of packed red blood cells over a ten day period. The investigation showed a regenerative anemia (hemoglobin 7.5 g/dl, MCV 83 fl, reticulocytes $90*10^9$/l), LDH 900 U/l (normal < 200). The direct antiglobulin test was positive (IgG3 + , IgA 2 +), uricemia 78 mg/l (normal 35–70).
An AHA with IgG and IgA autoantibodies direct against reticulocytes was suspected. Prednisone 0.5 mg/Kg/day was indicated and he returns to his baseline hemoglobin of 12 g/dl within 3 weeks of treatment.
Summary/Conclusions: The syndrome of AIHA with reticulocytopenia is not rare. The cause of reticulocytopenia is not well established but it is advised to examine patients for hyperuricemia.

P-461
PERCENTAGE TYPE OF CASES AIHA AT CENTRAL BLOOD TRANSFUSION SERVICE – INDONESIAN RED CROSS

E Merizka[1,2], F Rozi[3] and R Gantini[4]
[1]University of Muhammadiyah Prof. Hamka, Medical Technology [2]Research and Production [3]Blood Service [4]Head of Central Blood Transfusion Service, Central Blood Transfusion Service Indonesian Red Cross, Jakarta, Indonesia

Background: Immune hemolytic anemia is characterized by clinical and laboratory features of hemolytic anemia with direct antiglobulin test (DAT) positivity. It could be autoimmune hemolytic anemia (AIHA), alloimmune, or drug-induced hemolysis based on the antigenic stimulus.

P-463
ANTIBODY ANTI-G: AUTO OR ALLOANTIBODIES?

S Mahjoub[1], W Amara[2], A Chakroun[2], H Baccouche[3] and N Ben Romdhane[4]
[1]Hematology [2]11 rue jebel lakhdar [3]11 rue jebel lakhdar, Hopital La rabta [4]Hematology, La RABTA, Tunis, Tunisia

Background: G antigen of Rh blood group system is present either along with D and/or C positive red cells . Serologically anti-G presents with the similar picture as that of multiple antibodies (anti-D + anti-C). Differentiating them is important in pregnancies because of hemolytic disease.
Aims: This case report highlights a rare case of auto anti-G without anti-D and anti-C in a myelodysplastic patient. This report disseminates knowledge on identification of anti-G and its importance in transfused patient.
Methods: Case report.

Results: Three months after a D- female was transfused with three units of D- red blood cells (RBCs), the results of a standard pre-transfusion antibody screen detected an incompatible cross match. Immunohematologic investigations: The direct antiglobulin test (DAT) was positive to IgG (3 +) and alloantibody identification panel detected anti-C+D in his serum. This report was interpreted by his physician to be evidence of alloimmunization to the D antigen, and C antigen which triggered concern that the patient had been transfused previously with D+, C+ RBCs as the result of an error in blood typing or personal identification. Differential adsorption and elution testing were performed to distinguish anti-G from anti-D + anti-C. This auto-antibody did not seem to cause significant in vivo hemolysis.

Summary/Conclusions: Autoantibodies with mimicking specificity are rarely encountered in the routine practice. Investigation must be done to accurate rapid diagnosis and transfusion antigen negative RBC units.

P-464
FREQUENCY AND RISK FACTORS FOR RBC ALLOIMMUNIZATION IN PATIENTS UNDERGOING SURGERY IN TEHRAN, IRANTHE ROLE IN IMPROVING TYPE AND SCREENING TESTS

S Moradinasab[1] and A Gharehbaghian[2]

[1]High Institute for Research and Education in Transfusion Medicine [2]Hematology and Blood Bank, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran

Background: Today, blood transfusion has become a major part of healthcare system and alloimmunization is an important adverse effect for the patients undergoing blood transfusion. During pre-transfusion testing, the patient's blood is screened for alloantibodies and an inappropriate screening test is one of the main reasons for missing immunized patients. Therefore, performance of proper and reliable pre-transfusion tests are necessary in order to minimize the hemolytic reactions related to RBC alloantibodies.

Aims: This study was set out to determine the frequency and specificity of RBC alloantibodies detected during pre-transfusion tests in addition to risk factors of alloimmunization in the hospitalized population in Tehran, Iran.

Methods: In this retrospective study, the characteristics and type of alloantibodies in 31 alloimmunized patients among 6029 hospitalized patients (2047 males and 3982 females) with the age of 1 year to 90 years were examined in the year 2016. We carried out pre-transfusion tests, including ABO group and Rh-D type, antibody screening and compatibility testing for all the patients applied for blood transfusion. We performed antibody screening by testing a patient's plasma against a reagent of O red blood cells. Albumin was used to enhance the antigen antibody reactions. For the samples that were positive in antibody screening test, antibody identification were done with 11-cell panel, covering the US Food and Administration-recommended RBC antigens. For alloimmunized patients, demographic characteristics including sex, age, medical history, transfusion history, and pregnancy or abortion history were collected. The data were analyzed by using statistical software SPSS version 23.0 and Excel 2016, Microsoft Corporation.

Results: Totally, 50 clinically significant alloantibodies were found in 31 patients, demonstrating the alloantibody prevalence of 0.5 percent in this study with the male: female ratio of 1:5.2 (5 males, 26 females). Among alloimmunized patients, 20 patients (64.5%) had single antibody, whereas the remaining 11 patients (35.4%) had multiple alloantibodies. The 8 frequent identified alloantibodies were anti-D 15 of 50 (30%), anti-E 12 of 50 (24%), anti-K 6 of 50 (12%), anti-C 5 of 50 (10%), anti-c 4 of 50 (8%), anti-e 4 of 50 (8%), anti-jk b 2 of 50 (4%) and anti-s 2 of 50 (4%). Of all alloimmunized patients, 28 patients (90.3%) had the history of transfusion. In 26 alloimmunized females, 23 patients (88.4%) had history of pregnancy or abortions. Alloimmunised patients were between 6–78 years. Interestingly, the prevalence of alloantibody detection was significantly different between various age groups, the highest frequency was identified in patients aged 21–30 years. Patients aged more than 70 years were alloimmunized at least.

Summary/Conclusions: In this study on non-transfusion dependent hospitalized patient in Tehran, Iran, the alloimmunization rate were relatively low compared to previous studies. We investigated multi-variant factors effecting alloimmunization and female sex, age, history of transfusion and pregnancy are the risk factors of alloimmunization. In order to avoid transfusion reactions, more sensitive pre-transfusion tests for all patients in the need of blood transfusion and also the precise documentations for alloimmunized patients should be considered.

P-465
RED BLOOD CELL ANTIGENS AND RED CELL ALLOIMMUNISATION IN SCD PATIENTS IN GHANA

LA Boateng[1,2], A Campbell[3], R Davenport[4], A Akoto[5], H Schonewille[6] and S Hugan[4]

[1]Medical Laboratory Technology, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana [2]International Public Health, Liverpool school of Tropical Medicine, LIVERPOOL, United Kingdom [3]Paediatrics, George Washington School of Medicine and Health Sciences, Washington, DC [4]Blood bank and Transfusion Services, University of Michigan Health systems, Ann Arbor, United States [5]Child Health School of Medical Sciences, Kwame Nkrumah University of Science & Technology Ghana, Kumasi, Ghana [6]Department of Experimental Immunohematology, Sanquin, Amsterdam, Netherlands

Background: Transfusion therapy is vital in the management of patients with sickle cell disease (SCD). Alloantibody formation against red blood cell (RBC) antigens is a common complication of transfusion therapy. In Ghana, the practice is to transfuse ABO and D compatible RBCs without screening for RBC antibodies. The prevalence of RBC alloimmunization as well as the frequency of blood group antigens other than ABO and D in transfused sickle cell patients in Ghana is not known.

Aims: We therefore studied the prevalence and specificities of RBC antibodies and the frequencies of some minor blood group antigens in transfused SCD patients at Komfo Anokye Teaching Hospital, Kumasi, Southern Ghana.

Methods: A cross-sectional study was performed, involving SCD patients who had received at least one previous RBC transfusion. Participants' basic data on demography, transfusion and medical history were recorded. In Ghana, patients' RBC were typed serologically for D, C, c, E, e, K, Fy[a], Fy[b], Jk[a], Jk[b], S and s antigens using the tube method. Serum samples were screened and typed for RBC antibodies using column gel technique at University of Michigan reference lab, USA. Molecular genotyping was performed on patients who made antibodies to antigens they possessed.

Results: A total of 154 SCD patients, 87 males and 67 females were recruited. The number of RBC transfusions ranged from 1–20. Majority of patients received 2–4 transfusions. Only one patient received >10 transfusions.

Antibodies against 13 RBC antigens were detected in ten (6.5%) patients. One patient each had anti-E, anti-D+C, anti-C+e, anti-E+C$_w$ and an antibody against a low frequency antigen of unknown specificity, respectively. Two patients had anti-D and three patients anti-M. The patient with anti-C+e and two patients with anti-D typed serologically as C, e and D positive respectively.

DNA sequencing results for these three patients showed that the patient who made anti-C+e possessed partial C and e antigens. The two serologically D+ patients lacked the RHD gene and had variant RHCE gene that encodes for ceAG variant. Other D-like antigens occurring on RHCE previously observed had polymorphisms in exon 5, however for these two patients, the polymorphism occurred in exon 2.

Due to limited reagent availability, RBC antigen typing was performed for 105 to 133 SCD patients for the various antigens. Antigen frequencies were D 96.2%, C 36.8%, E 28.0%, c 100%, e 98.5%, K 0%, Fy[a] 4.3%, Fy[b] 3.8%, Jk[a] 75.0%, Jk[b] 46.5%, S 39% and s 94%.

Summary/Conclusions: The prevalence of RBC alloimmunisation in transfused SCD patients in Ghana was 6.5% and these antibodies were mainly directed to the rhesus antigens. Almost 40% of the Rh antibodies made were due to alteration in the RH allele.

Our findings suggest that there is the need to screen for RBC antibodies in SCD patients before blood transfusion in Ghana, however to effectively avert alloimmunisation limited antigen matching and molecular genotyping for Rh antigens are essential in the future.

P-466
ALOIMUNIZATION FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

M Raos[1], I Bojanic[1], R Serventi Seiwerth[2] and B Golubic Cepulic[1]

[1]Clinical Department of Transfusion Medicine and Transplantation Biology
[2]Department of Internal Medicine, Clinical Hospital Centre Zagreb, Zagreb, Croatia

Background: In almost all patients treated with allogeneic hematopoietic stem cell transplantation (HSCT), there is a certain degree of disparity in red blood cell (RBC) antigens. Major, minor and bidirectional ABO incompatibility can cause acute hemolysis or delayed erythropoiesis recovery in the post-transplant period. Non-ABO red blood cell alloantibodies may cause similar complications if the recipient or donor RBC expresses a specific antigen. New immunization after allogeneic HSCT, although rare in occurrence (1 to 8.7%), can also cause hemolysis.

Aims: The aim was to investigate the frequency of non-ABO alloimmunization following allogeneic HSCT, the cause of their occurrence and the specificity of alloantibodies.

Methods: Data for the patients following allogeneic HSCT in UHC Zagreb from 1991 to 2016 were retrospectively reviewed. Of the 40 patients with alloantibodies, the alloantibodies were detected before allogeneic HSCT in 19 patients, and after HSCT in 21 patients. Out of the 21 patients with alloantibodies detected after HSCT, 18 patients developed de novo immunization, in 2 passive transfer of alloantibodies with blood components was suspected and in 1 RhD immunoprophylaxis was applied.

Results: Data for a total of 772 patients were analyzed; 439 (56.9%) were male and 333 (43.1%) female. In 39 (5.1%) patients, second HSCT was performed. Out of a total of 811 transplants, 526 (64.9%) were related and 285 (35.1%) unrelated. According to the type of transplant, bone marrow (BM) was transplanted in 468 (57.8%) cases, peripheral blood stem cell (PBSC) in 319 (39.3%), cord blood (CB) in 13 (1.6%), selected CD34 + cells in 5 (0.6%), BM + PBSC in 4 (0.5%) and PBSC + CB in 2 (0.2%). The recipient and the donor were ABO identical in 405 (52.5%) of the HSCT. Major incompatibility appeared in 166 (21.5%) HSCT, minor incompatibility in 156 (20.2%), and bidirectional incompatibility in 45 (5.8%). The recipient and donor were RhD identical in 616 (79.8%) and RhD was incompatible in 156 (20.2%) HSCT. Alloantibodies were detected before HSCT in 19 (2.5%) patients and in 2 (0.2%) donors. After allogeneic HSCT, 18 (2.5%) patients developed a new immunization. None of the patients with de novo immunization had been previously immunized. Seven patients developed one alloantibody, and 11 of them had multiple alloantibodies; a total 33 alloantibodies of different specificities. The most frequent were antibodies from the Rhesus blood group system: anti-E (10), -C (7) and -D (6). The average time from transplantation to alloantibody detection was 10.5 months. The causes of new immunization were: donor lymphocyte exposure to the recipient's RBC (6), transfusion with blood components after HSCT (3), combination of the first and second cause (4), antibodies possibly generated by the B lymphocytes of the recipient (1), and in 4 patients the cause of alloimmunisation was unknown due to missing data.

Summary/Conclusions: In patients treated with allogeneic HSCT, there is a risk of developing new alloimmunization, due to exposure of donor lymphocytes to RBC of the recipient, or transfusion therapy with antigen incompatible blood components. After allogeneic HSCT, our patients developed alloantibodies of the Rhesus, Kell, MNS and Lutheran blood group systems that can cause significant hemolysis and complicate the course of recovery. Since some patients develop alloantibodies despite intensive immunosuppressive treatment, continuous immunohematological monitoring is required for patients following HSCT.

P-467
ALLOIMMUNIZARTION RATES IN THALASSEMIA MAJOR PATIENTS

L Kasraian[1], M karimi[1] and N naderi[2]

[1]Blood Transfusion Research Centre, High Institute for Research and Education in Transfusion Medicine, Shiraz, Iran, Blood Transfusion Research Centre, High Institute for Research and Education in Transfusion Medicine, Shiraz, Iran
[2]Anesthesilogy Department, Shiraz University of Medical Science, Shiraz, Islamic Republic of Iran

Background: Development of antibodies (alloantibodies and autoantibodies) against (RBC) antigens is one of the most significant side effects of chronic blood transfusions This study was conducted to estimate the rate of immunization to red blood cell (RBC) in thalassemia major patients.

Aims: The ultimate aim of this study was to evaluate the frequency and causes of immunization to RBC in TDT patients to facilitate future developments in the treatment of these patients.

Methods: This cross -sectional study was conducted on 732 thalassemia major patients in Shiraz, Iran.. The frequency and the type of antibodies were surveyed by coombs test, antibody screening, and antibody identification tests

Results: RBC immunization was found in 93 patients (12.7%). Indirect agglutination test (IAT) was positive in 59 patients (63.4%) while direct coombs tests (DAT) was positive in 41 (44%) of the immunized patients. In addition,7 patients (7.52%) showed positive results for both DAT and IAT. The most frequent antibodies were against Kell (34.4%), D (17.2%) and E (14%).

The results indicated that gender, age of starting transfusion and splenectomy did not have any impact on the immunization rate

Summary/Conclusions: In this study, the alloimmunization rate was 9.01%. Antibodies against Rh and Kell system were found to be the most frequent antibodies. The findings showed that at least RBC matching, for Rh and kell antigens also must be considered for preparing blood in thalassemia patients

P-468
PREVENTION AND MANAGEMENT OF RED BLOOD CELL ALLOIMMUNIZATION IN THALASSEMIA

A Pourfathollah and A Sedaghat

High Institute for Research and Education in Transfusion Medicine, Iranian Blood Transfusion Organization, Tehran, Islamic Republic of Iran

Background: Since Iran is located on the "thalassemia belt", the prevention and treatment of thalassemia major is one of the priorities of national health governance in the country. Currently there are more than 18000 patients of thalassemia major in Iran.

Aims: - Provides constant compatible, safe and adequate blood and blood products for thalassemia patients.
- Prevention and treatment of thalassemia major is one of the priorities of national health governance in the country

Methods: The national thalassemia prevention plan was started in 1997. Considering the few number of new patients, it has been proved as one of the successful plans in developing countries. The prevalence of alloimmunization among Iranian thalassemia patients has not been decreased from 1994 to 2013 in Iran. However, the rate is considerably low comparing to other countries. Although there are some strategies to reduce the risk of RBC alloimmunization, finding compatible RBC units for patients with thalassemia has remained a big challenge. IBTO provides constant compatible, safe and adequate blood and blood products for thalassemia patients. Also, pre-storage leukoreduction is applied to all thalassemia patients. There is reference and subsidiary clinical centers throughout the country which provide health services to the patients according to the protocols set by the Iranian Ministry of Health.

Results: As a part of mitigation strategy to manage the alloimmunization, IBTO is recommended to perform matching protocol for K antigen of Kell system for the most prevalent of Rh alloantibody in patients with thalassemia like D, C and E of Rh system. Secondly, personalized medicine and giving the most appropriate transfusion before the formation of alloantibody prevents the severe complications to find the compatible RBC units. Lastly, performing the screening programme to find the donors with the same phenotype of RBC-specific antigens may be helpful to make a pool of donors with the same expression of the most immunogenic RBC antigens such as Kell and Rh other than D antigen.

Summary/Conclusions: In conclusion, by appropriate policymaking and defining more sensitive pre-transfusion tests like molecular typing of D variants, the prevalence alloimmunization may reduce dramatically in Iran.

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RED BLOOD CELL ALLOANTIBODIES: PREVALENCE AND SPECIFICITY AMONG BLOOD DONORS IN BIKANER (RAJASTHAN), INDIA

S Vashistha, D Arya, N Mahawar, A Bharti, K Purohit, M Mehra, S Raheja and K Mehra

Department of Immuno Haematology & Transfusion Medicine, Sardar Patel Medical College & Associated Group of Hospitals, Bikaner, India

Background: Alloantibodies against red blood cell (RBC) antigens can significantly complicate blood transfusions and can cause difficulties in pre transfusion compatibility testing causing delay in the availability of blood units even in emergency indications.

The prevalence of alloimmunization is extremely variable depending upon the population being studied. In India, till date, most literature on alloimmunization is limited to multi-transfused patients, with a very few studies on healthy blood donors.

Blood donors are the only source of all kinds of blood components for various transfusion therapies. They must be "typed and screened" to make the right blood units available to the needy ones at the right time.

Aims: This study was aimed to determine the prevalence and specificity of RBC alloantibodies among healthy blood donors in India.

Methods: ABO-Rh(D) typing, antibody screening and identification tests were performed on the samples collected from blood donors (n = 19231) on Immucor Galileo Neo fully automated immunohematology analyzer, during the period from April 2017 to October 2017.

ABO-RH(D) blood grouping was performed using Direct Hemagglutination Microstrips with reagents provided by the manufacturer.

Screening and identification were performed using commercially prepared Capture LISS, Capture-R Ready-Screen Pooled cell, 3 cell and Ready-ID 14 cell panels based with Solid Phase Red Cell Adherence (SPRCA) technology.

Results were interpreted using the antigram supplied. Appropriate statistical tests of significance were applied and results were analyzed using SPSS version 16, PRIMER and MS Excel software with Yate's correction applied.

Results: 0.12% (23/19231) donor samples were screened positive for RBC alloantibodies. 80% (4/5) cases from 18–25 years of age group, 25% (1/4) cases from 36–45 years of age group and 12.5% (1/8) cases from 26–35 years of age group had developed multiple alloantibodies (P = 0.041).

Out of 23 positive cases, 17 were identified to have 23 alloantibodies (0.12% prevalence). Alloantibodies against MNSs system antigens were observed to be the most frequent (8/23 cases, 34.8%), followed by Rh system (6/23, 26.1%) and Kell system antigens (5/23 cases, 21.7%). The most common individual alloantibody identified was anti K (5/19231, 0.03%), followed by anti M antibodies (3/19231, 0.02%). Anti D, Anti Fyb, Anti N and Anti S revealed to have frequency of (2/19231, 0.01%) each. 2 cases were classified as exhibiting Solid Phase Phenomenon (SPP), since all the panel cells were reacting on solid phase but no positive reaction was observed on other techniques (tube and column) in liquid phase. Specificity of 4 cases could not be determined on the cell panels used and methods adopted in the study.

Alloimmunization rate was observed significantly higher among females (1.84%; 5/272) as compared with that among males (0.09%; 18/18959) (P < 0.001%). No significant association was observed between ABO/Rh(D) blood group types and alloimmunization.

Summary/Conclusions: Occurrence of alloantibodies is not uncommon among the blood donors; being more prevalent particularly in female donors, mostly because of child bearing. The pattern of specificities of alloantibodies identified in this study tells us that alloantibodies of MNSs, Kell and Rh blood group systems are the most commonly encountered.

Blood Banks should be sensitized for the importance of antibody identification and it should be performed on hundred percent donor samples along with the patient samples so as to make compatible blood units available to the needy ones on time.

P-470

TRANSFUSION THERAPY IN PATIENTS WITH COMPLEX ANTIERYTHROCYTE ALLOIMMUNIZATIONS IN THE BLOOD TRANSFUSION INSTITUTE OF SERBIA IN 2017

N Mladenovic, B Zivotic, N Strbac, B Vasiljevic Jovanovic, A Vlatkovic, S Milutinovic, R Dinic, V Lukic and G Bogdanovic

Blood Transfusion Institute of Serbia, Belgrade, Serbia

Background: It is often very difficult to timely secure adequate RBC units for alloimmunized patients, especially for patients with complex alloimmunizations. On 21st February 2013, the Lombardy rare donor programme defined criteria for complex antierythrocyte immunizations: patients with 3 or more antibodies, 2 or more alloantibodies with autoantibodies and antibodies to high frequency antigens, thus suggesting establishment of rare blood type donor registers and banks of rare blood types. In February 2012, formation of the National Typed Donors Register (NTDR) was initiated at the Blood Transfusion Institute of Serbia (BTIS), a database with over 1,500 members.

Aims: Incidence and analysis of complex alloimmunizations from 1st January till 31st December 2017 in patients at the Department of pretransfusion testing, blood and blood products distribution and hemovigilance of the BTIS, as well as the methods of their transfusion treatment.

Methods: Retrospective study performed from January 1st till December 31st 2017, was based on data collected from the register and the ISBT IT database including 33 650 patients, for which pretransfusion testing was performed. All clinically significant antierythrocyte antibodies were identified at +37°C using gel method on Bio-Rad anti IgG rabbit ID Liss/Coombs or Bio-Rad NaCl cards/enzyme, using standard or papain treated ID Bio-Rad panel Cells. Antibody identification at +4°C and at room temperature was performed by tube method using Rea Cell commercial test erythrocytes. Blood type phenotypes were determined using different test reagents (Sanguin-Pelikloon, Bio-Rad and Lorne).

Results:: In 630 (1,9%) patients, it was necessary to identify antierythrocyte antibodies due to positive antibody screening, positive interreactions and problems in blood group determination. There were 13 (2.06%) patients with three detected alloantibodies, four had 4 antibodies (0.64%), one (0.2%) had 5 antibodies, i.e. total of 19 patients with complex immunisation (0,06% of the total number of patients for which pretransfusion testing was performed). The most frequent combination with three antibodies was D+C+E in Rh negative patients. All patients with complex immunization had at least one Rh antibody. The most frequent antibodies were of E and Kell specificity. Complex antibodies were most common in hematological (36.8%) and oncological (21%) polytransfused patients, age 50 to 60 years (31.6%)

and female patients (68.4%). For the majority, adequate RBC units were provided by negative interactions and typing of those RBC to antigens against which antibodies were not produced. Finding one unit with negative interaction mostly required testing of up to 10 RBC units, and in one case even 82 units. Thanks to the NTDR, blood was provided for 4 patients (11 donations in total) and for 1 patient autologous transfusion (3 predeposits) was used.

Summary/Conclusions: Alloantibodies were identified in 1.9% of patients, out of which 0.06% had complex alloimmunisation. Establishment and enlargement of NTDR contributed to the increase of typed blood stocks, which facilitated and shortened adequate blood searching procedure needed for patients with complex immunizations, especially in emergency situations.

P-471

FOUR ALLO ANTIBODIES IN A MULTIPLY TRANSFUSED SICKLE CELL DISEASE PATIENT AT SEYED AL SHOHADA HOSPITAL IN ISFAHAN, IRAN: A CASE REPORT

S Hemmati Bardehshahi[1], A Talebi[2] and M Jalali Far[3,4]

[1]Blood Bank, Seyed Al Shohada Hospital of Medical Science University of Isfahan [2]Pathology, Isfahan University of Medical Sciences, Isfahan [3]Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran [4]Health Research Institute, Research Center of Thalassemia & Hemoglobinopathy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Islamic Republic of Iran

Background: Sickle cell disease (SCD) is congenital homozygote hemolytic anemia. Blood transfusion for sickle cell disease (SCD) is a common therapeutic method, however, Allo-immunization due to blood transfusion remains the main Complications for patients with frequent transfusion background. Similarly, delayed hemolytic transfusion reactions(DHTR) is one of the life-threatening reactions which triggered by undetectable titer of alloantibodies produced during previous transfusion. The most frequent Allo-antibodies in SCD patients belong to the Rh, Kell, Kidd, Duffy, and MNS blood group systems respectively.

Aims: In this study we are focusing on reporting an unprecedented case of sickle cell with vaginal hemorrhage who represent unexpected reduction on hemoglobin level and incompatibility in cross matches after transfusing one red blood cell unit. Despite the intensive efforts both in Isfahan's and Tehran's blood transfusion organization, finding compatible red blood cells among donors, was not successful.

Methods: A 36 years old woman with SCD diagnosis and vaginal hemorrhage was referred to Seyed Al Shohada hospital (specialized center for cancer and other hemoglobinopathies in Isfahan city, Iran). To control the patient's condition, one packed blood cell unite was transfused. After transfusion her hemoglobin represent 0.5 mg/dl unexpected reduction. Indirect anti-globulin test (IAT) and direct anti-globulin test (DAT) were performed by using standard blood bank's methods (saline, 37°C with albumin, and Coomb's phases) to determine formation of Allo- antibodies and Auto-antibodies. In order to identify Allo-antibodies screening cells (Sets of 2 or 3 vials) and Panel Cells (At least 10 vials per set each of the panel cells has been antigen typed and an auto-control should also be run) are conducted and Patient RBCs are serologically phenotyped by commercial anti-serums for C, c, E, e, K, k, M, N, S, s, Fya, Fyb, Jka, Jkb in order to confirm the accuracy of antibody specification.

Results: Screening cells and Panel cells determined formation of 4 Allo-antibodies in patient serum. (Anti-C, Anti-e, Anti-s, Anti-Jkb). Patient RBCs phenotype The patient's phenotype is as follows: C-, c+, E+, e-, K+, k+, Fya+, Fyb-, Jka+, Jkb-, M-, N+, S+, s-.

Summary/Conclusions: Since Rh System Antigens cause the major number of Allo-immunization in sickle cell patients, providing matched red blood cells in Rh system would decrease Allo-immunization rate. Although, regarding to the local potential antibodies among the sickle cell patients we can apply appropriate strategies to prevent Allo-immunization, there is no authenticated data over the frequent Allo-antibodies among Sickle cell patients and common antigens of indigenous donors in Isfahan city Which requires further research in this regard.

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RED BLOOD CELL ALLOIMMUNIZATION IN A PORTUGUESE HOSPITAL

C Monteiro, L Gonçalves, A Leite, H Sousa, B Fortunato, T Ventura, J Baldaque, F Baia and C Koch

Department of Transfusion Medicine and Blood Bank, Centro Hospitalar São João, EPE, Porto, Portugal

Background: Individuals exposed to red blood cell alloantigens through transfusion, pregnancy or transplantation may produce antibodies against alloantigens. Since June 2009, its our policy when feasible to transfuse women of child bearing potential and transfusion dependent patients with Rh and K phenotype-matched blood.
Aims: Centro Hospitalar São João, EPE is the biggest hospital in the north of Portugal. It is a highly specialized tertiary hospital with 1142 beds, level 1 trauma centre, a large cardiothoracic surgery centre and a hemato-oncology department. The aim of this study is to report the frequency and specificity of red blood cell (RBC) alloantibodies in Centro Hospitalar São João, EPE (CHSJ) and evaluate our transfusion policies.
Methods: A total of 32069 recipients of blood products were analysed in order to evaluate the alloantibodies detected, during the period of 2010 to 2017. Data from January 2010 to December 2017 were retrieved from the blood bank database. The following information was collected: age, gender, the number and specificity of alloantibodies and whether the patient had previous alloantibody screening negative (new alloantibodies).
Results: 1031 recipients had positive screening for alloantibodies: 562 had alloantibodies at admission and 469 recipients had new alloantibodies detected following transfusion. Our detection frequency was 3,16% and our immunisation frequency was 1,46%. In the group of recipients with new alloantibodies, Anti-E was the most frequent alloantibody detected, followed by anti-D and anti-K, with no significant differences between genders. Our distribution pattern was E> D> K> Jk^a> C. We also monitor compliance with our policy regarding transfusion practice in women of child bearing potential.
Summary/Conclusions: The identification of RBC alloantibodies developed after transfusion in our hospital allowed us to detect errors in blood components selection. In order to increase safety in transfusion practice, several measures can be applied, as performing a repeat Rh/K phenotype of blood donors or identify RhD variants in apparently Rh D negative donors.

P-473

EDUCATING RARE DONORS – WHY IS THIS IMPORTANT?

T Powley, B Wilson, Y Liew and J Daly

Clinical Services and Research, Australian Red Cross Blood Service, Brisbane, Australia

Background: During a follow up conversation about routine full blood count results a donor mentioned that he had an unusual Gerbich blood group to the Blood Service Medical Officer.
Aims: The Medical Officer contacted the Red Cell Reference Laboratory team who were unable to find anything in the donor's record to suggest a known history of this rare type. The donor was contacted for additional information to assist with further investigation and to provide a sample for testing.
Methods: Following a number of conversations with the donor it was established that the donor's rare blood group was identified twenty years earlier when the donor's father was being treated in the UK and it was identified that his father had a rare Gerbich blood type making blood transfusion difficult. The donor stated that his mother and ten siblings were all tested in the UK and they all have the same rare blood type. The family is Caucasian but the donor alluded to "other" ethnic groups in his ancestry. The Australian Red Cell Reference Laboratory contacted the International Blood Group laboratory (IBGRL) in the UK for any information they may have about this donor and his family whilst further testing was conducted.
Results: The IBGRL confirmed that this donor was known to them and had been tested in a very large family study twenty years earlier. Their results indicated that the donor was Ge:-2,3,4 due to being a compound heterozygote GPC.Ge/GPC.Yus (deduced by immunoblotting studies). Testing was performed by the Australian Red Cell Reference laboratory and serology testing revealed the donor was O RhD positive GE:-2,3 and blood group targeted DNA sequencing analysis predicted the GE*01.-02/*01.03 genotype confirming the GE:-2,3,4 phenotype, which is the very rare Yus type.
Summary/Conclusions: This donor is a particularly rare and useful phenotype not only for transfusion, but as a reagent red cell for serology investigations and has been donating in Australia for 9 years before being identified as a rare donor

through a routine unrelated conversation with a Medical Officer. The Blood Service missed 15 whole blood donations that may otherwise have been frozen for future transfusion and have unwittingly recruited this donor to apheresis plasma missing out on valuable whole blood donations.
Better education of our rare donors and the use of cards to identify donors or patients with rare blood groups may help with self-identification as a rare donor. It is also important that our staff within donor recruitment and collection have the information necessary to ensure donors that do self-identify are managed effectively. Education is a key part in ensuring that we do not miss the needle in the haystack.

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POLYMORPHISM OF DIEGO BLOOD GROUP AND FREQUENCY OF IGG-DI^A IN SHAANXI PROVINCE

Q Zuo

Blood group laboratory, Shaanxi Blood Center, Xi'an, China

Background: Diego blood group antibodies can cause hemolytic disease of the newborn and hemolytic transfusion reactions. Not the same as the European, Chinese population have a high frequency of Di^a antigens. Thus, there have a higher probability of IgG-Di^a antibody by random blood transfusion and maternal-child blood group incompatibility.
Aims: To investigate the distribution of Diego blood group polymorphism in Shaanxi population and the frequency of IgG-Di^a antibody in transfused patients.
Methods: Genomic DNA was extracted from 1068 blood donors in Shaanxi province. Diego blood group was genotyped by touchdown polymerase chain reaction. IgG-Di^a frequency was identified by indirect antiglobulin test and statistical analysis in 386 blood transfusion patients with irregular antibody during 2016–2017.
Results: One Di (a+b-), 52 Di(a+b+), 1 015 Di (a-b+) and no Di (a-b-) have been detected in 1068 blood donors. The frequency of Di^a antigen and gene was 0.049 63 and 0.025 28 respectively, and the frequency of Di^b antigen and gene was 0. 999 06 and 0.974 72 in blood donors. 19 IgG-Di^a were identified in the 386 patients who were positive for irregular antibodies screening, the frequency was 0.049 22.
Summary/Conclusions: In this study, through detecting and analysing the Diego blood group in blood donors in Shaanxi Province of China, we discovered the Diego blood group polymorphism which play a vital role in genetics/forensics and blood transfusion. Our study first reported that high frequency of IgG-Di^a antibody occurred in the clinical specimen with irregular antibodies in China, so we should be pay special attention to it. Because the important clinical significance of IgG-Di^a antibody, when detected irregular antibodies, the panel cells we used in routine work should include Dia antigen to avoid false negative results of IgG-Di^a in antibody screening.

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THE MNS VARIANTS IN THAI BLOOD DONORS

K Kerdkaewngam, P Ovataga, J Tubrod, U Tingtoy and U Charoonruangrit
National Blood Center, Thai Red Cross Society, Bangkok, Thailand

Background: The MNS variants are very complex. The antibodies of this subsystem have been found 43.3% of total antibodies in Thai patients. Therefore it is necessary to carefully select cells for antibodies screening cells, since some subclasses such as GP.Hut (MiII) and GP.Hop (MiIV) failed to react with some of MNS variant antibodies.
Aims: To study MNS variant phenotypes in Thai blood donors in order to select suitable donors for screening cells production.
Methods: A total of 1,019 blood samples were phenotyped by using saline standard tube technique for anti-Mur and column agglutination technique (Bio-Rad) for anti-MUT, anti-Vw, anti-Hil, anti-Hop and anti-Anek (anti-Hop+anti-Nob). These mentioned antibodies were kindly supplied by Kanto-Koshinetsu Block Blood Center, Japanese Red Cross, Tokyo.
Results: It is revealed that 6 donors (0.59%), 935 donors (91.76%), 9 donors (0.88%) and 69 donors (6.77%) were GP.Hut (MiII), GP.Mur (MiIII), GP.Hop (MiIV) and GP.Bun (MiVI) respectively.
Summary/Conclusions: The results showed that GP.Mur (MiIII) was the most MNS variant subclasses in Thais. GP.Hut (MiII), GP.Hop (MiIV) and GP.Bun (MiVI) were rare phenotypes. The previous study in Thais by Chandanyingyong et.al. (1975) indicated that the most common was GP.Mur (MiIII) which was confirmed by this study. These results were useful for selecting suitable red blood cells for our screening cell production.

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AN ATTRAVTIVE REPORT OF VARIENT M-ANTIGENE

H Sheibani[1] and M Moghaddam[2]

[1]Immunohematology, Blood Transfusion Center, High Institute for Research Center and Education in Transfusion Medicine [2]Immunohematology, Blood Transfusion Center, High Institute for Research Center and Education in Transfusion Medicine, Tehran, Islamic Republic of Iran

Background: Following the discovery of the ABO blood group system, the MNS system was the second blood group system to be recognized. 22–30% of the peoples lack the M antigen on their red blood cells and therefore are capable of producing anti-M when exposed to the antigen. Anti-M is discussed a naturally occurring antibody that is usually active at temperatures below 37°C and is thus of no clinical significance. This antibody, if present in an individual, can lead to a discrepancy between forward and reverse ABO grouping and then creates diagnostic difficulties for blood bank staff.

Aims: We report a case of variant M-antigen that was referred to the immunohematology laboratory as blood group discrepancy.

Methods: A blood sample of a 28-year-old lady was received to Immunohematology Reference Laboratory as blood group discrepancy. She was admitted to the hospital for delivery. Her hemoglobin was 7.0 g/dl and she never received any blood transfusion. Cell grouping of patient was A positive, while reverse (serum) grouping showed agglutination with A1cell. Antibody screening was done using Low Ionic Strength Solution (LISS) with both gel technique (ID microtyping system) and conventional test tube method. Her serum tested with commercially available three cell panel. Result showed positive reaction with panel I and III, while negative with panel II. For antibody Identification, 11-cell panel was used which identified anti-M antibody and it was confirmed by selected cells antibody ID panel. Patient's sera showed 4 + reaction with M+N-cells, 3 + reaction with M+N+ cells, but negative with M-N+ cells. Subsequently, patient phenotype was considered completely. The anti-M titers were 64 with M+N-homozygous cell, while 16 with M+N+ heterozygous cell at AHG phase. It was interesting that, the patient's blood with two M-antisera from different companies [(Immundiagnostik, LOT: 0MM113, Clone NO: M-11H2) and (SIFIN, LOT: G40710, Clone NO: M-11H2)] showed a positive reaction, despite the third antisera (LORNE, LOT:31160A) that no reaction was seen. It is remarkable, both of antisera with positive reaction had a same clone number and negative antisera was polyclonal. In addition, direct antiglobulin test (DAT) and autocontrol were negative.

Results: it is important to type specificity of anti-M antibody with accuracy as it can influence clinical outcome and strict warm conditions should be maintained during the procedure and results should be read immediately.

Summary/Conclusions: Anti-M is more common in children than adults, and it is not uncommon for pregnant M-woman to produce anti-M but to give birth to an M-body. Very few cases have been reported of anti-M to be Ig-G type and there is no clinical consensus on the management of HDN caused by anti-M alloantibody. On high titer IgG plus IgM anti-M was responsible for neonatal red cell aplasia and caused a substantial reduction in proliferation of erythroid cells in culture. Anti-M antibodies with high titer and high affinity may react strongly at room temperature and cause hemagglutination to carry through 37°C and the antiglobulin test phase, therefore, it is important to type specificity of anti-M antibody with accuracy as it can influence clinical outcome and strict warm conditions should be maintained during the procedure and results should be read immediately.

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FREQUENCY OF DEL VARIANT IN CHILEAN BLOOD DONORS

J Caamaño[1,2], J Moraga[2], A Contreras[2], C Iturra[2], F Moraga[2], D Navarrete[2] and N Saavedra[3]

[1]Medicina Interna, Universidad de La Frontera de Temuco, Chile [2]Facultad de Salud, Universidad Santo Tomas [3]Ciencias Básicas, Universidad de La Frontera, Temuco, Chile

Background: Routinely, individuals are classified as Rh positive or negative depending on the presence or absence of D antigen on the membrane of red cell. However, D antigen might present qualitative and quantitative alterations that are more difficultly detected. Among them, DEL variant is characterized by an extremely weak expression of D antigen, which cannot be detected by conventional testing and therefore is mistyped as Rh D negative. Molecular analysis of DEL individuals showed an intact D gene or a partial DEL with losing of detectable D epitope, being these phenotypes associated with some genetic variants. In Chilean population the frequency of RhD negative phenotype has been previously reported. However, the frequency of D variants including DEL and DNA alterations related to these D variants remains unknown.

Aims: To describe the frequency of DEL phenotype and 1227A>G and M295I genotypes in Chilean blood donors.

Methods: 125 RhD negative samples were selected from unrelated blood donors attended at the Blood Bank in Hernan Henriquez Aravena Hospital (Temuco, Chile), which were classified using Anti-D (Rho) IgM/IgG monoclonal antisera by direct agglutination test. Then, resulting D negative samples were analyzed by indirect antiglobulin test using gel cards. Additionally, Rh DEL phenotype was detected by adsorption/elution test. The 1227A>G and M295I genotypes were detected by polymerase chain reaction.

Results: 118 samples (94.4%) were positive to adsorption/elution test, confirming DEL phenotype. Then, molecular analysis performed on these samples showed frequencies of 27.97% (n = 33) and 10.17% (n = 12) for 1227A>G and M295I variants, respectively. Moreover, 46.61% (n = 55) of analyzed samples showed the presence of both genetic variants.

Summary/Conclusions: The data demonstrated a high frequency of the DEL phenotype in the population studied. The molecular analysis of 1227A> G and M295I shows that these variants are present in a high percentage and can be used as useful genetic markers for RhDEL in Chile, in replacement of the adsorption-elution test.

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DETERMINATION OF WEAK "D" ANTIGEN AMONG RHESUS NEGATIVE PAKISTANI BLOOD DONORS

M Ahmad[1,2], M Saeed[3], U Waheed[4], A Hanif[5], M Hamid Rahmani[6] and N Awan[1]

[1]Department of Chemical Pathology,, University of Health Sciences, Lahore, Punjab, Pakistan [2]Department of Blood Bank/Transfusion Medicine, Punjab Institute of Cardiology [3]Department of Pathology, Allama Iqbal Medical College Lahore, Lahore [4]Safe Blood Transfusion Program of Pakistan, Safe Blood Transfusion Program of Pakistan, Islamabad [5]Medical Laboratory Technology, Government College University, Faisalabad [6]Department of Pathology, Sahiwal Medical College, Sahiwal, Pakistan

Background: Until the 19th century the blood transfusion procedure was unsafe, but this mystery was solved in 29th century with the discovery of ABO and Rh blood group antigens. The discovery of Rh system by Levine and Stetson in 1939 was great to break through in transfusion medicine. It is the most significant blood group system after ABO. Studies have shown that a significant proportion of patients who's RBCs lack "D" antigen makes anti-D, if they have exposed to the "Weak D" antigen by blood transfusion. Therefore, determination of Rhesus (Rh) phenotype is of critical importance.2 Anti-D of the Rh blood group system is clinically important. It causeshemolytic transfusion reactions (HTR) and hemolytic disease of newborn (HDN).

Aims: This study was planned for the determination of weak "D" antigen, to highlight the importance of "Weak D antigen Testing" among the Rhesus-negative blood donors.

Methods: Five different tertiary care and four secondary care hospitals of Lahore and six different institutes/universities including individuals visiting to blood banks for determination of their blood groups were included in study. Two ml of blood sample was collected in EDTA-containing vial and analyzed for determination of ABO/Rhesus (Rh) typing; all Rh-negative samples were further processed for the Weak D antigen Testing according to standard protocol and commercially available monoclonal antibody.

Results: Out of total 55,874 participants only 8.0% (n = 4,454) were Rh-negative. Among these Rh-negative samples, 99.0% (n = 4,410) samples were negative even after "Weak D Testing". Only 0.98% (n = 44) were weak "D" positive, in Rh-negative samples.

Summary/Conclusions: Every Rh-negative individual should be processed for the detection of Weak "D" antigen by "Weak D antigen Testing" as it may not be detected by immediate spin tube method.

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PREVALENCE OF RH BLOOD GROUP ANTIGENS IN BLOOD DONORS AT THE BLOOD BANK OF VOJVODINA

J Grujic, Z Budakov Obradovic, Z Gulan, B Pekovic, M Krga Milanovic and G Dimitrijevic

Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia

Background: The Rhesus (Rh) blood group system was discovered more than 70 years ago and became second in importance after ABO blood group in transfusion medicine, due to its highly immunogenicity.

Highly polymorphic genes RHD and RHCE encode Rh blood group antigens There are more than 50 antigens in Rh blood group system but most significant are D, C, E, c and e.
Aims: To establish the frequency of major Rh blood group antigens in voluntary blood donors in Vojvodina.
Methods: A prospective study was conducted on 1000 blood donors during one year in 2017. Rh blood group typing was performed by standard gel technique. Statistical significance was analyzed with chi-square test and descriptive statistics for the categorical variables were performed by computing the frequencies in each category.
Results: A total of 1000 blood samples were phenotyped. Blood group O in tested samples was present in 71,5% among tested blood donors, blood group A in 25%, B in 2,5% and AB in 1%. Results showed that the most common Rh is "e" antigen (98.5%), followed by D-85,2%, C-71,7%, c-83,3% and E-28.8%. Among Rh positive donors the most common phenotype is DCcee (66.4%) and the least common phenotype is Dccee (0.1%). Analysing results of Rh negative blood donors it showed that the most common phenotype is ddccee (99,8%) and the rarest were ddCcee (0,1%) and ddccEe (0,1%).
Summary/Conclusions: Phenotyping red cells routinely in Rh blood group system would decrease alloimmunization of patients and occurrence of delayed hemolytic transfusion reaction. The presence of database with phenotyped blood donors would help providing antigen negative blood to patients and improve blood safety

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ABO AND RH PHENOTYPE FREQUENCIES IN DRUZE POPULATION IN NORTHERN ISRAEL

HJ Morani[1], S Arshed[1], O Salalha[1], M Matanes[2], E Eshel[1], Y Zivony[1] and N Dally[1]
[1]Blood Bank, Ziv Medical Center, Safed [2]Blood Bank, Ziv Medical Center, Mielya, Israel

Background: ABO and Rh Phenotype frequencies of local populations can influence the management of blood bank stock and supply in order to better serve the patient population. In Northern Israel where the Druze population is approximately 30% of hospital patients, no blood bank data has previously been presented regarding ABO and Rh phenotype frequency
Aims: This study examined the ABO and Rh phenotype frequency in the Druze patient population of the Ziv Medical Center
Methods: ABO and RhD were examined in 1,000 Druze patients through retrospective record analysis. Rh phenotype and Kell phenotype were prospectively examined in 100 Druze patients over 2017
Results: Within the Druze population the frequency of ABO blood groups was found to be: A 45%, B 14%, O 35%, and AB 6%. The antigen frequencies were: RhD 82%, Kell 5%, C 29%, E 11%, c 88%, e 95%, cw 1%. The current frequency of ABO blood groups in the international Caucasian population is: A 43%, B 9%, O 44%, and AB 4%. The antigen frequencies are: RhD 85%, Kell 9%, C 68%, E 29%, c 80%, e 98%, cw 2%
Summary/Conclusions: The overall Israel frequency of blood type A differs from the international Caucasian population: 36% vs 43%. The Druze population is similar in frequency to the international Caucasian population, however blood bank stocks are based upon local frequency. Thus, in the northern area of Israel which serves the Druze community, it is important to increase the available stock of type A blood units. More importantly, our novel finding of the significantly lower C antigen frequency in the Druze population reveals an increased risk for developing anti-C antibodies. This may majorly impact the transfusion policy in the hospitals serving the Druze community by providing blood units which are C negative

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PREVALENCE AND SPECIFICITY OF RED CELL ANTIBODIES IN A SRI LANKAN TAMIL POPULATION IN NORTHERN PROVINCE OF SRI LANKA

CD Senevirathne[1], I de Alwis[2], D Kodithuwakkuarachchi[3], T Sarmila[4] and U Gunawardhana[5]
[1]Transfusion medicine, Teaching Hospital Jaffna, Jaffna [2]Transfusion medicine, National Blood Transfusion Service, Colombo [3]Transfusion medicine, District General Hospital Mullaithivu, Mullaithivu [4]Transfusion medicine, District General Hospital Kilinochchi, Kilinochchi [5]Transfusion medicine, Base Hospital Point pedro, Point pedro, Sri Lanka

Background: Sri Lanka is a country of multiple ethnicities and its population comprises of 75% with Sinhalese, 11.2% with Sri Lankan Tamil, 9.3% with Sri Lankan Moors, 4.1% by Indian Tamil, 0.2% with Sri Lankan Malays.

The Sri Lankan Tamils; the second largest ethnic group of the country, live in all parts of the country. But 43.49% of them live in Northern Province (NP).
Aims: This study is to determine the prevalence and the specificities of red cell antibodies in Sri Lankan Tamil population who mostly inhabit in NP.
Methods: Retrospective analysis was done in antenatal mothers and hospitalized patients who underwent pre-transfusion compatibility testing, in four major hospitals in NP during 1st of January 2015 to 31st of December 2017. All samples were tested for ABO and Rh D typing and for red cell antibodies with 3 cell panel by 37°C Indirect Antiglobulin test.
All antibody screening positive samples were sent to Immunohematology reference laboratory (IHRL) at National blood center (NBC) to identify the specificities using commercial red cell panel from Orthoclinical Diagnostics and Diamed.
Results: Total antibody screenings were 63, 936 from antenatal mothers and patients for pre- transfusion compatibility testing. Red cell antibodies were detected in 110 samples with 0.17% prevalence. The allo-antibody prevalence was 0.13% (89) and auto antibody prevalence was 0.03% (21).
The results showed that frequencies of antibody specificities are Anti D in 28 (25.4%), Anti Le [b] in 26 (23.6%), Anti Le[a] in 11(10%), Anti Le[a]+ Le [b] in 06(5.4%), Anti E in 03(2.7%), Anti Mur in 03 (2.7%), Anti D+ Anti Le [b] in 02(1.8%), Anti Fy [a] in 02(1.8%), Anti c in 02(1.8%), Anti Jk [a] + Auto antibody (Cold) in 02(1.8%), Anti Fy [b] in 01 (0.9%), Anti Jk [b] in 01(0.9%), Anti Jk [b] + Auto antibody in 01 (0.9%), Anti M in 01 (0.9%), Cold auto antibody in 08 (7.2%), Warm auto antibody in 05 (4.5%), Both Cold & Warm auto antibody in 07 (6.3%).
There is significant association between the whole Sri Lankan and Northern Tamil populations in Anti D (χ^2 = 24.008, P = 0.001), Anti Le[b] (χ^2 = 5.04, P = 0.024), Anti Le[a]+ Le[b] (χ^2 = 8.651, P = 0.032), and Anti E (χ^2 = 5.934, P = 0.014)
Summary/Conclusions: The frequencies of antibody specificities found among Sri Lankan Tamils are different compared to island wide data according to a study that was done in 2009 at IHRL NBC, analyzing samples from all parts of the country. Antibodies were detected in 191 samples. The frequencies of antibody specificities were Anti D: 5.7%, Anti Le[b]: 36.2%, Anti Le[a]: 15.7%, Anti Le[a] + Le[b]: 17.2%, Anti E 10.4%, Anti c: 2.6%.

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IRREGULAR ANTIBODIES IN ECUADORIAN BLOOD DONORS

JI Acosta
Centro Zonal de Fraccionamiento, Hemocentro Nacional – Cruz Roja Ecuatoriana, Ambato, Ecuador

Background: The identification of irregular antibodies is one of the steps to carry out a safe transfusion practice. The search and identification of these antibodies is carried out using the indirect antiglobulin technique and is mandatory in blood donors. Knowing if donors have developed alloantibodies is necessary because in our environment a large number of these people have received transfusions or have been pregnant, the main causes for the development of irregular antibodies, which could cause transfusion reactions. The alloantibodies have been divided into two groups, antibodies of clinical importance, and those that are not significant in transfusion medicine. They should all be traced and identified in blood donors as a prelude to the release of the product s for transfusion step.
Aims: To evaluate the presence of irregular antibodies in Ecuadorian donors.
Methods: Irregular antibodies were screened in the plasma of volunteer blood donors from the central highlands of Ecuador, who visited the Fractionation Zonal Center of Ambato of the National Hemocenter of the Ecuadorian Red Cross, during the period January - December 2017. For the screening of the alloantibodies, three reactive screens were used by the column agglutination technique. From the positive samples, the identification of the antibody was made using the panel of 11 cells in the same technique.
Results: Results A total of 17155 were analyzed donor samples blood volunteers, where 11,401 (66.46%) correspond to male donors and 5754 (33.54%) to female donors. Positive results were obtained for the detection of irregular antibodies in 60 (0.35%) samples, of which 24 (40%) corresponded to the male sex and 36 (60%) to the female sex. The most frequent specificities identified were Anti-Lea (48.3%), Anti-E (21.7%), Anti-D (8.3%), Anti-K (3.3%), Anti-C (1.7%), Anti-Fya (1.7-%) and Anti-N (1.7%), while eight (13.3%) positive results we could not identify the antibody and therefore these were categorized as indeterminate.
Summary/Conclusions: The antibody most commonly found in blood donors is Anti-Lea, considered of little clinical importance despite reports of transfusion reactions. Anti-E is the antibody most commonly found in Ecuadorian blood donors referring to the clinically significant ones, followed by Anti-D and Anti-K. There are antibodies classified as indeterminate that must be studied deeply in order to evaluate if they are clinically significant. The Anti-D antibodies found were all identified in female donors with at least one pregnancy prior to donation.

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ESTABLISHMENT AND UTILIZATION OF A TRANSFUSION RECIPIENT REGISTRY IN KOREA: ESTIMATING THE FREQUENCIES OF SPECIFIC ANTIGEN–NEGATIVE BLOOD UNITS

D Shin[1], H Kim[1], Y Chung[1,2], Y Hong[1,3], K Park[1,3] and K Han[4]

[1]Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul [2]Department of Laboratory Medicine, Myongji Hospital, Goyang [3]Department of Laboratory Medicine, Seoul National University Bundang Hospital, Seongnam [4]Department of Laboratory Medicine, Myongji Hospital, Seoul, Republic of Korea

Background: More than 300 blood group antigens have been recognized, and their frequencies vary among communities and ethnic groups. To ensure a stable supply of blood units, predicting the probability of obtaining compatible blood units is important.
Aims: Using data from the Korean national registry, this study was conducted to establish the Korean national registry, to evaluate the distribution of unexpected antibodies, and to determine the frequencies of specific antigen-negative blood units.
Methods: Data added to the Korean national registry between July 2013 and April 2016 were analyzed. The distribution of unexpected antibodies and frequencies of specific antigen-negative blood units were estimated.
Results: In total, 3,513 cases from 22 institutes were registered. The most common single alloantibodies were anti-E, anti-Le[a], and anti-M. The most common multiple alloantibodies were anti-E with anti-c, anti-C with anti-e, and anti-Le[a] with anti-Le[b]. The frequencies of E-, Le[a]-, and M-negative units were 42.3%, 56.9%, and 20.2%, respectively.
Summary/Conclusions: The distribution of unexpected antibodies and frequencies of specific antigen-negative blood units were investigated using data from the Korean national registry. The results provide useful data to predict the number of blood units to be tested to obtain compatible blood units.

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ANTIBODIES AGAINST HIGH FREQUENCY ANTIGEN DETECTED IN POLISH PATIENTS BETWEEN 2000 AND 2017

M Pelc-Kłopotowska[1], K Guz[1], A Orzińska[1], H Łopieńska[1], J Bednarz[1], H Mazowiecka[1], B Michalewska[1], M Uhrynowska[1], V Karamatic Crew[2], N Thornton[2] and E Brojer[1]

[1]Department of Immunohematology, Institute of Hematology and Transfusion Medicine, Warsaw, Poland [2]IBGRL Red Cell Reference Laboratory, NHSBT Filton Blood Centre, Bristol, United Kingdom

Background: Detection and identification of antibodies to high frequency antigen (>99%, HFA) is a great challenge for blood transfusion laboratory. Some of them are clinically significant and have the potential to cause haemolytic disease of the foetus and newborn or haemolytic transfusion reaction after incompatible transfusion. In such cases providing compatible blood for transfusion is a challenge. The information about the specificity of antibodies in the current population is important to develop the policies for blood donor typing for rare blood groups.
Aims: We present data regarding the alloantibodies to high frequencies antigens, identified over a 17 year period, to investigate the prevalence of rare antibodies in the Polish population
Methods: Blood samples from 316 patients, including 41 (13%) pregnant women, tested between 2000 and 2017. Antibodies detected in the samples reacted with all or the majority of panel cells. Specificity of the antibody was determined with routinely applied panel of red blood cell (RBCs) by RT saline test, enzyme test at 37°C and DiaMed IAT with untreated, papain treated and DTT treated cells (for differentiation of reactions). For confirmation: 1) of suspected specificity appropriate antigen negative samples of RBCs and serum with the corresponding antibody for phenotyping patient cells obtained from SCARF (Serum, Cells and Rare Fluid) Exchange were used; 2) a patient genotype was established using RBC-FluoGene Rare (Inno-Train, Kronberg/Taunus, Germany), in-house real-time protocols for LWa/b (abstract ISBT-1152); RHCE*02.08.01; LU*02.14 or sequencing (LAN, Jr). In some cases specificity of antibodies to HFA was determined by IBGRL, UK.
Results: Of the tested samples with alloantibody against (HFA) 24 specificities were determined, mostly confirmed by patient genotype. Antibodies always regarded as clinically significant were detected in 36 (11%) patients (10 anti-Kpb, 5 anti-Dib, 4 anti-k, 4 anti-Rh17, 4 anti-H in Oh individuals, 3 anti-PP1Pk, 2 anti-P, 2 anti-Rh51-like, 1 anti-Ku, 1 anti-Jk3) among them 4 anti-Kpb, 1 anti-k, 2 anti-Dib and 1 anti-Rh17 were detected in pregnant women. Antibodies classified as sometimes but rarely destroying incompatible RBCs were found in 108 (34%) patients (50 anti-LWa, 45

anti-Yta, 28 anti-Lan, 13 anti-Lub, 10 anti-Jra, 4 anti-Ge2, 3 anti-Coa, 3 anti-Gya, 2 anti-Lu8). Not clinically significant antibody within HTLA specificities in 122 patients (39%) (63 anti-Ch, 24 anti-JMH, 18 anti-Kna, 15 anti-Rg and 2 anti-Yka) were found. In 144 cases it was necessary to consider searching for antigen negative donors.
Summary/Conclusions: Our data illustrates a broad range of antibodies to high frequency antigens present in the Polish population. Data studies such as this are essential for establishing a suitable rare donor screening program, and tailoring a rare blood provision strategy and policy development for a population.

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AN ANTIBODY AGAINST A NOVEL HIGH INCIDENCE ANTIGEN IN THE INDIAN BLOOD GROUP SYSTEM

C Henny[1], N Thornton[2], S Lejon Crottet[1], L Baglow[2], J Graber[1], C Niederhauser[1] and H Hustinx[1]

[1]Interregional Blood Transfusion SRC, Berne, Switzerland [2]International Blood Group Reference Laboratory, NHSBT, Bristol, United Kingdom

Background: The Indian (In) blood group glycoprotein CD44, is the predominant cell surface receptor for hyaluronan and other components of the extracellular matrix. The protein is encoded by the CD44 gene on chromosome 11, consisting of 19 exons of which 10 are variable. The hematopoietic isoform is composed of exon 1 to 5, 15 to 17 and 19. The Indian blood group system consists of 4 high prevalence antigens IN2 (In[b]), IN3 (INFI), IN4 (INJA) and IN5 (INRA) and one low prevalence antigen IN1 (In[a]). IN:-3, IN:-4 and IN:-5 have been reported in only a few cases. IN1, which is antithetical to IN2, is more prevalent in the Arabic, Iranian and Indian population with up to 10% being IN:1,2.
Aims: A sample from a patient of Sri Lankan origin was investigated for antibody specificity due to pan reactivity. A sample from the brother of the patient was also investigated.
Methods: Serological investigations were performed by IAT (tube and column agglutination). Papain and trypsin treated cells were also utilised. Soluble recombinant In blood group proteins (In-rBGP) (Imusyn, Germany) were used in neutralization tests. The clinical significance of the antibody was assessed by a monocyte monolayer assay (MMA). Genomic DNA was isolated from whole blood and the samples were further characterized by PCR amplification and Sanger sequencing including flanking intronic regions of the hematopoietic isoform of CD44 (exons 1–5, 15–17 and 19).
Results: The plasma of the patient and his brother reacted positive with all cells tested, except their own, by IAT and trypsin IAT, but negative in papain and saline tests. The antibody was neutralized with In-rBGP, thereby confirming In specificity. The patient and his brother were found to have the IN:2 phenotype. The monocyte index (MI) for the patient was <3%. Sequencing of CD44 revealed the mutation c.276C>A in a homozygous state for both the patient and his brother. This mutation leads to amino acid change p.H92Q. The patient's serum was compatible with cells from his brother. Cells from the patient's brother were found to be IN:3,5. IN:-3 and IN:-4 cells were found to be incompatible with the brother's plasma.
Summary/Conclusions: We report the case of a patient of Sri Lankan origin whose cells lack a novel high prevalence antigen of the In system and his plasma contains the corresponding anti-In antibody. Lack of the novel In antigen is due to homozygosity for a novel mutation c.276C>A in exon 3 of CD44. His brother was found to have the same genotype and was serologically compatible with the patient's plasma. As the patient and his brother apparently have not been transfused, we presume that the antibody is naturally occurring. An MI <3% suggests that the antibody is not clinical relevant.

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THE PREVALENCE AND IDENTIFICATION OF A HIGH–FREQUENCY ANTIGEN ANTIBODY OF ANTI–JK3: FIVE YEARS ANALYSIS AT A MEDICAL CENTER

H Chen, C Chung and P Tsai
Pathology Center, Chi Mei Medical Center, Tainan, Taiwan, Republic of China

Background: The Kidd blood group system was discovered in 1951 that consists of two major antigens, Jka and Jkb. In 1959, the null phenotype, Jk(a-b-) was found, and the antibody which recognized both Jk[a] and Jk[b] later named anti-Jk3. In Asian population, Jk(a-b-) is rare, so if patient with anti-Jk3, the transfusion support is quite difficult.

Aims: The aims of this study were to analyze the prevalence of anti-Jk3 and reported the results of 4 cases in our institution.

Methods: The present study was also a prospective study. From January 2013 to December2017, a total of 53819 samples were tested for antibody screening, if screening test was positive, identification test would be performed then. Standard serological principles of AABB technical manual were applied to present study.

Results: In the past five years, there were 53819 samples tested for antibody screening, 1947 samples were identified as RBC-specific antibody, and the rate of RBC-specific antibody was 3.6%. Among all the antibody-specific cases, only 4 cases were anti-Jk3, the prevalence was about 0.2%. Patient 1, 2 and 3 were DAT negative and all their plasma reacted pan-agglutination with all panel cells by CAT (ID-CARD, Bio-Rad), saline-IAT and MP (manual polybrene method) IAT. The grading agglutination reactions of CAT (2+/3+) were stronger than MP method (1+/2+). Red cell phenotype of three patients showed Jk(a-b-), so demonstrated their antibody specificity as anti-Jk3. For patient 4, the DAT/ auto-control were positive and antibody were pan-reactivity with all panel cells, too. After checking her transfusion history, we learned her first time antibody screen was negative and received 2 units RBCs 7 days ago, just before her second time antibody screen. We rechecked her first sample for phenotype, it presented Jk(a-b-), supporting her antibody specificity was anti-Jk3; her DAT and auto-control of second sample results were influenced by her transfusion.

Summary/Conclusions: In general, Kidd antibodies are not easy to detect because some positive agglutination reactions are weak or absent that could use enzyme-treated cells to give more sensitive results in identifying. Anti-Jk3 is a clinical significant antibody, it also can cause acute or delayed hemolytic transfusion reactions but rarely cause of HDN. Anti-Jk3 reacts with Jka(+) and Jkb(+) red cell antigen, but not with a Jk(a-b-) phenotype that would be a serious problem with transfusion because the frequency of positive Kidd antigen is quite high in our country; hence, if a patient need to transfuse RBC products, we only could ask local blood center to support and offer Jk(a-b-) red cells for transfusion. In addition, from the results we showed above, CAT method is more sensitive than MP method to detect anti-Jk3; however, MP method is a routine technology for antibody screening and cross-match in our laboratory. Therefore, for the weak expression or negative results in panel cells while identifying anti-Jk3, further confirmation by CAT method is needed.

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THE FIRST EVIDENCE OF THE KANNO − PHENOTYPE AND ANTI-KANNO IN AN INDIVIDUAL OF INDIAN ORIGIN

B Jones[1], V Karamatic Crew[1], R Musa[2], N Ahmad[2], G Muniandi[2], A Hassan[2], N Abu Amin[2] and N Thornton[1]

[1]International Blood Group Reference Laboratory, NHS Blood & Transplant, Bristol, United Kingdom [2]Immunohaematology Division, National Blood Center, Kuala Lumpur, Malaysia

Background: The first example of anti-KANNO was detected in 1991 in a Japanese female. The Japanese blood service have described a further 27 cases of KANNO− individuals with anti-KANNO, the majority of which were females with a history of pregnancy. The first example of anti-KANNO found outside of Japan was described in 2014, however the patient was thought to be of Japanese origin. KANNO is a high frequency antigen sensitive to papain, trypsin, α-chymotrypsin and pronase treatment but resistant to AET and DTT treatment. Anti-KANNO has the characteristics of a high titre low avidity (HTLA) antibody. No cases of anti-KANNO in a non-Japanese individual have been previously described.

Aims: To describe the first case of the KANNO− phenotype and anti-KANNO in an individual of non-Japanese origin.

Methods: Blood samples from a 24 year old male patient of Indian origin, with a diagnosis of single ventricle for Fontan operation, were investigated due to the detection of an unidentified alloantibody to a high frequency antigen. Serological tests were performed by standard LISS tube IAT. Artificially C4 coated cells were achieved by incubating cells with 10% sucrose and human AB serum. Cells were treated with papain, trypsin, α-chymotrypsin, pronase and DTT. Inhibition studies were carried out using the following soluble recombinant blood group proteinsCR1, Yt[a], JMH and In[b].

Results: The patient's plasma reacted with moderate strength by LISS IAT with all untreated panel cells but no reactivity was observed with papain treated cells. The patient's cells were found to be positive for the following papain sensitive antigens: Kn[a], Yt[a], JMH, In[b], En[a], Ge2, CD99. C4 coated cells were found to react the same strength as uncoated cells, thereby indicating the antibody was not anti-Ch/Rg. Inhibition tests with the patient's plasma and soluble recombinant CR1, Yt[a], JMH and In[b] proteins

showed no inhibition. The patient's plasma was negative with trypsin, α-chymotrypsin and pronase treated cells; whereas DTT treated cells were positive. The reaction profile indicated possible anti-KANNO. The only cells found to be compatible with the patient's plasma were autologous cells and an example of KANNO− cells. The patient's cells were typed with three examples of anti-KANNO and found to be KANNO−.

Summary/Conclusions: We have described a new case of a KANNO− individual with anti-KANNO. This is the first reported case of this rare phenotype in a non-Japanese individual. The serological presentation of the antibody showed the distinctive reaction profile with enzyme treated and chemically modified cells, in accordance with previously reported examples of anti-KANNO, which provides a useful tool for identifying this rare antibody.

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AN IGM MONOCLONAL ANTIBODY DIRECTED AGAINST THE VEL ANTIGEN

MV Van Der Rijst[1,2], S Lissenberg-Thunnissen[2], P Ligthart[3], R Visser[2], A Bentlage[2], E van den Akker[1], G Vidarsson[2] and C Van der Schoot[2]

[1]Hematopoiesis [2]Experimental Immunohematology [3]Immunohematology Diagnostic Services, Sanquin Blood supply, Amsterdam, Netherlands

Background: Alloimmunisation against the Vel blood group can be caused by blood transfusions or through pregnancies and may result in transfusion reactions or haemolytic disease of the new-born. Correct typing for the Vel blood group is therefore crucial for patient and donor. At present typing is performed using patient sera containing anti-Vel antibodies. However, these sera are limited available, subject to donor variability, and unable to discriminate between Vel-weak and Vel-negative donors. Therefore, there is need for an unlimited source of anti-Vel reagents, that is also reactive with weak Vel expressing red blood cells (RBCs).

Aims: Production and characterization of a monoclonal antibody against the Vel antigen.

Methods: CD19-positive cells of an alloimmunised patient (3 months after child birth) were incubated with Vel-positive ghosts. Cells with affinity to the ghosts were single cell sorted and expanded on EL4B5 feeder cells to generate B cell clones producing antibodies [Dohmen et al., JI 2005]. RNA was isolated from clones that produced antibodies reacting with Vel-positive, but not with Vel-negative RBCs. The variable Ig regions were amplified from cDNA, and sequenced. The variable heavy (VH) and light (VL) domains were cloned into pcDNA3.1 harbouring the constant domains of heavy and light chains of IgG or IgM. Freestyle 293 cells were transfected to produce the antibodies, which were purified by chromatography. The reactivity of the antibody was tested by flow cytometry, using an array of RBCs with variable or no Vel antigen expression and using 239T cells ectopically expressing SMIM1. Complement activation upon antibody binding was determined by measuring C3 and C4 deposition by flow cytometry.

Results: The antibody titre of the patient was 1:64, containing predominantly IgM antibodies. 3.2×10^5 CD19+ B-cells were isolated, of which 695 cells with affinity to Vel-positive ghosts were single cell sorted. From 272 antibody producing clones one clone, M3F5S, produced IgM and κ Vel specific antibodies. No somatic hypermutations were detected. The VH and VL chains of M3F5S were cloned into expression vector pcDNA3.1. The recombinant IgM antibody, but not the IgG antibody, was specific for the Vel antigen, as it reacted both in direct agglutination and in flow cytometry with a panel of Vel-positive RBCs and not with Vel-negative RBCs. Furthermore, the antibody was only reactive with SMIM1 expressing HEK293T cells. The recombinant IgM antibody induced complement activation. The different expression levels of Vel, caused by the heterozygous deletion in SMIM1 and/or the SNP rs1175550 in intron 2, were detected by flow cytometry and serology. However, serology was more sensitive. Direct agglutination with the moAb M3F5S identified one donor as Vel weak whereas in the same test a human anti-Vel serum did not react with these cells. The Vel expression of this donor was confirmed with other anti-Vel sera.

Summary/Conclusions: We have generated a recombinant IgM moAb specific for the Vel antigen. This antibody is at least as sensitive as currently used human sera and can be used in direct agglutination assays.

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Abstract has been withdrawn

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PRODUCTION OF HUMAN HYBRIDOMA SECRETING MONOCLONAL ANTIBODY AGAINST RH (E) ANTIGEN

S Ponsen, S Phonimit, N Premprayoon, K Kerdkaewngam, U Tingtoy and U Charoonruangrit

National blood center, Thai Red Cross Society, Bangkok, Thailand

Background: Anti-E reagent from National Blood Center, The Thai Red Cross Society, recently involves significant cost because of the expensive importing supernatant.

Aims: To produce human hybridoma secreting anti-E monoclonal antibody from human B lymphocytes.

Methods: We first isolated human B lymphocytes producing anti-E from buffy coated, packed red cell or whole blood using ficoll-hypaque density gradient centrifugation and subsequently transformed them with Epstein-Barr virus (EBV). Next we fused the transformed secreting cell lines with human myelomas (JMS-3) using 50% Polyethylene Glycol (PEG) to produce hybridoma. We also investigated whether the hybridoma-secreting molecules could aggregate Rh (E) antigen on red blood cells. After that, we saved secreting clones by limiting dilution. Following expansion of these hybridomas, we assessed their supernatant in detail by checking their specificity against panel cells, their reactivity to different Rh (E) antigens, and antibody titer by testing sequential dilution with both of saline and indirect antiglobulin (IAT) technique.

Results: We established 4 different cell lines stably expressing anti-E, namely 4C91A2, 4C91B9, 4C91F9 and 4C91G5.The titers of their antibody with R1R2 cell were 1:512, 1:256, 1:256 and 1: 512w, respectively. These anti-E reagents reacted perfectly with E positive cell, whereas they did not react with E negative cell at all. This result indicates that our reagents fulfill the quality of the current anti-E reagent.

Summary/Conclusions: Although further serology testing in required, our 4 different cell lines could stably produce anti-E reagent. This will substitute the supernatant from oversea import and will reduce financial cost in medical services in the future.

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A CASE OF UNEXPECTED ANTIGEN TYPING

E Bessette[1], M Ng[1], J Cote[2] and G Clarke[3]

[1]Canadian Blood Services, Calgary [2]Canadian Blood Services, Ottawa [3]Canadian Blood Services, Edmonton, Canada

Background: At Canadian Blood Services, blood donors are selected for phenotype testing based on ABO group and number of historical donations. This testing is done primarily on the Immucor Gamma automated NEO instrument. Recently, we found a donor who previously tested as negative for the small s antigen but currently is testing as small s positive on the NEO instrument. Testing with Immucor monoclonal Anti-s antisera using manual tube method found the donor to be small s negative.

Aims: Review the results from an automated instrument and from manual testing for a donor with a discrepancy for the small s antigen and incorporate results of genetic testing to resolve the discrepancy. Demonstrate a process used to resolve this apparent antigen phenotype discrepancy.

Methods: The Immucor Gamma NEO uses a Capture-R solid phase technology which is based on the principle of the indirect antiglobulin test. This Anti-s antisera is prepared from pools of human serum containing polyclonal antibodies. The manual testing method is a room temperature incubation for 15 min using Immucor monoclonal antisera. The Immucor monoclonal Anti-s antisera is prepared from IgM antibodies from the human/murine heterohybridoma cell line P3BER. The genotyping is completed using the Grifols/Progenika IDCORE[xt] kit.

Results: The historical small s result from manual testing using Immucor monoclonal antisera was negative. The current testing on the NEO instrument using Immucor polyclonal antisera was 2+ positive. The small s testing on the NEO was repeated using the same NEO instrument and on four other NEO instruments. We were able to reproduce the positive result (2–3+ positive) on all automated NEO instruments. The same donor sample was manually tested using monoclonal antisera and was small s negative. DAT testing was completed with Anti-IgG reagent and was negative. The donor sample was genotyped with a predicted phenotype of S+s-. The package insert for the polyclonal antisera used on the automated instrument indicates that only some low prevalent antigens had been excluded from this reagent. Further phenotype testing for the presence of a low prevalent antigen which may cross react with the polyclonal Anti-s antisera was performed on this donor's red cells. The donor is Wr(a+) which hindered further testing of the low prevalent antigens in the MNS system.

Summary/Conclusions: With advances in technology, Blood Group Serology testing is becoming more automated and less of a manual process. Automation should bring more accuracy, efficiency, and decreased risk of errors. However, the discrepant small s phenotyping for this donor shows that there are limitations with automation. In this case, the difference between the polyclonal and monoclonal antisera is likely responsible for the discrepancy, with the polyclonal Anti-s showing cross reactivity with a low prevalence antigen for which this donor is positive. A routine process for resolving apparent discrepancies must use a variety of techniques and reagents in a standardized fashion to ensure accurate phenotyping information on donors.

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HEMOLYTIC TRANSFUSION REACTION DUE TO AN ANTI-H ANTIBODY IN A SICKLE CELL DISEASE PATIENT

E Lazarova[1], V Pede[1], A Muylaert[1], P Vandekerckhove[1], C Folman[2], M de Haas[2] and V Compernolle[1]

[1]Blood Services, Belgian Red Cross-Flanders, Mechelen, Belgium [2]Department of Immunohematology Diagnostics, Sanquin Diagnostic Services, Amsterdam, Netherlands

Background: Clinically significant alloanti-H can be produced only by H-deficient Bombay (Oh) phenotypes and H-partially deficient para-Bombay (Ah, Bh, ABh) phenotypes. Furthermore, autoanti-H/IH can be found in healthy people, most commonly in A1or A1B individuals who express very little H antigen. These antibodies are generally IgM type and are reactive at 4°C and rarely at room temperature (RT). They have been also reported in individuals with cold agglutinin syndrome. However, unusual cases of transfusion reactions due to wide thermal range anti-H/IH antibodies have been also described.

Aims: Here we report a case of a sickle cell disease (SCD) patient, blood group B, who presented a hemolytic episode after transfusion of antigen-matched packed RBC (pRBC) of blood group O.

Methods: All serologic testing was performed on EDTA patient samples. Panel studies were performed in a gel-card format or by tube testing by a saline method at RT, 37°C, indirect antiglobulin test (IAT) using monospecific anti-IgG reagent and with enzyme-treated reagent cells. The patient's plasma was treated with dithiothreitol to determine the immunoglobulin class of the reacting agglutinins.

Results: Case report: The patients was a 17-year-old young woman with homozygous SCD, blood group B positive, C- E- c+ e+ K- k+ Fya- Fyb+ Jka+ Jkb- M+ N- S- s+ Lan+ Ata+ Jra+ P+, and known with the following alloantibodies: anti-C, anti-E and anti-Jkb from 2009, when she received two O negative pRBC in our institution. She was also transfused in 2013 with one O negative pRBC. She was admitted in May 2017 with painful crisis and severe anemia (hemoglobin (Hb) of 34 g/l) and received 2 antigen-matched (for all clinically significant antigens) and cross-matched O negative pRBC with no adverse events; Hb raised to 68 g/l. Ten days later, she was readmitted with painful crisis and anemia with Hb of 46 g/l. The direct antiglobulin test was negative and the plasma showed a panreactivity at room temperature and at 37°C, in IAT and with enzyme treated test cells with all test cells, except the autologous control. During the following h the Hb dropped to 35 g/l and one antigen-matched O negative pRBC was transfused in an emergency. The transfusion was inefficient as the patient continued to deteriorate and the Hb decreased till 29 g/l. In the meantime, the diagnostic of strong large thermal amplitude anti-H antibodies of IgM type reacting also at 37°C in IAT was established. Afterwards, the patient was efficiently transfused with two thawed antigen-matched and cross-matched B negative pRBC delivered by the Sanquin cryobank and Hb raised to 58 g/l.

Summary/Conclusions: This is a rare case of wide thermal range anti-H autoantibodies behaving as alloantibodies and causing severe hemolysis. As the hemolysis appeared 12 days after the transfusion episode of O negative pRBCs and was accelerated by the following transfusion of one more O negative pRBC, we could here stipulate also about a delayed hemolytic transfusion reaction, a complication that is particularity life-threatening in SCD patients. This case, together with the other 5 similar cases with anti-IH from the literature, confirm that both ABO-identical matching and phenotypical matching should be considered in SCD settings.

P-493

MULTIPLE INCOMPATIBLE TRANSFUSIONS IN A GE:-2,-3 PATIENT IMMUNIZED WITH AN ANTI-GE2: WHAT TEST TO PERFORM IN ORDER TO SELECT THE MOST APROPRIATE BLOOD WHEN RBC UNITS ARE SCARCE?

VL Thonier[1], G Laiguillon[1], K Cazabat[1], B Elmasmouhi[2], M Le Bras[3], J Babinet[1] and T Peyrard[1]

[1]CNRGS, Institut National de la Transfusion Sanguine, Paris [2]Site de Poitiers, Etablissement Français du Sang, Poitiers [3]Site d'Angers, Etablissement Français du Sang, Angers, France

Background: Individuals harboring the Gerbich phenotype (GE:-2,-3) lack the Ge2 and Ge3 antigens. They can develop an anti-Ge2 or/and an anti-Ge3. Anti-Ge2 antibodies are the most common. They may be naturally or immune occurring. Their clinical significance is regularly discussed in the literature. Regarding the risk of an acute transfusion reaction, data are overall reassuring. Ge2- units are scarce because no Ge2 screening is routinely implemented. Most donors are recruited through family studies or as former immunized patients. Few of them are discovered during donor testing if a natural antibody is present.

Aims: To report the transfusion management of an immunized Gerbich patient in a hemorrhagic shock whom required 4 transfusion episodes a few days apart. Our frozen stock was 3 group O and 6 group A and no fresh units.

Methods: Standard haemagglutination techniques and biochemistry tests were performed.

Results: Our patient, group A, Ge:-2,-3, was rushed to hospital after an overdose of vitamin K antagonists. Massive hepatic bleeding was diagnosed. Before the transfusion, the anti-Ge2 had a titer of 8 in LISS-IAT-IgG column-agglutination technique. Four group O incompatible units were transfused with a protocol of intravenous immunoglobulins (IVIG) and steroids. Hemolysis was monitored with hemoglobin, haptoglobin, lactate dehydrogenase (LDH) and bilirubin. Since day 2, they highlighted hemolysis, whereas the transfusion yield was satisfying. The scarcity of Ge2- units forced us to monitor the hemolysis with other markers: antibody screens, antibody (anti-A and anti-Ge2) titrations, DAT, elution and ABO typing. The anti-A titration was performed to evaluate the risk of an hemolysis due to passive anti-A antibodies after the IVIG prophylaxis. Transfusion was needed 4 days later. The DAT became positive just after the first transfusion. In the serum, no anti-Ge2 but weak anti-A was detected. Because an ABO mixed-field reaction was still present, group O incompatible units were selected. On day 9 and 10 the patient required transfusion, then the Ge2 antibody's titer was 16 and anti-A was still weakly detected as a new injection of IVIG was already made in case of a new incompatible transfusion. One O Ge2- unit was thawed and transfused. A fresh unit O Ge2- was collected just in time for the last episode.

Summary/Conclusions: Hemolysis markers present bias. Haptoglobin is very sensitive and it drops rapidly. It may be reduced in patients with liver damage and might be overestimated in case of acute inflammation. As LDH is present in many tissues, it lacks specificity. The drop of hemoglobin is a sign for hemolysis only if bleeding has stopped. When these parameters are difficult to interpret, using direct markers of the destruction of the transfused red blood cells (in our example group O units) helps to evaluate the intensity of the hemolysis. A mixed-field reaction is reassuring. Cross matching the units with the serum and the eluate, monitoring the titer and strength of the antibodies helped us to select the most appropriate units. This case again illustrates that anti-Ge2 is not responsible for severe transfusion reactions, as no clear evidence of hemolysis was observed.

P-494

AN INTERESTING CASE OF NATURALLY OCCURRING ANTI-E MIMICKING ANTI-A1

D Gupta, V Rajendran, R Nair and S S

Transfusion Medicine, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala, India, Thiruvananthapuram, Kerala, India

Background: Solving problems in Immunohematology are always challenging and at the same time interesting. Recently we have encountered an interesting case of discrepancy in blood grouping. Anti-E is usually an acquired type of IgG antibody like the other Rh Antibodies. Rarely they can occur naturally also. Apart from Anti-D, Anti-E can also occur naturally among the Rh antibodies.

Aims: We are reporting a similar case that deals with the presence of naturally occurring Anti-E in the blood of an elderly male.

Methods: A 61-year-old male with no past history of transfusion was admitted at our centre for Cardiopulmonary Bypass Surgery. Blood samples were sent to blood

centre for ABO grouping and Rh typing. Forward grouping showed as A RhD positive. On reverse grouping, a weak agglutination was observed with 'A' cells. The reaction with pooled A cells strengthened on incubation at 37°C. No reaction was obtained against pooled 'O' cells in saline. Red cells were negative upon testing with Anti-A1 lectin. A2 group with Anti-A1 was suspected. Compatibility was performed in gel card with two randomly chosen A RhD+ RBC units. Auto-control was negative at room temperature and 37°C. 1+ agglutination reaction was observed at 4°C probably due to insignificant cold auto antibodies.

Compatibility testing:

Patient's serum with Unit 1: Incompatible

Patient's serum with Unit 2: Compatible

Results: The red cells of Unit 2 were found to be A1 positive. Thus, possibility of Anti-A1 was ruled out. Antibody screening was performed with 3 cell panel which revealed the possibilities of Anti-E. Patient's cells were found to be RhE negative (R1R1 phenotype). Unit 2 which was found compatible was also found to be RhE negative while Unit 1 was RhE positive. One of the donor units used in preparing the pooled 'A' cells for reverse grouping was found to be 'E' positive. Antibody screening against pooled papainised group 'O' cells gave a strong positive result (2+). 4 units of RhE negative and 4 units of RhE positive red cells were cross matched with patient's serum. All 4 RhE-positive cells were agglutinated by the serum at room temperature and at 37°C. No reaction was observed with RhE negative cells. The specificity of Anti-E was now confirmed.

A portion of the serum was treated with Di-thiothreitol (DTT) and titrated in parallel with untreated serum. O+ cells of R_zR_z phenotype were used for titration. A titre of 2 was observed at Anti-Human Globulin (AHG) phase in the untreated serum. Antibody was undetectable in the DTT treated serum.

Summary/Conclusions: Initially we thought it as Anti-A1 and later found it as anti-E. Considering the reactivity with E antigen positive 'A' cells at saline phase and disappearance upon treatment with DTT, it was most likely to be an IgM antibody with a wide thermal amplitude. Even though Naturally occurring Anti-E is not clinically significant, corresponding antigen negative red cell should be issued for transfusion.

P-495

CASE REPORT EXAMPLE OF ANTI–LUB ANTIBODIES

A Djozo[1], M Raos[2], B Golubic-Cepulic[2] and J Kurilic[1]

[1]Immunohaematology, Blood transfusion institute of FB&H, Sarajevo, Bosnia and Herzegovina [2]Clinical Department of Transfusion Medicine and Transplantation Biology, University Hospital Center Zagreb, Zagreb, Croatia

Background: The Lutheran b blood antigen is a high prevalence antigen occurring in 99.8% of population. Consequently, antibody formation against Lutheran b is very rare.

We describe one case of pregnancy complicated by Lub alloimmunization.

Aims: The "Lutheran" antibody was first described by Callender, Race, and Paykog (1945) in the serum of patient who developed number of antibodies in response to multiple transfusions of blood. While this antibody can cause hemolytic reactions in adults, there is limited clinical information on its effects on the fetus and newborn. The main challenge of the case like this is how to obtain antigen negative blood for possible maternal and foetal transfusion.

Methods: Blood samples were screened by two automated systems IH- 500 BioRad and AutoVue Ortho as well by tube technique.

Results: A twenty eight years old women in 32nd weeks of gestation had one normal pregnancy seven years before. The sample is obtained from another hospital blood center. Antibody screening was positive, but its specificity remained unknown. In our Institute as well as in the University Hospital Centre in Zagreb, Croatia, The Clinical Institute for Transfusion Medicine and Transplant Biology, the results were identical.The serum of pregnant woman gave panagglutination with all test cells and mixed field phenomena by the antiglobulin test. The strength of the reaction was 2+ at 37C° and 1+ at 20C° using tube and microcolumn technique, as well as by enzyme technique (papain). Titration score was 1:32. The autocontrol was negative and direct antiglobulin test, too. The presence of an antibody against an antigen of high frequency was suspected. The Lu phenotype in women was found Lu(a+b-). HLA antibodies were excluded. Anti-Lub antibody confirmed in International Blood Group Reference Laboratory Bristol.

The baby was bom at term after vaginal delivery with a negative direct antiglobulin test. There was no clinical evidence of haemolytic disease of the newborn. Unfortunately, we could not do family testing because of the unavailability of the blood samples.

Summary/Conclusions: The learned lesson could be that we should think about of high frequency antigen in routine work, however rare they were.It would be

recommanded to review options to maximize perinatal and postnatal outcome. This case emphasizes the importance of perinatal surveillance by transfusion medicine specialists, the importance of sensitive and specific tools for antibody screening and identification and the existence of national or regional Register of rare blood donors, for transfusion support of mother and child. The cooperation between the centers and collegues is desirable and even necessary.

P-496
ANTI–HI ANTIBODY IN PREGNANT WOMAN

L Nikolic[1] and O Kontic-Vucinic[2]
[1]Clinic for Gynecology and Obstetrics, Laboratory for Hematology and Transfusion
[2]Clinic for Gynecology and Obstetrics, Clinical Center of Serbia, Belgrade, Serbia

Background: Cold agglutinins, naturally occurring, are predominantly IgM antibodies and react predominantly at 4°C.The naturally antibodies belong to the ABO, Hh, Ii, Lewis, MN, P blood group systems. Alternatively, they may be associated with Mycoplasma infection and malignant diseases. Anti-HI is a complex antibody, commonly benign in nature with preferential action in cold temperature.
Aims: The aim of this report is to describe a clinically significant anti-HI antibody with a wide thermal range which was recognized during laboratory testing in pregnancy.
Methods: Case report.
Results: A 29-year-old pregnant woman at 37 week of gestation was admitted to our Clinic for monitoring pregnancy and delivery planning. Pretransfusion tests demonstrated A_1 group D positive on forward grouping. Reverse grouping showed an agglutination with B and O cells. Agglutination with O cells was stronger at 4°C.The subgroup of A antigen was confirmed as A_1 using anti-A_1 and anti-H lectins (Lorne UK, and CE Immunodiagnostics, Germany). Erythrocyte phenotype was C+, c-, D+, E-, e+, M+, N-, I+. Antibody identification with the commercially available panel (BioRad, Diapanel, Switzerland) revealed pan-agglutination at 4°C and at room temperature (4+).The reaction was gradually weakened at 37°C (2+) and with Coomb's phase (1+). Autocontrol and direct Coomb's test were negative. Antibody titre at 4°C and at room temperature was 64. Immunological tests for antinuclear antibody, antineutrophil cytoplasmic antibody, anticardiolipin antibody and rheumatoid factor were negative. Mycoplasma antibody IgG and IgM test was also negative. Additionally, patient sera was tested with 11 adult A blood group (10 A1 and 1 A2 group) and cord blood (5 O and 5 A group). Reaction was negative with all ten A1 cells and positive (2+) with A_2 cells. There was no agglutination with O and A cord cells. Anti-I and anti-H was ruled out as patient serum reacted with adult O cells but not with O cord cells and adult A1 cells. We concluded that it was an anti-HI antibody. The patient's blood was found to be compatible with A_1 cells but not with O cells and group A1 units of red cell concentrates were selected for cross-matching tests. Due to obstetric reason decision was made to deliver a child with the Cesarean section at 39 week of gestation. A healthy 2500-g boy was delivered. Apgar score in the first minute was 8, haemoglobin was 221 g/l and direct Coomb's test was negative. Unlike anti-H and anti-I antibodies, anti-HI reacts only in the presence of both antigens together. Anti-HI is seen in individuals with A_1B, A_1, and B blood groups. Its reactivity depends on the amount of H antigens on red cells.
Summary/Conclusions: This case describes anti-HI antibody with broad thermal amplitude which was recognized during pre-transfusion testing in pregnancy. This case report illustrates the presence of a clinically significant antibody (anti-HI), and the importance of reverse grouping and antibody screening. Clumped erythrocytes due to cold agglutinins may occlude microvasculature and based on our case report anti-HI can be associated with fetal growth restriction. Moreover, it draws attention to the fact that the blood group O is not always compatible with the A_1 and A_1B blood groups.

P-497
ANTI E ALLOANTIBODYITS SIGNIFICANCE IN A CASE OF ANEMIA

R Sood
Transfusion Medicine, Immunohematology & Blood Bank, VPS Rockland Hospital, New Delhi, India

Background: The Rh antigens are highly immunogenic .Majority of the Rh antibodies are of IgG type. Alloantibody induced hemolytic anaemia due to anti E - IgG antibody binding to red blood cell surface antigens is characterized by extreme

hemolysis, typically extravascular. If the most common causes of severe neonatal hemolytic disease such as Rh and ABO incompatibilities cannot be demonstrated in a newborn with significant hemolytic hyperbilirubinemia, anti-E hemolytic disease should strongly be considered in the differential diagnosis. A very severe form of minor group antibody hemolytic disease characterized by anemia and severe hyperbilirubinemia requiring many exchange transfusions may be encountered during the course of the disease (1)
Aims: To detect alloantibody induced hemolysis.
Antibodies directed against the Rh antigen E have been detected frequently after blood transfusions and sensitization of pregnancy. On rare occasions anti-E has been thought to be a natural occurrence, i.e., to be present without obvious preceding antigenic stimulation. The usefulness of a panel of blood cells of known antigenic make-up in identifying such antibodies is emphasized.
Rh antibodies rarely activate complement .Majority are IgG type. They bind to RBCs and mark them for destruction in spleen (extravascular hemolysis).They typically cause delayed hemolytic Transfusion Reaction. They are also the most common cause of HDN.
Methods: A 35-year-old female patient started developing fever, with generalized weakness, loss of appetite, nausea, vomiting, jaundice and anemia progressing to pancytopenia and splenomegaly.
There was a continuous fall in hemoglobin. There was also a continuous evidence of extravascular hemolysis in spleen, since last 15 days (the Rh antibodies bind to the RBCs and mark them for destruction in the spleen) .Also hematuria was noted after blood transfusion.
Peripheral smear showed anisopoikilocytosis, spherocytosis and a pancytopenic picture. Reticulocyte count was on the lower side (0.5%).
Immunohematology Testing: Forward and reverse blood grouping showed no group discrepancy. The direct antiglobulin test DCT performed on the patients' blood sample revealed positive (1+) agglutination with polyspecific antihuman globulin (anti-IgG and anti-C3d) .The ICT, Indirect Coombs Test, was positive2+(Antisera for DCT & ICT of make Tulip Diagnostics).
Owing to the history of multiple transfusions, and the occurrence of hematuria, the patient's serum was tested against the cell panel with screening red cells using the gel technology (LISS-Coombs Card, Ortho Biovue System, Ortho Clinical Diagnostics). It reacted against cells containing the E antigen and behaved as an incomplete antibody. The identification panel (Ortho Biovue System, Ortho Clinical Diagnostics) confirmed the presence of anti-E antibody with titer of 1:8 (tube method). Auto-control was negative.
An eluate was obtained from red cells using the commercial acid elution kit (Make Ortho Clinical Diagnostics), which confirmed the specificity to be anti-E. The extended red cell typing of the patient showed cells negative for E antigen. Di-thiothreitol treatment of the serum confirmed the presence of IgG type of antibody only. Enzyme treatment showed increased reactivity.
Results: Patient was diagnosed as a case with alloantibody anti E, based on the test results.
Summary/Conclusions: Detecting blood antibodies: auto, allo, cold or warm, is important. The role of transfusion medicine and Immunohematology laboratory in the diagnosis of patient with hemolysis and anemia is emphasised.

P-498

Abstract has been withdrawn

P-499
ALLO–ANTIBODIES MASKED BY AUTO–IMMUNE COLD ANTIBODIES IN REGULARLY TRANSFUSED EGYPTIAN PATIENTS

MS Saleh
Issuing, NBTS Egypt, Giza, Egypt

Background: Autoimmune cold antibodies are clinically non-significant but they can interfere with the pre-transfusion tests like (antibodies screening, cross-matching, etc…..) by masking the presence of other antibodies that may be clinically significant
Aims: The aim of the study is to find out:
The prevalence of autoimmune cold antibodies among regularly transfused Egyptian patients.
The prevalence of allo-antibodies masked by autoimmune cold antibodies.

Methods: The study conducted on transfusion dependent patients (2000 patients) with Thalassemia, aplastic anemia, leukemia, renal failure and anemia of chronic diseases; presented to Egyptian NBTC for blood transfusion.

According to National Egyptian Testing Strategy, Patients were subjected to:

Screening for allo-antibodies against group O reagent RBCs (panel of 3 cells) using appropriate IAT at 37°C by CAT.

Antibody identification for positive screening samples against group O reagent RBCs (panel of 11 cells) using appropriate IAT at 37°C by CAT.

Screening at room temperature to detect the presence of cold antibodies.

Screening for allo-antibodies against group O reagent RBCs (panel of 3 cells) using appropriate IAT at strict 37°C with pre-warming of both serum & reagents (in case of positive results of Screening at room temperature)

Antibody identification for positive screening samples to identify the specificity of allo-antibodies masked by autoimmune cold ones against group O reagent RBCs (panel of 11 cells) using appropriate IAT at strict 37°C with pre-warming of both serum & reagents.

Results: A total of 2000 patient were examined for the presence of autoimmune cold antibodies & allo antibodies that may be masked by them.

Out of a total of 2000 we found that 185 (9.25%) patients had autoimmune cold antibodies and the co-incident prevalence of masked allo-antibodies was as follows:

Autoimmune cold antibodies only:129 out of 185 patients (69.7%)

Allo-anti D: 3 out of 185 patients (1.6%)

Allo-anti C: 7 out of 185 patients (3.8%)

Allo-anti E: 15 out of 185 patients (8.1%)

Allo-antic: 13 out of 185 patients (7%)

Allo-anti K: 7 out of 185 patients (3.8%)

Allo-anti Fy^a: 1 out of 185 patients (0.5%)

Allo-anti Jk^a: 7 out of 185 patients (3.8%)

Allo-anti S: 3 out of 185 patients (1.6%)

Summary/Conclusions: Pre-warming techniques are helpful in differentiation between cold non-significant Abs and warm Abs, for proper pre-transfusion testing of the patients' samples

P-500

ACCURACY OF ADSORPTION-ELUTION TEST AND ITS INCORPORATION INTO DEL TYPING STRATEGY FOR D-NEGATIVE KOREAN DONORS

T Kim, Y Hong, H Kim, E Song, K Park, J Song and K Han

Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

Background: DEL, the weakest RhD variant, is serologically detected only via an adsorption-elution test. Transfusion of red cells with a DEL phenotype, if mistyped as D-negative, has the potential to elicit anti-D alloimmunization.

Aims: The aim of this study is to identify accuracy of the adsorption-elution test and establish a cost-efficient laboratory protocol for DEL identification in serologically D-negative Korean donors.

Methods: Serologically D-negative samples were determined using the indirect antihuman globulin test and subsequently tested for DEL phenotype using an adsorption-elution test. The samples were also tested for RhCE phenotypes. Real-time PCR and melting curve analysis were performed to identify hitherto reported DEL alleles in the Korean population.

Results: Of the 674 serologically D-negative cases, D antigens were detected in 142 cases (21.1%) by an adsorption-elution test. DEL alleles were detected only in 93 (65.5%) out of the 142 cases. Of the 532 D-negative cases in the adsorption-elution test, 5 cases (0.9%) were found to harbor DEL alleles. No DEL alleles were found in serologically D-negative samples with RhC (-).

Summary/Conclusions: An adsorption-elution test combined with RhC phenotyping can be used as a cost-efficient screening tool for Korean DEL donors despite high false-positive rates. The adsorption-elution test is also helpful to overcome inherent limitations of genotyping assays.

P-501

ANTIGEN INTEGRITY AFTER STORAGE OF RED CELL ALIQUOTS IN LIQUID NITROGEN FOR OVER 30 YEARS

J Cote, J Morden, S Pigneau, C Welch and C Pambrun

[1]Canadian Blood Services, Ottawa, Canada

Background: Cryopreservation of red cells in liquid nitrogen (LN$_2$) may be used to store aliquots of red blood cells. Storage of red cells may cause antigen deterioration over time, especially in the Duffy, MNS, P1, Knops (Kn^a, McC^a) blood group systems and the Bennett- Goodspeed (Bg) Antigen. Red cell aliquots have been added to the rare inventory at the Canadian Blood Services' immunohematology reference laboratory since 1975 for use in antibody identification or compatibility testing. A comprehensive inventory of well characterized rare red cells is essential to the immunohematology reference laboratory.

Aims: To determine the red cell antigen integrity after frozen storage in LN$_2$ for greater than 30 years.

Methods: The selected rare red cells were all frozen more than 7 days after collection and had been frozen for more than 30 years. Thirty-one rare red cells, frozen in LN$_2$ at −196°C per the method described by Gibbs et al (1962), were thawed and serologically phenotyped for M, Fy^a and Fy^b using licensed commercial antisera following the manufactures instructions. Heterozygous red cells were used as positive controls (e.g., MN, Fy(a+b+)). Monospecific anti-IgG was used if antihuman globulin was required. The phenotypes were compared to those obtained when the cells were fresh cells or at another time point during frozen storage.

Results: The results obtained were 100% concordant with the previously obtained M, Fy^a and Fy^b phenotypes for all 31 rare red cells. The strength of reactivity of all positive test results was equal to or greater than the strength of reactivity observed with the heterozygous positive controls.

Summary/Conclusions: The rare red cells maintained frozen in LN$_2$ for greater than 30 years did not show any serological evidence of antigen loss for the M, Fy^a and Fy^b antigens. Though the Duffy and MNS blood groups are known to deteriorate during storage, freezing in liquid nitrogen at −196°C, based on our findings, appears to protect the antigen integrity over long periods of time.

P-502

DOES THE TREATMENT OF RED BLOOD CELLS WITH DTT 0.014 M AND THEIR STORAGE IS BETTER THAN THE STANDARD?

C Coello De Portugal Casana[1], J Garcia Hinojosa[2], A Rodriguez Hidalgo[2], J Palomar Perez[2], R Palma Fernandez[2], M Flores Sanz[2], C Fanara[2], B Eguia Lopez[2] and A Pajares Herraiz[3]

[1]CTRA-STRA [2]Centro Regional de Transfusion Toledo-Guadalajara, Toledo, Spain [3]Direccion, Centro Regional de Transfusion Toledo-Guadalajara, Toledo, Spain

Background: Treatment of red cells (RC) with dithiothreitol (DTT) at 0.2M makes it possible to resolve the interference in the immunohematological tests produced by Daratumumab. This technique has improved safety in transfusion, but it still has disadvantages since it only allows crossmatching and antibodies screen (AS) just one.

Aims: To demonstrate that the treatment of RC with DTT at 0.014M obtains the same results as with the current technique (0.2) achieving less or equal degree of hemolysis and better interpretation of gel results. Observe the degree of hemolysis during the storage of RC treated with 0.014 DTT, comparing them with 0.2, using different methods of preservation and that this RC treated with DTT allows crossmatching and AS up to 15 days after the treatment therefore allowing a reduction of the pretransfusional time.

Methods: We selected a patient under treatment with Daratumumab with known erythrocyte genotype and 5 phenotyped units of blood donors (ABO, Rh, Duffy, Kidd MNSs). We use commercial IMMUCOR RC (IRC) as control. In day 1: We perform the crossmatch of the units and IRC without DTT treatment to check for interference. We treated 1 cc RC and IRC with DTT ratio ¼ reconstituted in PBS pH 8 at 0.014 and 0.2. We checked the erythrocyte phenotype (EP) of RC treated (ABO, Duffy, Kidd and MNSs). We performed 2 crossmatchs: one with patient plasma and another with the addition of 50 μl of IgG antisera known for clinically significant Antibodies (Rh, Duffy, Kidd, Kell and Ss) (Bio-Rad; IMMUCOR, Grifols). We Stored 250 μl of washed RBCs treated at 0.2 and 0.014 with 1 cc of different preservation media for 15 days and the degree of hemolysis (DH) was analyzed. At day 7 and 15: The DH was measured by COBASc 702 (ROCHE). We performed the Crossmatch with 50 μl of IgG antisera known for clinically significant Antibodies (Rh, Duffy, Kidd, Kell and Ss) with each sample in each preservation medium.

Results: At day 1 samples with 0.014 are equivalent to 0.2 and eliminates the interference with DTT with a lower degree of hemolysis. With AS there were similar reaction with 0.014 vs 0.2 for Rh and Ss, and there were less discrepancies with heterozygous Duffy and Kidd in 0.014 vs 0.2 respectively. Day 7: the Crossmatch was similar with 0.14 vs 0.2 in all the preservation medium, with higher hemolysis with 0.2. In the AS Duffy and Kidd heterozygotes phenotypes had higher discrepancies in the 0.2 group. The DH with LISS 0,014 was better. The group with PBS 0.2 was the worst. Day 15: the crossmatch remains viable in PBS, Alsever and Liss at 0.014 and Alsever and Liss with 0.2 There were a greater degree of hemolysis in the 0.2 vs 0.014 group.

Summary/Conclusions: Treatment with DTT of the RC with 0.014 M is similar that the RC treated with 0.2 M. There were less hemolysis in the group 0.014 vs 0.2 during the storage of the RC, especially with Liss and Alsever preservation mediums. There were less discrepancies in the AS at day 7 and 15 with RC treated with 0.014.

P-503

Abstract has been withdrawn

P-504

Abstract has been withdrawn

P-505

A NEW RAPID INDIRECT ANTIGLOBULIN TEST USING M-TRAP® AND ONYX® TECHNOLOGY

L Soufflet, S Barradeau, C Betremieux, A Dambron and P Desmet
R&D, DIAGAST, LOOS, France

Background: A new Blood Group Serology technique has been developed based on membrane technology. Indirect antiglobulin technique using this innovative process of M-TRAP® on the ONYX® automated system is intended to detect unexpected antibodies in plasma. This new generation of IAT is based on the detection by anti-immunoglobulin and/or complement reagent, of immune complexes (RBC + Antibodies) after retention of sensitized cells onto a spot on a porous membrane. This simple technology without centrifugation step allows a very convenient time to result of 15 min.

Aims: The present work reports the results obtained by the Indirect Antiglobulin Test (IAT) detection of unexpected red-blood cell antibodies using the M-TRAP® assay with the ONYX® automated system and compares sensitivity and specificity against the more classical centrifugation-based gel tests.

Methods: The red blood cell panels are incubated with plasma samples in microtiter plate during 10 min, then transferred on a membrane spot in the presence of a polycation, forming a red cell spot. The polyvalent antiglobulin is so added in order to detect the antibodies and consolidate the cell's network. After washing, the pan agglutination effect is eliminated resulting in red blood cells elimination white spot for negative samples and retention of a red blood cell spot if unexpected antibodies are fixed on RBC. In this first automated study, a cohort of negative and positive samples, respectively selected from the Transfusion laboratory of the Lille Hospital Center (France) or screened in the French Blood Banks was tested. The samples were also tested with a gel test system.

Results: A panel of 50 positive samples (antibodies to RH/KEL/DUFFY/KIDD/MNS/Lewis, P1...) has been tested with the new M-TRAP ® test using the ONYX® automated system and with a gel test as reference test ranking the sensitivity agreement between the two techniques near 100%. Moreover, the anti-D French National reference sample can be detected as low as 2.5 ng/ml depending of used red blood cell's panel. All the negative samples (n = 200) were found negative in all techniques. Interestingly, time-to-result (TTR) is shortened to 15 min with the M-TRAP® assay compared to about 25 min with the gel test system.

Summary/Conclusions: This comparative study shows that IAT performed with the simple and rapid M-TRAP® method is as specific and sensitive as the usual gel filtration tests for the detection of red blood cells unexpected antibodies. We conclude that this new generation of test is an efficient and fully automated alternative to gel filtration centrifugation-based tests. The shortened TTR makes the M-TRAP® assay particularly attractive, especially in case of emergency transfusion.

P-506

15 MINUTES TO PERFORM COMPLETE BLOOD GROUP SEROLOGY TESTING WITH A NEW TECHNOLOGYM–TRAP® AND ONYX® AUTOMATED SYSTEM

A Delanoë, K Ganier, M Dupont, C Betremieux and S Barradeau
R&D, Diagast, LOOS, France

Background: A blood transfusion is a potentially hazardous procedure. Thus, complete blood compatibility should be tested prior to transfusion. However, in situations where a delay in testing might jeopardize a patient who urgently requires red blood cell transfusion, getting the compatibility test results may be an issue. This is especially due to the time needed to perform indirect antiglobulin tests. The new fully ONYX® automated system using M-TRAP® tests (ABO-RH1 typing test and antibody screening IAT) can provide complete blood group serology results within 15 min and minimizes the risk of blood incompatibility during emergency transfusions.

Aims: The present work reports the time-to-result data obtained by the M-TRAP® technology (ABO-RH1 blood typing tests and antibody screening- IAT) and the ONYX® automated system.

Methods: We performed two studies:

For each test, time-to-result is compared to a standard automated gel filtration technique. This time is measured from the loading of the sample to the display of the result. Time to result was evaluated for specific tests and in combination:

- 96 samples for the antibody screening IAT

- 150 samples for the ABO-RH1 typing test (including reverse typing).

Combined tests were launched for 36 samples to evaluate the time-to-result .when complete blood group serology testing is required.

Results: Each antibody screening test is performed within only 15 min. Each ABO-RH1 test, including reverse typing, is performed in less than 8 min. Considering the combined test (ABO RH1+ Reverse typing + Antibody screening), time-to-result obtained from the loading of sample to the display of the result is less than 15 min. Thanks to the management of ABO-RH1 test which is performed during the 10 min incubation of red blood cell panel with plasma sample for the antibody screening test, each combined test is performed in less than 15 min. We observed 100% of concordance between the M-TRAP® technique and the gel filtration technique used as a standard.

Summary/Conclusions: These results show that the M-TRAP® technology and the ONYX® automated system is offering a fast and secure solution to test the blood compatibility in case of emergency in transfusion.

P-507

MULTICENTRE EVALUATION OF THE NEW M-TRAP® IN ABO/RHD SYSTEM IN TAIWAN

MT Lin[1], Y Chou[1], C Chen[2], T Lee[3], F Chu[3] and J Chang[1]
[1]Department of Pathology and Laboratory Medicine, Taoyuan Armed Forces General Hospital, Taoyuan [2]Division of Transfusion Medicine, Department of Pathology and Laboratory Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei [3]Department of Clinical Pathology, Far Eastern Memorial Hospital, New Taipei, Taiwan, Republic of China

Background: Implementation of manual blood group confirmation of ABO/RhD for pre-selection of donors, blood group control of blood bags, it reduces human errors, allows economic, high throughput and improves turnaround time.

Aims: We aimed at evaluating the ease of use and the efficiency of the ABD PAD® (DIAGAST, French) in comparison to the clinical tube method in three different laboratories.

Methods: ABD PAD® technology is based on the immobilization of antibodies covalently bounded to a porous membrane. Only the red blood cells having the corresponding antigen are fixed into the membrane revealing immediately the reaction. 3 steps procedure allows a manual blood group confirmation in 30 s in a safe and standardized way. After initial training, ABD PAD® was used in parallel to Tube method following the daily workload. A total of 480 individual samples were run ABD forward grouping: 373 samples from patients, 53 samples from military health examination, 47 samples from blood bags and 5 specific cases.

Results: The ABD PAD® was more rapid than Tube method, need not to centrifuge. For 5 specific cases, two A2 subtypes show A type and three B3 subtypes show B type, respectively. Others are consistent in two methods. Regarding the ease of use, ABD PAD® was intuitive and user friendly.

Summary/Conclusions: ABD PAD® brings appreciated new features that could further patient's bedside and for outside lab's purpose (mobile blood collection, ambulances, military etc.), thus accommodating a wide range of clinical needs. We

suggest the ABD PAD could setup ABD reverse grouping for AB subtypes in the future.

P-508

INTRODUCTION OF AUTOMATED HIGH TITRE ANTI-A AND/OR ANTI-B SCREENING IN AUSTRALIAN BLOOD DONORS

T Powley[1], M Suarez[2], S Ismay[3], J Daly[1] and J Pink[1]

[1]Clinical Services and Research [2]Scientific & Technical Services, Australian Red Cross Blood Service, Brisbane [3]Manufacturing, Australian Red Cross Blood Service, Sydney, Australia

Background: Historically, the Australian Red Cross Blood Service (Blood Service) performed high titre antibody (HTAB) testing manually. The testing was restricted to group O apheresis platelet donations because all previously reported cases of haemolysis from minor ABO incompatibility involved Group O donors. The Blood Service commenced a review following two reported serious transfusion reactions due to non-group O components containing high titre anti-A and/or anti-B, including one Group A apheresis platelet with an extremely high titre anti-B transfused to a group AB recipient.

Aims: To identify and evaluate alternate testing methodologies to enable increased testing of group A and B apheresis donations and other high volume clinical plasma components.

Methods: A literature review was conducted to determine existing international practice. Automated HTAB screening using the Beckman Coulter PK7300 is utilised by the National Health Service Blood and Transplant (NHSBT) in England and the Scottish National Blood Transfusion Service (SNBTS) and an evaluation of the suitability of these methods was completed in 2016. In 2017 the Blood Service completed the design control and validation for a modified Automated HTAB screening test based on the NHSBT and SNBTS methods. Two HTAB tests using different dilution ratios are tested in parallel, with the lower dilution ratio (32) which approximates a conventional tube saline direct agglutination titre of 128 differentiates between low and high titre anti-A and anti-B. The second dilution ratio (64) which is the highest dilution ratio available on the Beckman Coulter PK7300 is used to identify donations that may have exceptionally high titre anti-A and/or anti-B and require further testing. The diluted donor plasma is tested separately against a group A1 and a group B cell (Beckman Coulter PK System Reverse Grouping Cells), with the reported result from the PK7300 being based on the combination of the results with the individual cells. Negative results must be obtained for both cells for an overall negative result to be reported.

Results: During the evaluation and validation testing 1498 samples were tested with 24% (372) of samples testing positive for HT32 (PK dilution ratio 32). A further 122 samples returned an indeterminate (?) result which defaults to a positive result interpretation, increasing the rate of donations with high titre anti-A and/or anti-B to 33%. In total 60% or 297 of the 494 samples testing positive for HT32 were also positive with the higher dilution ratio HT64.

Summary/Conclusions: The Australian method has been registered as an accredited in-house class 3 IVD with the Australian regulatory bodies. All apheresis platelets and clinical plasma components that are tested and found to be negative in the HT32 test are labelled as "Low anti-A/B" on the component release label. Implementation of this new automated test will improve access to low titre anti-A/B clinical plasma components and apheresis platelets reducing the risk of transfusion reaction where the intended recipient is ABO incompatible and transfusion is unavoidable.

P-509

AUTOMATED ABO ANTIBODY TITRATIONS ON THE NEO IRIS™ – CONSISTENCY AND REPRODUCIBILITY

E Preuss[1], B Berst-Susanto[2], S Oldekamp[1], J Muehl[1], A Gellerer[1], D Ruebsamen[1], S Gurnik[1], D Fung[1], R Whitmarsh[1], O Meyer[2] and M Spigarelli[1]

[1]R&D, Immucor GmbH, Dreieich [2]ZTB Zentrum für Transfusionsmedizin und Zelltherapie Berlin gemeinnützige GmbH, Ein Gemeinschaftsunternehmen der Charité – Universitätsmedizin Berlin und des DRK-Blutspendedienstes Nord-Ost, Berlin, Germany

Background: ABO antibody titrations for IgM and IgG antibodies are clinically relevant in several areas such as ABO-incompatible stem cell and solid organ transplantation, blood group O donor characterization for transfusion as well as ABO-incompatible pregnancies. The most common methods for the determination of ABO

antibody titers, including conventional tube test and column agglutination technique, are time consuming, poor in accuracy and reproducibility, and are subjective with respect to interpretation of the titer end point.

Immucor's Capture® based fully automated IgM and IgG ABO titration assays have been validated for use on the Galileo NEO®. Those ABO titration assays have now been validated internally and in a clinical study on Immucor's newly developed platform, the NEO Iris™.

Aims: The aim of the study was to evaluate the performance of fully automated IgM and IgG ABO titration assays on the NEO Iris™ platform internally and in clinical settings.

Methods: The NEO Iris™ offers fully automated IgG full range assays with dilutions from neat up to 128 (low titer assays) and 16 to 4096 (high titer assays) as well as full range IgM assays from neat to 128 for A1, A2 and B cells. All methods are fully automated with the titer result provided by the instrument without manual intervention.

For reproducibility and repeatability of fully automated ABO titration assays, donor plasma was tested and evaluated with low titer IgM and IgG as well as high titer IgG configuration. Two donor specimens per assay were tested in triplicates in the morning and afternoon on five non-consecutive days within 21 days on three NEO Iris™ instruments resulting in 180 titer results per assay. To verify titer consistency studies were performed internally and in clinical settings. In the clinical study, at least 80 patient specimens per IgM and per IgG assay (low and high titer combined) were tested utilizing the automated ABO titration range assays on the NEO Iris™ versus Galileo NEO®.

Results: The automated ABO titration assays demonstrate very high reproducibility across different NEO Iris™ instruments and different time points. 180 titer results were analyzed for each IgM and IgG assay. On average, 77% of all assays show the same titer, 23% differ by one doubling dilution and only 0.1% differs by two doubling dilutions. High consistency between NEO Iris™ and Galileo NEO® was demonstrated internally. Clinical studies confirmed high consistency of titer results (titer results within two doubling dilution steps) for all assays under evaluation.

Summary/Conclusions: Fully automated ABO titration assays offer an excellent reproducibility and repeatability across several NEO Iris™ instruments and high consistency as demonstrated internally and in a clinical study. Immucor provides a complete and highly consistent IgM and IgG ABO titration assay set on the Galileo NEO® and NEO Iris™ which may help to overcome currently labor intensive and less precise manual techniques.

P-510

PERFORMANCE EVALUATION OF THE NEW VERSION INSTRUMENT SOFTWARE V.04.07.02 FOR THE FULLY AUTOMATED BLOOD BANK ANALYZER IH-1000

F Pohlmann[1], Y El-Aini[2] and R Muniz[1]

[1]IHD Marketing, BIO-RAD, Cressier, Switzerland [2]GCO, BIO-RAD, Paris, France

Background: Delivering the right blood in a short time is one of biggest challenges of a laboratory. Requests for urgent blood delivery can arrive at any time throughout the day and must be handled in between the daily routine testing. The management and testing of urgent blood samples requires staff resources as well as additional resources on automated instruments. The management of STAT samples in automated instruments is essential to ensure an on-time delivery of urgent blood sample requests without delaying or interrupting the daily routine sample testing.

Aims: The aim of this evaluation is to determine, under optimal customer laboratory conditions, the performance of the immunohematology automation of IH-1000 in combination with the new instrument software version. In particular the management of STAT samples for ABO/D reverse + full Phenotype and antibody screening and antibody identification in routine testing.

Methods: Performance evaluation in a routine customer laboratory with the new IH-1000 instrument software V.04.07.2 by using the ID Gel System and a comparison to known and previously obtained data with the routine software version used (V.04.05.01).

Results: All results were compliant and according to the expected results known from previous testing in routine. No cross-contamination or carry-over has been observed. For ABO/D + full Phenotype STAT samples the average time to results was 15.7 min. Compared to the previous version this is an improvement of 21.7 min. A reduction of 58%. Also for Ab. Screening and Ab. Identification improvements in time to result have been observed. A reduction of 11.1 min (19.8%) for Ab. Identification and 14.1 min (27.8%) for Ab. Screening results.

Summary/Conclusions: In comparison to the software used in routine testing the IH-1000 instrument software V.04.07.02 shows significant improvements in time to

result for STAT and routine sample handling of full Blood Groups including Phenotype, Antibody Identification and Antibody Screening.

P-511

COMPARATIVE EVALUATION OF DAYMATE S AND IH-1000 FOR AUTOMATED ABO-RH TYPING

J Lee, J Shin, H Choi, S Kim and M Shin

Laboratory Medicine, Chonnam National University Hwasun Hospital, Hwasun, Republic of Korea

Background: It is important to obtain correct results of patients' ABO and RhD types for successful blood transfusion. Although ABO and RhD typing was traditionally performed by manual methods using slide and test tubes, it has been replaced by automated immunohematology analyzers.
Aims: This study was aimed to test the automated DAYmate S for validation of ABO and RhD typing by comparing manual method and IH-1000 system.
Methods: A total of 311 patients' samples was randomly collected and tested during 2 months at Chonnam National University Hwasun Hospital. ABO and RhD typing of each sample was performed using manual method, DAYmate S system, and IH-1000 system, respectively. Manual method was done as a reference procedure by slide or tube method. DAYmate S used column agglutination with gel and reagents added to empty wells.
Results: Among 311 samples, 106, 88, 80, and 37 samples were blood type A, B, O, and AB, respectively. There was only one Rh-negative type O sample. The concordance rates of ABO typing between manual method and automated system were 100% (331/331) for DAYmate S system and 99.7% (330/331) for IH-1000 system. One sample showed ABO discrepancy in IH-1000 system, which was as follows 4+ with anti-A, 4+ with anti-B, 1+ with A1 RBC, and 1+ with B RBC, respectively. That sample was obtained by the patient diagnosed as plasmacytoma. Comparing the correlations between manual method and automated analyzers using Pearson's correlation, the rho values of DAYmate S and IH-1000 were as follows 1.00 and 0.99 for anti-A, 0.99 and 0.99 for anti-B, 0.30 and 0.44 for anti-D, 0.97 and 0.97 for A1 RBC, and 0.95 and 0.94 for B RBC, respectively (all P < 0.001). Both automated immunohematology analyzers showed good correlation with manual method. Above all, DAYmate S system exhibited slightly better correlation with manual method than IH-1000 system in the respect of anti-A and B RBC.
Summary/Conclusions: The DAYmate S automated immunohematology analyzer showed appropriate concordances as well as good correlations with manual method for ABO and RhD typing. DAYmate S was sufficient for use in ABO and RhD typing with clinical samples.

P-512

COMPARISON OF AUTOMATED AND MANUAL ALLOANTIBODY TITRATION USING CAPTURE®, GEL AND TUBE

D Ruebsamen, A Gellerer, E Preuß and M Spigarelli

R&D, Immucor Medizinische Diagnostik GmbH, Dreieich, Germany

Background: The titration of alloantibodies to a red cell antigen is a semi-quantitative method to measure the strength of an antibody which is used to predict the fetal risk of suffering from hemolytic disease of the fetus and newborn (HDFN) or for donor/patient characterization in incompatible blood transfusions and organ transplantation. Due to technical and human factors the manual titration of antibodies remains highly variable and labor-intensive therefore, an automated solution is strongly desired. Immucor previously launched IgG and IgM specific Capture® based fully automated ABO titration assays which are available on Immucor's Galileo NEO® and NEO Iris™ platforms. Currently IgG specific assays for the titration of alloantibodies are in development.
Aims: The aim of the study was to compare IgG titer results obtained by different automated and manual techniques, i.e. automated solid phase (Capture®), manual column agglutination technique (gel) and manual tube test (IAT).
Methods: Patient, pregnancy and donor samples with different known alloantibodies as well as the 2nd WHO international standard for anti-D immunoglobulin were tested using 1) a Capture® based prototype assay including automated titration of the samples on the NEO Iris™, 2) a Capture® based prototype assay using manually diluted samples on the NEO Iris™, 3) manual gel card (Anti-IgG) with manually diluted samples, 4) gel card (Anti-IgG) with manually diluted DTT-treated samples and 5) indirect agglutination tube test with manually diluted samples.
Results: The titer results of the Capture® based assay using automated dilution of the samples are very consistent to the titer results of the manually diluted samples on the same assay type on NEO Iris™ (all titers within one doubling dilution). Capture® and gel titers are more comparable with DTT-treated samples than with untreated samples. IAT shows the highest variations compared to gel and Capture®.
Summary/Conclusions: The prototype assay for automated NEO Iris™ alloantibody titration is able to accurately pipette samples in doubling dilutions with minimum operator time or effort. Comparison to other techniques proves the assay to be specific for clinically relevant IgG alloantibodies.

P-513

COMPARATIVE ANALYSIS OF THE GEL TECHNIQUE AND THE SOLID-PHASE TECHNIQUE "CAPTURE-R" WHEN CONDUCTING CROSSMATCH TESTS BEFORE THE TRANSFUSION OF ERYTHROCYTE-CONTAINING MEDIA OF HEMATOLOGICAL PATIENTS

OS Kalmikova[1], I Dubinkin[1], A Rakhmani[2], M Danilevskaja[1], V Zuravlev[3] and T Gaponova[2]

[1]Laboratory of Quality Control and Safety of Transfusions [2]Department of Blood Cells Processing and Cryopreservation [3]Department of Clinical Transfusiology, National Medical Research Center for Hematology of the Russian Federation in Moscow, Moscow, Russian Federation

Background: Conducting cross-matching (a test for individual compatibility) before hemotransfusions is an important part in ensuring the immunological safety of the transfusion therapy. There are no crossmatch methods that would reliably reveal all clinically relevant anti-erythrocyte antibodies and would not give false-positive results. However, in a number of cases, application of particular crossmatch testing methods enables to select a compatible blood and have a safe transfusion, when other methods do not allow doing this.
Aims: To compare the gel technique and the solid-phase technique of crossmatch testing in individual selection of erythrocyte-containing media of hematological patients.
Methods: In 2017 4385 crossmatch tests before the transfusion of erythrocyte-containing media were conducted on the analyzer "Galileo Neo" Immucor (USA) using the method of solid-phase technique "Capture-R" for 1055 hematological patients with various nosologies between 18 and 76 years of age (average age – 45). Similar research and the direct Coombs test were conducted on gel cards Liss/Coombs "Bio-Rad" (USA).
Results:. 6 patients with a positive direct Coombs test (between 25 and 72 years of ages, average age 56), which makes 0,57% of the total number of hematological patients with the diagnoses: 2-AIGA (conducted with 3 hemotransfusion), 1 - myelogenous leukemia (2 hemotransfusions), 1 - multiple myeloma (3 hemotransfusions), 1 - clear cell carcinoma of kidney (2 hemotransfusions), 1- Waldenstrom macroglobulinemia (6 hemotransfusions) all the crossmatch tests in the gel technique "Bio-Rad" were positive (incompatible), while in the solid-phase technique "Capture-R" the same tests were negative (compatible). In other cases both methods demonstrated identical results. The test with selected compatible by the solid-phase method samples of the donors' erythrocytes was negative (compatible) with the recipients in all cases and all hemotransfusions of 6 recipients were without hemolytic incompatible blood transfusion reactions and were characterized by clinically relevant hemoglobin increase (>10 g/l).
Summary/Conclusions: In some pathological states there are anti-erythrocytic IgM, which do not have a clinical relevance and do not cause hemolysis. Gel techniques do not enable, without the processing of serum, to differentiate IgM from IgG. Adhesion methods at the solid phase allow revealing only IgG, which, in some cases, enables to select compatible erythrocytes. At the same time, one should bear in mind the possibility of presence of pure IgM against erythrocytic allotypic antigens erythrocytes of Rhesus system, Kell–Cellano system and others, which have hemolytic efficiency. Final decision about immunological compatibility and conducting a hemotransfusion is made based upon the compatibility test in vivo.

P-514
A MODIFIED ADSORPTION METHOD WITH PEG

G Gryfelt and A Wikman

KITM, Karolinska University Hospital, Stockholm, Sweden

Background: Adsorption is used to determine if a patient with WAIHA also have underlying alloantibodies. A common method for adsorption is to use PEG; plasma, RBC and PEG are mixed in equal proportions and incubated at 37°C for 15 min, and after centrifugation the supernatant is tested against a panel of RBCs by indirect antiglobulin test (IAT), either by tube or gel technique.

We have a slightly different approach, after the first incubation and centrifugation we mix 100 µl of the plasma-PEG supernatant with 50 µl 0.8% RBCs in LISS in tubes. Thereafter we incubate the mixture at 37°C for 15 min, and after one wash with PBS the pellet is transferred to a gel card containing anti-IgG.

A few years ago, we compared our modified PEG-method with three other PEG adsorption methods.

Aims: The aim was to identify the adsorption method that best detected underlying irregular erythrocyte antibodies.

Methods: Plasma with autoantibodies detected from 5 patients were auto-adsorbed and plasma with weak (titer ≤2.) alloantibodies (anti-D, anti-E, anti-c, anti-e, anti-K and anti-S) from 5 patients were allo-adsorbed using antigen negative RBCs.

Method 1: Our modified PEG-method, see background. Method 2–4: Different amounts of the plasma-PEG supernatant and 50 µl 0.8% RBCs in LISS was transferred to a gel card containing anti-IgG, incubated at 37°C for 15 min and centrifuged. Method 2: 100 µl plasma-PEG suspension. Method 3: 50 µl plasma-PEG suspension. Method 4: 25 µl plasma-PEG suspension. Only one sample with autoantibodies were adsorbed with method 4, and one sample with auto-antibodies were not tested with method 2. All four methods were used for testing plasma samples containing allo-antibodies.

Results: Autoantibodies: Three of five samples tested were still positive using methods 1–3 and one gave negative results with all methods tested. In the fifth sample an anti-D due to prophylaxis were discovered by methods 1 and 3 but not by method 4, method 2 not tested.

Alloantibodies: Three of six weak allo-antibodies tested were detected by all methods (anti-D, anti-c and anti-e). Two weak allo-antibodies (anti-E and anti-S) were detected by methods 1–2 and 1–3 respectively. The weak anti-K was not detected by either method.

Method 1 gave the strongest positive reactions and method 4 the weakest. Methods 2 and 3 were difficult to interpret, probably because of a large volume of PEG.

Summary/Conclusions: Method 1 resulted in strong specific reactions and is used in our laboratory both in auto- and allo-adsorption.

P-515
COMPARISON OF PERFORMANCE BETWEEN AUTOMATIC BLOOD GROUPING ANALYZER PK7300 AND NEO IN BLOOD GROUP SCREENING

T Xu[1] and M He[2]

[1]Department of laboratory [2]Department of research, Blood center, Wuhan, China

Background: ABO blood group and RhD blood group are the very important human erythrocyte blood group systems. They play an important role in clinical safety transfusion, organ transplantation, tissue matching and forensic identification. Accurate screening ABO and RhD blood groups are the prerequisites for safety blood transfusion. The automatic blood grouping analyzer PK7300 and NEO are widely used in blood stations, but their performance is rarely compared.

Aims: To compare the performance of automatic blood grouping analyzer PK7300 and NEO in screening ABO and RhD blood groups.

Methods: First,100 samples which had been determined were repeatedly detected for 3 times using automatic blood grouping analyzer PK7300 and NEO, to see whether the results were consistent. Second, ABO blood group and RhD blood group were detected using PK7300 automatic blood grouping analyzer and NEO automatic bold grouping analyzer, O cell agglutination and RhD negative specimens were sent to the blood transfusion research department of Wuhan Blood Center to identify.

Results: First, The results of repeated determination were consistent for 3 times .Second, The 24353 blood donors were detected, and the ABO blood group correct rate of PK7300 automatic blood grouping analyzer and NEO automatic blood grouping analyzer were 99.55% and 99.59%, respectively;the RhD blood group correct rate were 99.93% and 99.91%, respectively.No statistically significant. Third,32 cases doubtful samples were sent to the blood transfusion research department, and 18 cases with weak-plasma antibody, resulting in a pattern of A cell and B cell reaction

weakly. 4 cases with weak anti-A and anti-B, 4 cases were subgroup and 6 cases were irregular antibodies.

Summary/Conclusions: PK7300 automatic blood grouping analyzer may have good stability. There was no statistical difference between the results of PK7300 automatic blood grouping analyzer and NEO automatic blood grouping analyzer, and the results were comparable. Compared with NEO automatic blood grouping analyzer, PK7300 automatic blood grouping analyzer would have more convenient operation, faster speed, less reagent, more clear instrument picture and intuitive results, more convenient manual checking, which would be reliable and suitable for blood stations with large blood samples. The main reasons for doubtful ABO blood groups by automatic blood grouping analyzer were attributed to weak anti-B, anti-A and irregular antibodies.

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Abstract has been withdrawn

P-517
PERFORMANCE EVALUATION OF THE NEW ECHO LUMENA

G Cook

Royal Alexandra Hospital, Edmonton, AB, Canada

Background: Echo Lumena™ is the newly CE marked Immucor immunohematology platform used in blood bank laboratories. Current user of the Galileo Echo® in a large hospital did a clinical process evaluation of this new instrument.

Aims: The objective of the study was to assess the concordance of group and screen assays using Echo Lumena compared to the Galileo Echo and to evaluate the sensitivity and specificity of the new platform.

Methods: The performance of the new automated Echo Lumena was compared with Galileo Echo instrument over 10 days using patient samples as they came into the clinical laboratory. All specimen were run within 24 h of collection and the same reagent lot numbers were used on both platforms. A total of 124 blood groups, 116 screens, 25 antibody identifications and 20 ABO/Rh donor unit confirmations were performed in addition to 10 cord blood samples for ABO/Rh.

Results: After comparing results, Echo Lumena showed a 99% concordance (123/124) with Galileo Echo for Group Assay and 98.2% (114/116) for Screen assay. The Echo Lumena detected two additional clinically significant antibodies (anti-M and Anti-Fy[a]) not detected by Galileo Echo. The quality of image on the Echo Lumena was improved compared to the Galileo Echo.

Summary/Conclusions: Echo Lumena has shown concordance with the Galileo Echo and improved sensitivity to clinically significant antibodies. Staff feedback was positive with the shorter run time on the Echo Lumena. There was no change in operation to use the Echo Lumena so no training was required.

P-518
EVALUATION OF THE AUTOMATIC ANALYZER ORTHO VISION® MAX FOR PRETRANSFUSIONAL TESTS

S Villa[1], M Poretti[1], E Magnabosco[1], R Trotti[1], E Raspollini[1], M Pizzi[1], E Rozek[2] and W Malomgré[3]

[1]Centro Trasfusionale, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico [2]Ortho Clinical Diagnostics, Milan, Italy [3]Ortho Clinical Diagnostics, Turnhout, Belgium

Background: An increasingly demanding routine and the continuous reduction of available resources have called all the laboratories to do more, better and with fewer resources. For this purpose laboratories of any size can take advantage by using automation. The choice of the type of instrumentation best suited to their own reality must take into consideration performance, efficiency, safety and economy of scale. ORTHO VISION® Max is presented as an automatic tool with high performance volumes.

Aims: We aimed at evaluating the ease of use and the efficiency of the ORTHO VISION® Max Analyser (VISION Max) for routine use in our transfusion laboratory in comparison to manual method and Ortho AutoVue Innova.

Methods: Basic immunohematology tests have been performed: direct and indirect determination of ABO group, Rh type, Rh/K phenotype and Dweak, auto-allo

erythrocyte antibodies screening and compatibility tests. In addition, second level tests were performed: identification of auto-antibodies, typing of non-ABO/Rh systems and erythrocyte antibodies titration for a total of 2,057 tests.

The system has been evaluated for following times: startup time, periodic maintenance and execution of internal quality control (CQI): direct and indirect determination of ABO + type Rh + detection of erythrocyte antibodies for 4 samples; Turn-Around Time (TAT): group determination and phenotype with fully loaded machine; management of urgencies (STAT): group determination and antibody screening with fully loaded or empty machine; system efficiency (base protocol - PB): routine repetition of the 3 instruments currently in use in our laboratory for 2 days; (advanced protocol – PA): erythrocyte antibodies titration; assessment of reagent consumption; Reflex-Test; Crash-Test: maximum number of blood samples possible for the instrument with complete test profile: direct and indirect determination of ABO group, Rh type, Rh/K phenotype, allo erythrocyte antibodies screening.

Results: The startup time: 14', periodic maintenance: 14' daily, 18' weekly and 13' monthly; CQI: 27'; TAT: 84 samples, 252 tests,3 h14' time; STAT: fully loaded 26', and empty 18'; PB: 1554 tests in two days; PA: 33' each titrations, 15 tests performed; Crash-Test: 84 samples and 332 tests performed; Reflex-Test: was performed on 30 samples as expected; reagent optimization: dedicated cassette punch tools allows for a 97% efficiency use of wells.

The test results are in agreement with those obtained with the methods in use.

Summary/Conclusions: Experimentation has shown that ORTHO VISION® Max has an excellent impact on the Laboratory routine with a considerable reduction in test execution time, especially for urgent management, and reagent consumption. The possibility of performing the Reflex-test allows a uniform treatment of unexpected results and an optimization of reporting times. Titrations performed with Vision allow better standardization and efficiency (1/3 of the time to complete the test in tube).

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EVALUATION OF MORE THAN 1000 WEAK D ANTIGEN TESTS BY USING AUTOMATED AND MANUAL METHODS IN FARS PROVINCE BLOOD TRANSFUSION SERVICE DURING 2017 IN IRAN

A Salah[1], M karimi[1,2], M Jalali Far1[3,4], A Khosravi[3] and M Shirmohammadi Esfeh[1]

[1]Blood Transfusion Research Center High Institute for Research and Education in Transfusion Medicine Tehran Islamic Republic of Iran [2]Shiraz Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran [3]Blood Transfusion Research Center High Institute for Research and Education in Transfusion Medicine Tehran, Islamic Republic of Iran [4]Health Research Institute, Research Center of Thalassemia & Hemoglobinopathy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Khuzestan, Ahvaz, Islamic Republic of Iran

Background: The nature of laboratory tests prone to errors in every step. The heavy workload and the importance of accuracy and precision in maintain Good Laboratory Practice in blood transfusion caused the use the automation in many aspects of transfusion service. One of the important and vital parts of transfusion is Immunohematology and Blood group typing The ABO and Rh blood group system play great and vital role in the blood transfusion. Incompatible or wrong blood group typing may lead to mortality and morbidity due to hemolytic reaction or in Rh system cause sensitization in first exposure and then acute or delayed hemolytic reaction specially in blood dependent patients. There is some controversy about the conventional and automated blood group typing about advantages and disadvantages between two methods and we want to study and compare both of methods.

Aims: Evaluation and compare the manual with standard and routine methods with automated methods in blood grouping of blood donors.

Methods: In this cross sectional experimental study that we conducted from 15 March 2017 until 22 April 2017 on blood donors that admitted to Fars Blood Transfusion service. All blood samples tested by automated Qwalys Diagast instruments and for confirmation the presence of Weak D antigen among the Rh-negative samples, all Rh D negative samples checked by standard manual methods by using blend Rh antisera of Iranian Blood Refine and Fractionation (IBRF) and Cinna Gen IgM antisera for D- Antigen commercial kits and in parallel the samples were checked by using three automated Qwalys Diagast instruments and DIAGAST Anti-D WEAK kits. For checking the validity of performance of automated instruments 19 Rh D positive confirmed samples was randomly selected and Rh D typing again done for those samples. The data were collected and analyzed by SPSS18.

Results: The total blood donations that tested was 15889. Rh D positive was 14470 (91.07%) and 1419 (8.03%) showed D negative by automated procedure. By using manual methods and two different Iranian commercial kits 1422 samples was Rh D

negative. For three samples that was negative by manual methods we performed weak D procedure by IgG Cinna Gen antisera and one of them showed weak D positive reaction. Examination of 19 Rh D positive samples by automated showed that one sample could not read the result by two instruments and the third instrument showed negative Rh D for that sample.

Summary/Conclusions: According to our findings and with take in consideration of importance the Rh D in transfusion, implementation of automated procedures in centers with high number of blood donors and blood dependent patients is highly recommended and can prevent many errors that maybe happened during perform testing such as Variability in red cell concentration in red cell suspension, Lack of consistency in reading agglutination reaction and other human errors. Use the automated methods cause the saving the time and cost and at same time showed the highly sensitivity results. It also should take care about the quality of blood samples to avoid wrong blood group typing and the instruments must be validate all time to prevent the errors that happened in ours study.

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EXPERIENCE IN THE IMPLEMENTATION OF TYPE AND SCREEN – ABBREVIATED CROSSMATCH PROCEDURE (TAS-CIS) IN A BLOOD BANK OF A HOSPITAL EMERGENCY CENTER IN LIMA PERU

E Carrillo[1], E Santiago[2], S Arce[3], Y Laura[3] and A Laura[3]
[1]Hospital Rebagliati Essalud, Lima [2]UPCH, Lima [3]CELIM ESSALUD, Lima, Peru

Background: The transfusion of blood concentrates (CH) in an emergency center is of the utmost importance, because it will allow the rapid recovery of oxygen transport capacity in a critical patient. Compatibility tests include the largest major crossmatch (PC) and/or the Type and Screen - abbreviated crossmatch procedure (TAS-CIS), and these should allow the transfusion of compatible and timely blood. Since June 2016, TAS-CIS was implemented at the blood bank of the Emergency Center of Lima of the Rebagliati Healthcare Network following the Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories, BCSH

Aims: Implementation of TAS-CIS in a blood bank of a hospital emergency center to attend compatible and timely blood

Methods: The TAS procedure was performed in the Echo Lumena (Immucor). The blood group ABO/RhD, was performed with anti-A, anti-B, anti-AB, anti-D (IgM), anti-D (IgG + IgM) and A1, B cells. The screening of irregular antibodies (EAI) was carried out with the capture technology in solid phase (Immucor). The detected antibodies were identified in the Immunohematology Laboratory of Edgardo Rebagliati Martins Hospital. If the patient had previously registered an alloantibody in the e-delphyn software (Hemasoft) or the TAS-CIS detected an alloantibody, the major crossmatch was performed. If the need for blood was very urgent, the CH was released with ABO/RhD group and abbreviated crossmatch procedure. Then the TAS-CIS was continued. In the case of patients with positive EAI and direct positive Coombs without previous transfusion, we proceeded with the protocol of incompatible blood by AHAI.

Results: Between June 2016 and February 2018, 7067 TAS-CIS were processed to treat 5085 patients in a critical situation. 15671 CH units were reserved and 10,683 (68.2%) were transfused. TAS-CIS positive was found in 177 (2.5%) samples and TAS-CIS negative in 6890 samples (97.5%). We identified 68 antibodies: Anti-E (22), Anti-Dia (18), Anti-c (8), Anti-K (3), Anti-Fya (3), Anti-Jka (3), Anti-D (2), Anti-e (2), Anti-S (2), Anti-C (1), Anti-Jkb (1), Anti-Fyb (1), Anti-Lea (1), Anti-Lua (1). Patients with positive TAS-CIS were crossmatching before transfusing CH. The results of the compatibility tests (TAS-CIS and/or crossmatch) were 15226 (97.2%) compatible, 445 (2.8%) incompatible. Due to emergency situations, 29 (0.2%) "Less incompatible" units were transfused. The process time of the TAS-CIS was between 30 and 40 min, for the first application, and for the following ones it was 8 to 10 min. In cases of great urgency, requests were attend without major crossmatch and then the TAS-CIS was continued.

Summary/Conclusions: The implementation of the TAS-CIS in the CELIM has allowed to attend red blood cell concentrates with a single sample, within 72 h, in a safe and timely manner, with service times between 30 and 45 min. A TAS-CIS was processed for each 2.22 packed red blood cells, allowing the saving of 8604 major crossmatch.

P-521

MDMULTICARD® – A FAST AND RELIABLE NEW MEMBER FOR THE IMMUNOHEMATOLOGY TOOLBOX

G Rizzi[1], Y Song[1], A Zorbas[1], A Caesar[2], P Schwind[2], C Gassner[3], C Engstroem[1] and B Frey[1]

[1]Immunohematology, Blood Transfusion Service Zurich Swiss Red Cross, Schlieren
[2]Medion Grifols Diagnostics, Duedingen [3]Genetics, Blood Transfusion Service Zurich Swiss Red Cross, Schlieren, Switzerland

Background: The MDmulticard® Basic Extended Phenotype (Medion Grifols Diagnostics, Duedingen, CH) was launched in September 2016 and allows simultaneous typing for Jk^a, Jk^b, Fy^a, Fy^b, S, s antigens using lateral flow technique.
Aims: In order to implement the MDmulticard® as an additional analytic platform we examined a series of samples taken from patients suffering from clinical conditions known to hamper serological red blood cell (RBC) antigen typing.
Methods: Samples (n = 34) of patients suffering from positive direct antiglobulin test (DAT) (n = 26, including warm and cold autoimmune hemolysis (AIHA) and sepsis), sickle cell disease (n = 7), paraproteinemia due to Multiple Myeloma or Morbus Waldenström (n = 9) and samples of newborns (n = 3) as well as samples of healthy blood donors (n = 13, three with known weak Fy^x) were assessed by MDmulticard® Basic Extended Phenotype. In addition, ten samples which were stored at 4°C for at least one month, were included into the study. The results were compared with the findings by alternative test methods, either by standard serology typing (gelcard on Erytra®, Medion Grifols, Duedingen, CH or BioRad, Cressier, CH) or by commercial molecular typing (inno-train GmbH, Kronberg i. T., D).
Results: The MDmulticard® was easy to handle and provided rapid results (in average 9 min from test start) making the method suitable for emergency applications. Overall the results were confirmed by alternative methods or known pre-values.
Two of known Fy^a negative samples showed false positive reactions by MDmulticard® due to the patient's strongly positive DAT (3+ and 4+).
One sample delivered a weak Jk^b positive result by MDmulticard® although the patient was known to be Jk^b negative by PCR. Clinical evaluation revealed recent transfusion of Jk^b positive RBC concentrates. In two IgM-DAT positive samples, the predicted phenotype by PCR was accurately diagnosed by MDmulticard® upon washing the patient's RBCs with NaCl 0.9%. A similar observation was made with cord blood cells. Another sample from a patient with severe cold AIHA needed to be washed with warm NaCl 0.9%.
Summary/Conclusions: MDmulticard® allows reliable RBC typing even of DAT positive samples. MDmulticard® may be applied to samples of patients suffering from clinical conditions such as sickle cell disease, AIHA or paraproteinemia impairing standard serological typing. In pre-transfused patients or such with a strongly positive DAT, the distinct positive reaction by MDmulticard® allows to differentiate between false positive reactions and inherited antigen positive RBCs. For emergency situations, the MDmulticard® proves to provide rapid and reliable antigen typing which allows transfusing the patient with phenotype compatible RBC concentrates.

P-522

EVALUATION OF A NEW METHOD ABD PAD FOR ABO AND RH1 BLOOD GROUPING OF THE PATIENTS

O Fontaine, J Herlem, G Alluin, C Djobo, A Delsalle and A Manteau
FRANCE, EFS HFNO Lille, LOOS, France

Background: ABD PAD by DIAGAST is an innovative method for manual ABO and RH1 blood group determinations. It use the technology M-TRAP which is based on the antibodies covalently bounded to a porous membrane. Only corresponding antigens of red blood cells are fixed into the membrane revealing immediately the reaction.
Aims: The aim of our study was to test this method on 274 blood patient samples in order to estimate the exactitude of blood group determinations whatever the pathology or the biological abnormalities.
Methods: The samples which were chosen, are based on clinical informations provided by the laboratory.
The blood grouping with ABD PAD was compared with the usual methods of the laboratory: autoanalyser blood grouping QWALYS (DIAGAST) and manual techniques to confirm the ABO RH1 blood typing.
Results: We evaluated the impact of samples heterogeneity on ABD PAD method.
We have differentiated the 279 characteristics of the samples:: 110 red blood cell pathology (autoimmune hemolytic anemia, thalassemia, sickle cell anemia, macrocytic and microcytic MCV, schistocytes), 24 malignant hemopathies, 3 cold agglutinins, 15 leucocytosis, 4 thrombocytosis, 11 daratumumab therapy, 52 blood

protein disorders (hyperproteinemia, hypoproteinemia, monoclonal gammopathy, beta-gamma bridging, high and low plasma fibrinogen), 13 hyperbilirubinemia, 2 hypercholesterolemia, 9 abnormality of samples (chylomicrons with creamy layer in the test tube, hemolysis), 2 mixed-field agglutination after transfusion, 10 weak expression of the A blood group antigen, 15 weak expression of the RH1 blood group antigen, 4 red cell antibodies, 5 stem cell transplant.
The results obtained with the ABD PAD were in accordance with those of the methods used in the laboratory. The reactions of 2 samples with cold agglutinins were false positive and the blood typing was obtained with warm washed (37°C saline) red cells.
All the reactions with weak A blood group antigen and weak RH1 blood group antigen were positive.
We saw a particularity with the mixed agglutination after transfusion obtained with usual methods because the recipient antigen was always positive.
Summary/Conclusions: This method shows a high sensibility for the weak expression of A and RH1 blood group antigens.
It also has the benefit to be very fast to determine blood groups (about 30 s).
Our study confirms the use of this new concept for both donors and recipients.

P-523

ABD PAD®: EVALUATION OF A NEW MANUAL ABO/RH BLOOD GROUPING METHOD

A Villa, N Revelli, S Scognamiglio, A Manazza and D Prati
[1]Immunohematology Reference Laboratory, U.O.C. Centro Trasfusionale, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milan, Italy

Background: The ABD PAD® (DIAGAST, Loos, FR) is a new diagnostic device for a quick confirmation of the ABO blood group and the Rhesus (D) for donors and recipients. The kit uses M-TRAP® technology based on the immobilization of antibodies covalently bounded to a porous membrane.
Aims: The aim of our study was to evaluate the performance, reliability, sensitivity and specificity of the device.
Methods: The ABD PAD® method was compared with a full automated microcolumn (Innova, Ortho Clinical-Diagnostics, Raritan NJ) and a microplate (NeoGalileo, Immucor, Norcross GA, USA) methods. The study was carried out by 2 trained technicians according to the manufacturer's instruction. A total of 388 tests were performed on 325 blood donors samples, 51 segment of donation bags and 12 patient samples (4 cord blood, 1 patient treated with Daratumumab, 4 patients, with red blood cells antibodies, 1 patient with weak D, 1 patient with anti-HLA antibodies and 1 patient with cold Auto Immune Hemolytic Anemia (AIHA) were selected. All samples, collected in EDTA, were stored between 2–8° C and tested within 7 days of collection. The reaction of each ABD PAD® plate was read and interpreted immediately and again 24 h later. The concordance between methods was assessed with the expected and historical results. In case of discrepancy, the sample was re-analyzed with reference methods. If the discrepancy was not resolved, the test was also performed with tube test.
Results: Concordant results between the ABD PAD® and the reference methods were obtained in 387 (99%) of the 388 samples. All the results in donor samples and segments of donation were concordant, whereas a patient sample with a positive direct antiglobulin test was not concordant for the presence of a strong autoagglutination.
Summary/Conclusions: The ABD PAD® is an easy procedure that quickly provides confirmation of ABO/RH typing. The test is certainly faster than the methods currently in use because the ABD PAD® plates are ready to use. This method showed comparable results to the routine reference methods, suggesting that it can be useful to check the blood group or in emergency or at patient's bedside.

P-524

EVALUATION OF THE NEW BLOOD GROUPING DEVICE ABD PAD®

M Amouchas[1], B Gourou[2], S Iguerguaziz[2] and G Hariti[2]
[1]DIAGAST, LOOS, France [2]Bab-El-Oued University Hospital, Algiers, Algeria

Background: The confirmation of ABO/Rh blood group of donors and patients is a test performed at different steps of the transfusion chain. At the blood transfusion service of Bab-El-Oued University Hospital (Algeria), this control is performed on the blood bags tubing segments and on the second patient specimen using liquid antisera and plates.

Aims: The new ABD PAD® device (DIAGAST, Loos, France), which is suitable for this application, was evaluated prior to its commercial launch.

Methods: The routine method (liquid antisera associated with plates) was compared to ABD PAD®.

Results: The evaluation was carried out on 100 samples of red blood cell concentrate from tubing segments and demonstrated 100% concordance with regards to the expected results. The average satisfaction score for ergonomics was 3.7/4.

Summary/Conclusion: The device has shown its reliability for the blood group confirmation.

P-525

NOVEL RECOMBINANT CD38 FOR USE IN PRETRANSFUSION DIAGNOSTICS

M Binda[1], V Favaloro[2], N Piel[2], J Berry[2] and P Schwind[1]

[1]Medion Grifols Diagnostics, Duedingen, Switzerland [2]Grifols Diagnostic Solutions, Emeryville, United States

Background: Novel anti-CD38 drugs, such as daratumumab (DARA), used in treatment of multiple myeloma, interfere with diagnostic screening and identification of unexpected antibodies. They cause pan-reactivity of Reagent Red Blood Cells (RRBC), which complicates the detection of underlying allo-antibodies of potential clinical relevance. Strategies to overcome this problem include: 1) Pretreatment of RRBC with reducing agents, such as Dithiothreitol (DTT); 2) Issuing phenotype/genotype matched RBC units; 3) Pre-incubation of patient plasma with soluble CD38 (sCD38) or anti-idiotype antibodies (Oostendorp, Transfusion, 2015). This latter approach suffers from the unavailability of reagents of sufficient activity.

Aims: The aim of this study was to evaluate the diagnostic use of a novel recombinant CD38.

Methods: Part of the extracellular domain of CD38 was expressed in mammalian cells and purified as soluble CD38 to a nominal concentration of ~30 mg/ml.

For evaluation of diagnostic functionality, 25 µl of anti-CD38 spiked donor plasma (containing allo-antibodies or not) were mixed with 2 µl of sCD38 (or PBS as control) and incubated for 15 min at 37°C. Antibody detection was then performed by Indirect Antiglobulin Test (IAT) in tube technique or DG Gel technique according to the manufacturers' instructions (Medion Grifols Diagnostics, Duedingen, Switzerland; Diagnostic Grifols, Parets del Valles, Spain).

Alternatively, the pre-incubation was done directly in the incubation chamber of a DG Gel Coombs card (Diagnostic Grifols), followed by IAT, i.e. addition of 50 µl of RRBC suspension (Screen-Cyte 0.8%, Medion Grifols Diagnostics), 15 min incubation at 37°C and centrifugation.

The absence of anti-CD38 residual activity is indicated by negative results for all tested RRBCs, provided that the sample does not contain unexpected antibodies.

Results: 2 µl of recombinant sCD38 allowed for complete inhibition of anti-CD38 (0.5 mg/ml corresponding to a titer of 1:4096) in 25 µl of donor plasma. With this experimental setting, 16/16 antibodies spiked at barely detectable amounts into DARA-spiked donor plasma could be detected after incubation with sCD38. The antibody specificities comprised anti-D, -E, -c, -Cw, -K, -Fya, -Jka, -S, -s, -M, -Lua, -Cob.

Summary/Conclusions: The presented results show the inhibition of therapeutic plasma concentrations of daratumumab using a novel sCD38 at high concentration. Our data did not show interference of this pre-incubation step with blood group alloantibody detection. Nevertheless, it cannot be excluded completely that a very weak antibody may escape from detection due to the small dilution caused by the addition of liquid CD38. After neutralization, the plasma can be screened with commercially available routine techniques, such as tube and gel technique. An important advantage of using a sCD38 protein as a blocker is the fact that it allows for screening and identification of antibodies against all blood group antigens. Also, neutralizing plasmatic anti-CD38 instead of denaturing cellular CD38 reduces the workload of the pre-analytical process.

The highly concentrated sCD38 presented in this work may provide, in combination with IAT, a rapid and accurate screening and identification method of even weakly reacting allo-antibodies masked by anti-CD38.

P-526

COMPLICATION IN BLOOD COMPATIBILITY TESTING WITH DARATUMUMAB TREATMENT IN MULTIPLE MYELOMA: A CASE REPORT

S Pathak[1], A Gupta[2], R Dubey[1], S Kaushik[1], S Singh[1] and T Chakraborty[1]

[1]Department of Transfusion Medicine, Max Healthcare [2]Technical Support, Immucor India Pvt Ltd, New Delhi, India

Background: Multiple myeloma is a condition of neoplastic proliferation of plasma cells producing a monoclonal antibody by bone marrow, resulting increased serum protein concentration, unexplained anemia & hypercalcemia. Daratumumab, also known as Darzalex™, DARA, or Dara-T, is a new medication recently approved in Nov, 2015 in US by the FDA to treat multiple myeloma. Daratumumab is an IgG1 Kappa monoclonal antibody that recognize and target CD38 on myeloma cells. Single therapy of this drug is significantly effective in heavily treated patients with relapsed or refractory disease.

Aims: Here we present a case of a 56 years old male patient diagnosed with relapsed multiple myeloma and given daratumumab immunotherapy. Due to its activity of anti-CD38, DARA interferes in screening and identification of red cells alloantibodies, & cross matching. We manage to overcome this interference by using Warm auto antibody removal medium (W.A.R.M.™). During routine antibody screening and compatibility testing, patient plasma consistently causes positive reactions in ICT, 3 Cell Screen, Cell panels, & AHG crossmatches. However, anti-CD38 didn't interfere with ABO/RhD typing or with immediate-spin crossmatches.

Methods: Patient was tested for ABO & Rh and 3 cell antibody screening by solid phase method on fully automated immunohematology analyzer, Galileo-NEO (Immucor, Norcross, USA). By obtaining pan reactivity in 3 Cell panel, sample was tested for antibody identification by Capture Ready ID® on solid phase. This was also pan reactive. Collecting patient's brief clinical and therapeutical history it was further tested with W.A.R.M. treated panel cells. W.A.R.M. was used to remove/destroy CD38 structure (as it contains dithiothreitol), from panel cells. To treat with W.A.R.M. 1 volume of panel cells were mixed with 4 volume of reagent, and incubated at 37°C for 30–45 mins. After incubation cells were washed four times with PBS and re-suspended to 2–5%. There are some limitations listed below:

- W.A.R.M.™ or ZZAP-treated antibody screen would not detect antibodies against to Kell, Duffy, M, N, S

Results: W.A.R.M. treatment of panel cells reduced DARA binding by denaturing cell surface CD38. ABO compatible along with Rh & Kell pheno matched RBCs were also found compatible treated with W.A.R.M. reagent.

Summary/Conclusions: However there are several methods are introduced worldwide to resolve DARA interference with blood bank testing like:

- Soluble CD38 infusion to patient plasma to neutralize circulating Daratumumab drug.
- Daratumumab anti-idiotype antibody (anti-DARA by mouse) also to neutralize circulating Daratumumab drug.
- DTT (Dithiothreitol) or W.A.R.M. treatment, which destroy the structure of CD38 of reagent red cells.
- Extended Phenotyping of patient RBC and providing same phenotype red cells.
- Trypsin treated reagent RBCs, which cleaves CD38, and prevent antigen destruction as compared to DTT.
- Testing with Lu(a-b-) RBCs, these RBCs has low expression of CD38 on their surface.

These methods are new to introduce and required much cost and skills. Treating panel cells or blood units re cells with W.A.R.M. reagent is a robust method to prevent the DARA interference, enabling blood bank to provide blood to DARA-treated patients without delay or much expenditure.

P-527

A MODIFIED DITHIOTHREITOL PROTOCOL FOR ELIMINATING DARATUMUMAB INTERFERENCE

N Lone Akhtar[1], H Lorenzen[2], V Ljørring[1], M Nielsen[2] and L Svendsen[2]

[1]Department of Clinical Immunology, Herlev University Hospital, Herlev [2]Faculty of Health and Technology, Metropolitan University College, Copenhagen, Denmark

Background: Daratumumab (DARA) is a monoclonal antibody directed against the glycoprotein CD38, used as treatment for patients with Multiple Myeloma. DARA causes interference in serological antibody testing, complicating the detection of clinical significant alloantibodies prior to blood transfusion. The interference is eliminated by using dithiothreitol (DTT)-treated reagent red blood cells (RBCs). However, a disadvantage of the DTT-method is the time-consuming procedure and the

hemolysis observed during long-term storage of DTT-treated reagent RBCs. To overcome this challenge, the Department of Clinical Immunology, Herlev University Hospital, has developed a modified protocol for DTT treatment that improves stability of reagent RBCs by 33 days without any visual hemolysis and ensures detection of alloantibodies. This protocol is a modification of AABB's technical manual due to a reduced amount of DTT used for the treatment of reagent RBCs.The purpose of the modified protocol was to enable preparation of DTT-treated reagent RBCs in conjunction with regular reagent RBCs in order to improve laboratory efficiency and to reduce turnaround time for antibody detection.

Aims: The aim of this study is to validate the modified protocol for DTT treatment of reagent RBCs, and to measure the reduced time spent on detection of alloantibodies.

Methods: DTT treatment of reagent RBCs was performed, with DTT supplied by the manufacturer Sigma Aldrich, according to AABB's technical manual except for a RBC:DTT ratio of 30:25 (vol:vol). Multiple batches of DTT-treated reagent RBCs were continuously prepared and distributed to three transfusion services in The Capital Region and Region Zealand of Denmark from February 2017 to February 2018. Antibody screening tests were performed, at all three study sites, with untreated and DTT-treated reagent RBCs on plasma samples from DARA-treated patients (n = 50) and on plasma samples (n = 60) from patients with known clinically significant alloantibodies (n = 70). Antibody screening tests were performed using Column Agglutination Technology with Coombs anti-IgG ID Cards (BioRad Laboratories).Analysis time was measured and compared using both immediately and in advance prepared DTT-treated reagent RBCs.

Results: The outcome of the study showed that DARA interference was eliminated in all 50 samples from DARA-treated patients. 55 of 70 alloantibodies were detected and the remaining 15 alloantibodies within the Kell system were negative, using the modified protocol for DTT-treated reagent RBCs.DTT-treated reagent RBCs prepared in advance provided antibody screening test results within 37 min compared to 90 min with immediately prepared DTT-treated reagent RBCs.

Summary/Conclusions: Validation results show, that the modified protocol for DTT-treatment of reagent RBCs eliminates DARA interference and detects alloantibodies examined except for alloantibodies within the Kell system. DTT-treated reagent RBCs, prepared in advance, reduce antibody detection time by 53 min.

The present study show that a central preparation of DTT-treated reagent RBCs and distribution to transfusion services ensures quality, improves laboratory efficiency and therefore prevents delayed blood transfusions.

Red Cell Immunology: Molecular

P-528
VISUAL BLOOD GROUP GENOTYPING BY LATERAL–FLOW DIPSTICK

J Gomez-Martinez[1,2,3], M Silvy[3,4,5], J Chiaroni[3,4,5], C Fournier-Wirth[1,2,3], F Roubinet[3,6], P Bailly[3,4,5] and J Brès[1,2,3]

[1]Etablissement français du sang Occitanie [2]Pathogenesis and Control of Chronic Infections, Univ Montpellier, INSERM, EFS, Montpellier [3]Etablissement Français du Sang, Blood Cell Grand Sud, Montpellier-Marseille [4]Etablissement Français du Sang PACA Corse, Biologie des Groupes Sanguins [5]Aix Marseille Univ, CNRS, EFS, ADES, Marseille [6]Etablissement français du sang Occitanie, Toulouse, France

Background: Alloimmunization is one of the main side effects of blood transfusion that could severely complicate further red blood cell transfusions, especially for patients with diseases requiring multiple transfusions. Conventional pretransfusion determination of blood group phenotype based on hemagglutination may failed in certain clinical situations. Molecular typing offers an alternative to deduce blood group phenotype from genotype. However, current methods require a turnaround time and are not usually performed on-site at hospital, limiting their application in emergency situations. When rapid decision is needed, tests to be performed near or on-site are advantageous.

Aims: In this work, we report the development of a novel rapid multiplex molecular method to identify seven alleles in three clinically relevant blood group systems (FY*01, FY*02, FY02N.01, GYPB*03, GYPB*04, JK*01 and JK*02). The assay was designed for carrying out unitary testing, in specific clinical situations such as pretransfusion testing for patients when serologic methods failed or in emergency situations.

Methods: We aimed to develop a straightforward and rapid genotyping test. For this purpose, we chose a pre-PCR handling and DNA extraction-free procedure which include a multiplex linear-after-the-exponential (LATE)-PCR amplification performed directly from whole blood. The single-stranded amplicons migrate on a dry-reagent allele-specific nucleic acids lateral-flow dipstick. Gold nanoparticles, used as reporter, permit the detection of blood group SNPs by the generation of red dots visible to naked eye. The assay parameters were optimized and our test was validated on 108 blood donor samples with known phenotype.

Results: Optimization of the assay includes both multiplex LATE-PCR parameters (primer concentration and cycle number) and lateral flow parameters (migration/hybridization temperature and buffer composition). The final protocol enables determination of deduced phenotype within a total processing time of 1 h from receiving blood sample. Validation showed a 100% concordance rate between deduced and standard serologic phenotypes.

Summary/Conclusions: Our test allowed accurate determination of deduced phenotype for FY1, FY2, S, s, JK1 and JK2 antigens. Due to its simple handling, the assay can be operated by non-skilled blood bank staff members. The proposed assay offers a potential for developing others relevant SNP panels for immunohematology but also new applications in point-of-care testing such as infectious diseases in the near future.

P-529
TWO CASES OF CAUCASIAN BOMBAY AND THREE CASES OF PARA–BOMBAY PHENOTYPE REVEALED FIVE NOVEL FUT1 ALLELES

H Hustinx[1], J Stettler[1], C Henny[1], S Lejon Crottet[1], F Still[1], ML Ollson[2] and J Storry[2]

[1]Diagnostic, Interregional Blood Transfusion SRC Ltd., Bern, Switzerland [2]Department of Laboratory Medicine, Clinical Immunology and Transfusion Medicine, Office of Medical Services, Region Skane & Division of Hematology and Transfusion Medicine, Dept. of Laboratory Medicine, Lund University, Lund, Sweden

Background: The rare Bombay (O_h) and para-Bombay ($H+^W$) phenotypes have non-functional or partially functional $\alpha(1,2)$-fucosyltransferases. These enzymes are encoded by two highly homologous genes FUT1 (H) and FUT2 (Se). The α2FucT1 enzyme encoded by FUT1 is crucial for the synthesis of H antigen on red blood cells (RBCs), a precursor processed to form either the A or B antigens. The α2FucT2 enzyme encoded by FUT2 is responsible for the synthesis of H antigen in body fluids such as saliva and plasma (secretor phenotype). Bombay individuals neither express ABH antigens on their RBCs nor secrete H substance in their saliva due to inactive FUT1 and FUT2 alleles, respectively. Para-Bombay phenotype typically displays weakened H antigen expression. This can either result from FUT1 variant allele(s) diminishing enzyme activity in non-secretors or by a non-functional FUT1 in secretors.

Aims: Two samples (probands 1 and 2) of Caucasian origin were investigated due to the presence of anti-H in their plasma and three samples (probands 3, 4 and 5) were analysed because of discrepancies in ABO blood group typing.

Methods: RBC typing and antibody identification was performed using standard serological testing (BioRad, Cressier, Switzerland and tube test). Flow cytometric analysis with monoclonal antibodies to H, A and B antigens was also performed. Genomic DNA was isolated from whole blood and SSP-PCR detecting common ABO alleles was performed. Full-coding sequences of FUT1 or ABO were analysed using published and in-house primers. Secretor phenotype was either determined serologically or by SSP-PCR detecting SNP 428G>A. Samples from the parents of proband 2 were analysed for confirmation.

Results: Proband 1 and 2 had no detectable A, B or H antigens by serology or flow cytometry. Plasma from both probands contained strong anti-H reacting by IAT, compatible only with O_h RBCs. Proband 1 genotyped as ABO*A1.01/ABO*B1.01, proband 2 as ABO*A1.01/ABO*O.01.02. DNA sequencing of FUT1 revealed that proband 1 was homozygous for FUT1*01N.12 whereas proband 2 showed compound heterozygosity for FUT1*01N.12 and a novel mutation, FUT1 c.791_792insG (p.M265Hfs*5). Samples from the parents of proband 2 showed that the new FUT1 allele was inherited by the group A father. Probands 3, 4 and 5 showed reduced expression of A antigen (negative to weakly positive). ABO genotyping [SJ1] predicted A phenotypes. Anti-H(I) was detected in the serum of proband 3. Flow cytometric analysis of proband 3 RBCs demonstrated a para-Bombay-like (A_h) expression with monoclonal anti-A, but were nonreactive with monoclonal anti-H. Serum from proband 4 showed strong anti-A. Serum from proband 5 was antibody negative. Sequencing of FUT1 revealed homozygosity for c.396_398delCCC (p.Pro133del) in proband 3; proband 4 was heterozygous for FUT1*01W.04 and a novel mutation, FUT1 c.710delG (p.G237Afs*43); proband 5 was heterozygous for two novel mutationsFUT1 c.288T>A (p.Y96Ter) and FUT1 c.454delG (p.E152Rfs*6). SSP-PCR for FUT2 c.428 suggested that proband 3 and 5 are secretors, whereas proband 4 is a non-secretor.

Summary/Conclusions: Five novel mutations of the FUT1 gene were identified, resulting in a Bombay or para-Bombay phenotype in five unrelated individuals. Based on serological data, all five mutations apparently abolish or diminish the fucosyltransferase activity.

P-530

IDENTIFICATION OF A 24 BP DELETION IN THE ABO GENE RESULTING IN A HEREDITARY SPLICE SITE MUTATION: A NOVEL ABO A ALLELE FOUND IN AN AUSTRIAN FAMILY

EM Matzhold[1], A Wagner, C Drexler[1], C Bernecker[1], T Schreiner[2] and T Wagner[1]

[1]Blood Group Serology & Transfusion Medicine, Medical University of Graz, Austria
[2]Institute of Biochemistry, Technical University of Graz, Graz, Austria

Background: Two related blood donors with aberrant ABO blood group phenotype showed a prominent mutation in the coding sequence of their ABO genes (ABO*A1.01-like mut).
Aims: To define its hereditary character and to evaluate genotype-phenotype associations a family study was conducted.
Methods: Serologic ABO typing of 29 family members was performed. Adsorption-elution studies of RBCs by use of monoclonal anti-A and allele-specific sequencing of the ABO gene were carried out in selected samples. All family members were screened for the identified deletion by PCR.
ABO specific gene transcripts were amplified, cloned into mammalian expression vector pcDNA3.1 and transformed into E. coli. 60 clones of 7 different sample cDNAs were investigated by sequencing analysis. HeLa cells were used as recipients of DNA transfection experiments with plasmid DNA containing the mutation specific transcript variant. Transfectants were harvested and analyzed for A antigen expression by flow cytometry and adsorption-elution method.
Results: Sequencing analysis revealed a novel ABO*A1.01-like allele with a deletion of 4 basepairs (bps) (236-239delCGTG) at the 3′end of exon 5, continuing in a deletion of further 20 bps in intron 5. 16 out of 29 investigated family members showed this mutation in their ABO gene.Family members genotyped as ABO*O/ABO*A1*like mut, indicated ABO blood group O by antigen typing. Reactive anti-B was present in their sera, but only weak agglutination of anti-A1 and a lack of anti-A isoagglutinins were found in reverse typing. In two individuals carrying the mutated ABO*A101-like allele, adsorption- elution studies identified very weak A-antigen expression on their RBCs. In contrast, eluates prepared from RBCs of other individuals did not exhibit any anti-A specificity when exposed to anti-A.
Cloning of cDNA indicated at least four different transcript variants generated by alternative splicing. cDNA clones of four different individuals revealed mutated ABO transcript variants showing the deletion in exon 5, and/or a retention of nucleotides 21 to 55 of intron 5. Most interestingly, a cDNA clone of one sample (genotype ABO*B.01/ABO*A1.01-like mut), showed an ABO transcript related to a wild type ABO*A1.01 allele.
HeLa cells transfected with mutant ABO*A cDNA were negative for the expression of A-antigen.
Summary/Conclusions: Several members of an Austrian family carry a novel ABO*A allele variant causing a defect in mRNA splicing, realized by the retention of intronic sequences in the mutated ABO gene transcript. Since adsorption elution studies of different family member's RBCs showed diverse results concerning A-antigen expression, the functionality of the mutated ABO gene remains unclear. Transfection of HeLa cells with mutated ABO cDNA did not result in A-antigen positive cells. However, in one cDNA clone, recombination of the individual's encoded ABO*B and ABO*A1.01-like mut sequences may have resulted in the formation of a functional ABO*A1.01 allele transcript, restoring some ABO transferase activity.

P-531

STUDY ON THE MOLECULAR MECHANISM OF EXPRESSION REGULATORY IN A AND B WEAK SUBGROUP

Q Yu[1], Y Su[2], J Zhen[3], Z Deng[2], W Hong[2], L Lu[1] and W Zhu[1]

[1]Shenzhen Blood Center, Shenzhen, China [2]Shenzhen Institute of Transfusion Medicine, Shenzhen Blood Center [3]Baoan Maternal and Child Health Hospital, Shenzhen, China

Background: The ABO blood type has complicate expression regulation mechanism. Although more than 100 ABO subgroup-related variations detected in a 18-kb region explained weak expression of A/B histo-blood group antigens, the molecular mechanisms underlying some subgroups are still not completely understood. In addition, many factors can influence the synthesis and activity of the resulting glycosyltransferase, for example usage of alternative first exons and promoters, enhancer status and repressors of transcription, as well as the methylation status of the promoter. It has been reported that loss of antigen expression of histo-blood groups A, B and O associated with cancer was caused by methylation of the ABO gene.
Aims: Basing on identifying ABO blood group serology and genetic background of some rare A or B weak subgroups, to invest the level of CpG methylation in promoter of ABO gene and the correlation between it and ABH antigen expression, and further studying on epigenetics may partly revealed ABO gene expression mechanism.
Methods: A total of 13 unrelated individuals including 6 A weak phenotypes and 7 B weak phenotypes were studied in this paper while 10 normal A or B antigen expression samples were randomly chosen as controls. 13 samples were detected ABO blood group by standard serum technique. All seven ABO exons, five introns, promoter plus the 5′-region including the CCAAT-binding factor/Nuclear Factor Y (CBF/NF-Y) binding enhancer were direct-sequenced. ABO transcript levels were measured by reverse transcription-PCR (RT—PCR). The level of methylation of the CpG island in ABO gene promoter was further analyzed by bisulfite and sequencing after cloning.PCR amplification was performed after genomic DNA performed bisulfite using the following primer sequences: 5 '- TTGTTGGGTGTATTTTGTATTTT – 3, 5′- AACCCCAAAATACCAAC- 3′. The PCR product was diluted 20 times, and 1uL was used as the template for the second round of amplification. 10 positive clones of each sample were randomly selected and directly sequenced.
Results: The serological characteristic of these samples showed that A or B antigen was obviously decreased. 13 samples including Ay, AelB (n = 2), AwB (n = 3), Bel, ABx,ABw (n = 2), Bw (n = 3) phenotype were genotyped as A102/A205, A102/B101 (n = 2), A101/B101, A102/B101(n = 2), B101/O02, A102/B101;A102/B101(n = 2), B101/O01, B101/O02(n = 2) respectively.
There were no mutations in the full-length coding sequences and splice receptor sites.The nucleotide characteristics of the 5′-UTR was consistent with common allele type and no any abnormity was identified in the promoter, enhancer regulatory sequence regions in 12 samples except a sample of Ay phenotype which enhancer polymorphism was A102/A201 while a haploid sequence is four 43-bp repeats and G at position 41 in the first repeat. The integrative cDNA transcript of ABO gene was obtained and no new splicing isoform was found.37 CpG island methylation sites in the ABO gene promoter region were analyzed. As compared with control group, the different methylation levels at 37 CpG sites of ABO gene promoter region appeared in 13 samples. −26 C residues of 4 samples were partially methylated.
Summary/Conclusions: The methylation status of the CpG island of ABO gene promoter region may cause weak expression of the A or B antigen.

P-532

FOUR TANDEM REPEAT UNITS IN REGULATORY REGION OF A ALLELE IS RESPONSIBLE FOR A NOVEL AWEAK PHONETYPE

J Wang[1], Y Gu[1], C Wang[1], Q Pan[2] and Q Fu[2]

[1]Department of Transfusion [2]Department of laboratory medicine, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China

Background: The ABO blood group system is highly important in clinical transfusion and transplantation medicine. Lot of weak expression of ABO phenotype have been discovered, which not only caused by the single nucleotide polymorphisms (SNP), but also relate to hybrid formation between the common alleles or mutation in the untranslated region (UTR). It indicated that one or four 43 bp-repeats were in the CBF-NF/Y-binding domain of the enhancer minisatellite, approximately 4 kbp upstream from the translation start codon in the UTR of ABO gene.
Aims: This study aims to investigate the molecular basis of ABO gene in a patient with serologic ABO blood group discrepancy.
Methods: The patient, 11-year-older girl, enrolled was from Shanghai Children's Medical Center. Serologic blood group identification, Coombs' test and antibody screening were detected with DG Gel Confirm cards, Neutral cards, Coombs cards by WADiana/8XT Compact Analyzer (from Diagnostic Grifols, S.A). The enhancer, promoter, exon 1~7 and their adjacent intron region of ABO gene were amplified by using polymerase chain reaction (PCR) method, the PCR products were directly sequenced to identify the gene mutation.
Results: The patient's red blood cells showed weak agglutination with anti-A(++) and anti-H(++), no agglutination with anti-B. The patient's serum showed strong agglutination with A1 cell, B cell, no agglutination with O cell. The direct antiglobulin test (DAT), indirect antiglobulin test (IAT) and antibody screening were all negative.

The ABO gene sequencing result showed four 43 bp short tandem repeat units in enhancer region (-3899~-2618 bp), which was three more than the normal A allele. This characteristics of the O allele were revealed.

In addition, one variation in exon 3 (106G>T), two variations in exon 4 (188G>A, 189C>T), a deletion and one variation in exon 6 (261delG, 297A>G), no variation in exon 1,2,5,7 of ABO gene were identified compared with the reference sequence of A101 allele.

Summary/Conclusions: Based on the Blood Group Antigen Gene Mutation Database, the patient was identified as A101/O02. The reason for weak A101 expression was four 43 bp tandem repeat units in enhancer region. The novel variation in the enhancer of A glycosyltransferase gene may cause weak A phenotype.

P-533
NOVEL GROUP B ALLELE IDENTIFIED IN A GROUP AB OBSTETRICAL PATIENT WITH AN APPARENT GROUP O NEONATE

JS Drouillard[1], M Knier[2], K Bensing[2], G Denomme[2,3] and A Carterson[1]

[1]Immunohematology Reference Laboratory, Heartland Blood Centers, part of Versiti, Aurora, IL [2]Immunohematology Reference Laboratory, Blood Center of Wisconsin, part of Versiti [3]Blood Research Institute, Milwaukee, WI, United States

Background: Maternal and cord blood samples were referred to our laboratory for the investigation of a Group AB obstetrical patient after delivery of an apparent Group O neonate.

Aims: To resolve a maternal-neonatal ABO inheritance discrepancy using a genomic DNA sequencing strategy of the ABO gene.

Methods: Maternal and neonatal red cells were phenotyped using several examples of commercial anti-A, anti-B, and anti-A, B. Neonatal red cells were incubated with commercial anti-A, anti-B, and anti-A, B for 15 min at room temperature, 18[o]C, and 4[o]C. Maternal plasma was tested for ABO isoagglutinins; this testing was omitted for the neonate's sample. ABO exons 6 and 7 were polymerase chain reaction (PCR)-amplified from genomic DNA and sequenced by Sanger dideoxy method using the BigDye Terminator v3.1 Cycle Sequencing Kit with complementary M13 primers. The results were aligned to ABO NG_006669.1.

Results: Maternal RBCs were DAT negative (IgG and C3) and strongly agglutinated at immediate spin by commercial anti-A and anti-B antisera. There was no evidence of anti-A or anti-B in maternal plasma.

Neonatal red cells were DAT negative (IgG and C3), nonreactive with reagent anti-A, anti-B, and anti-A, B at immediate spin, and weakly reactive with anti-B after a 15 min room temperature incubation. Microscopic mixed field reactivity was observed following 18[o]C and 4[o]C incubation of cord red cells with anti-A and anti-B indicating probable contamination of the sample with maternal red cells.

Genomic DNA from maternal and neonatal blood were used to sequence ABO due to discordant serological findings. A 261delG allele was identified in exon 6 of the neonate, representing the common nonfunctional Group O01 allele, which was absent from the maternal DNA, and therefore denoted the paternal allele. The remaining allele contained single nucleotide polymorphisms (SNPs): 297G, 523A, 526G, 657T, 703A, 796A, 803C, 820T, 930A. This allele is closely related to the B110 allele, represented by the 523A, with an additional 820T SNP. This allele was also identified within the maternal sample.

Summary/Conclusions: The B110 allele is reported to have normal expression of antigen; however the 820T SNP is a missense (V247L) mutation, not previously reported. Therefore, this represents a novel Group B allele. Until now, the 820A (V277M) has only been observed in Group A alleles. This novel mutation has an unknown effect on B antigen expression. Red cells may show weak mixed field B antigen expression similar to the 820A on A antigen expression. Our case suggests strong expression of the B antigen is possible and that expression may be very weak at birth. Therefore, the observation of Group O typing of the neonate is consistent with the combined effects of the 523A and 820T missense mutations in addition to the fact that ABO antigens are not well developed at birth. Further, the absence of anti-B in our maternal patient's plasma indicates production of B isoagglutinins is not expected for individuals possessing this novel allele.

P-534
THE MAJOR B ALLELE ACCOUNTING FOR B$_M$ AND A$_1$B$_M$ PHENOTYPES IN THE JAPANESE POPULATION

K Ogasawara[1], T Miyazaki[2], S Ito[3], R Yabe[4], M Uchikawa[4], T Enomoto[5], N Yokoya[6], Y Hori[7], M Kumamoto[8], S Watanabe[9] and M Satake[1]

[1]Research and Development, Japanese Red Cross Central Blood Institute, Tokyo
[2]Blood Group Laboratory, Japanese Red Cross Hokkaido Block Blood Center, Sapporo
[3]Blood Group Laboratory, Japanese Red Cross Tohoku Block Blood Center, Sendai
[4]Blood Group Laboratory, Japanese Red Cross Kanto-Koshinetsu Block Blood Center, Tokyo [5]Blood Group Laboratory, Japanese Red Cross Kanto-Koshinetsu Block Blood Center, Higashimatsuyama [6]Blood Group Laboratory, Japanese Red Cross Tokai-Hokuriku Block Blood Center, Seto [7]Blood Group Laboratory, Japanese Red Cross Kinki Block Blood Center, Osaka [8]Blood Group Laboratory, Japanese Red Cross Chu-Shikoku Block Blood Center, Hiroshima [9]Blood Group Laboratory, Japanese Red Cross Kyushu Block Blood Center, Kurume, Japan

Background: B$_m$ and A$_1$B$_m$ phenotypes are the most frequent ABO variants in the Japanese population. The B antigen on B$_m$ red blood cells is only detectable by adsorption and elution tests, and plasma B-transferase activity is usually detected at half or less levels compared with that of common B. Recently, a B allele lacking an erythroid cell-specific transcription enhancer element in intron 1 of the ABO gene (B^{m}5.8 with a c.28 + 5110_10889del) was identified from individuals with B$_m$ and A$_1$B$_m$ phenotypes, which could explain the unique serologic properties of B$_m$. Other B^m alleles with a 3.0 kb deletion including the element (B^{m}3.0; c.28 + 4077_7107del) or with a GATA-1 binding site mutation in the element (B^{m}GAGA; c.28 + 5861T>G) have been identified.

Aims: We investigated the occurrence and distribution of B^m alleles, B^{m}5.8, B^{m}3.0, and B^{m}GAGA, within both B$_m$ and A$_1$B$_m$ subgroups in the Japanese population.

Methods: In the Japanese Red Cross Society, eight Blood Centers tested blood samples from donors throughout Japan, and collected blood samples from 888 B$_m$ and 419 A$_1$B$_m$ individuals by an automated blood grouping system (PK7300, Beckman Coulter) followed by standard tube tests. Genomic DNA was extracted from whole blood and the B^{m}5.8 allele was typed by polymerase chain reaction (PCR) or PCR-sequence specific primer (SSP). When the B^{m}5.8 typing was negative, nucleotide sequencing was performed. The nucleotide sequence of GenBank accession no. NG_006669.1 was used as a reference.

Results: DNA analysis revealed that 1,304 of 1,307 (99.77%) individuals had the B^{m}5.8 allele. Only three individuals had a negative result by PCR-based B^{m}5.8 screening. Nucleotide sequencing revealed that one individual had the B^{m}3.0 allele. The other two individuals had a B^{m}GAGA allele; one individual was a non-secretor and the other was a secretor.

Summary/Conclusions: Our results clearly demonstrate that the B^{m}5.8 is a predominant allele accounting for 99.77% of the B^m alleles in the Japanese individuals with B$_m$ and A$_1$B$_m$ phenotypes. This allele may have been inherited over a long time period and spread over the Japanese population. In contrast, the B^{m}3.0 and B^{m}GAGA may be generated by recent events, and these are sporadic in the population. The widely distributed B^{m}5.8 allele can be typed by a conventional method such as PCR-SSP.

P-535
LINKSĒQ™ FOR ABO, A MOLECULAR BASED TYPING SOLUTION FOR THE ABO BLOOD GROUP

W Lane[1,2], H Mah[1], J Rodriguez[1], T Viard[3], R Russnak[3], V Yuen[3], R Haddad[3], I Kim[3], R Li[3] and Z Antovich[3]

[1]Pathology, Brigham and Women's Hospital [2]Harvard Medical School, Boston
[3]Thermo Fisher Scientific, South San Francisco, United States

Background: ABO is the most important blood group system in transfusion medicine because A and B are the most immunogenic blood group antigens. ABO compatibility between donors and recipients is so critical for transfusion success that ABO typing must be performed before every single transfusion on two samples collected at different times. Laboratories typically use serological methods to perform ABO typing. However, serology has significant limitations including (i) recently transfused patients may exhibit mixed field agglutination wherein both the patient's and recent donor's antigens are detected, and (ii) both forward and reverse typing must be performed, but may yield discordant results. These limitations are most problematic with phenotypes involving weakly expressed antigens. Laboratories can overcome these drawbacks with a combination of genotyping solutions (SSP, sequencing, etc), but these methods are time- and labor-consuming, and require interpretation by subject matter experts.

Aims: Most ABO variants are caused by single-nucleotide polymorphisms (SNPs). ABO molecular typing is currently performed with labor intensive techniques such as

PCR-SSP, a method that utilizes time-consuming post PCR analysis steps, or Sequence Based Typing (SBT). SBT requires substantial financial investment, long turnaround times and extensive technical expertise. The aim of this study was to evaluate an alternative ABO genotyping solution recently introduced by Thermo Fisher Scientific.

Methods: The Thermo Fisher Scientific solution is based on its LinkSēq real-time PCR technology, which was developed over 10 years ago for genotyping the complex Human Leukocyte Antigen (HLA) system. LinkSēq ABO analyzes 19 reactions that identify multiple relevant SNPs located within the ABO gene. We evaluated this solution by analyzing 40 archived DNA samples, including blood blank samples for which serotyping failed or produced discordant results, and samples from deceased solid organ donors.

Results: Genotyping results generated by LinkSēq were 100% concordant with typing obtained by traditional methodologies. In two cases, serology couldn't provide conclusive results and typing had to be reflexed to lectin tests or SBT. LinkSēq overcomes the major challenges of molecular typing by providing a robust, automated approach that increases laboratory productivity and reduces turn-around time. With less than 10 min of hands-on set-up, no further operator intervention with reagents, and SureTyper™ software fully automating all analysis, LinkSēq delivers genotyping and predicted phenotyping results in approximately 90 min.

Summary/ConclusionsWe conclude that LinkSēq can provide a simple, effective and robust method for ABO typing including accurate A_2 subgrouping.

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Abstract has been withdrawn

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A NOVEL C.810C>G MUTATION IN B SUBGROUP THAI BLOOD DONOR

N Anukul[1], N Leetrakool[2], P Tanan[2], P Palacajornsuk[1] and P Klangsinsirikul[1]

[1]Division of Transfusion Science, Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University [2]Blood Bank Section, Maharaj Nakorn Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Background: B allele encodes D-galactosyltransferase transferring the sugar D-galactose to H antigen to produce B antigen. B allele is located on the ABO gene consisting of 7 coding exons. Polymorphisms on B alleles are mostly found in exon 6 and 7 and can cause decreased activity and specificity of transferase enzyme leading to B subgroups. For ABO typing, serologic testing is performed using either the tube test or column agglutination test (CAT). Basically, the B_3 subgroup can be identified by observing the mixed-field agglutination (MFA) with anti-B and B_3 red cell suspension in the forward grouping, while with B_{weak} only weak agglutination can be observed (e.g. 2 + or 1 + or w+). With the advance of molecular technology implemented ABO genotyping, it can be used as the confirmation test. Eight and 34 different alleles are reported for B_3 and B_{weak} subgroups, respectively, according to the ISBT 001 blood group allele table. These mutations have been reported in Caucasian and Asian populations, however, there is no report in Thai population. For the first time we describe the mutation positions found in suspected B subgroup within Thai blood donors.

Aims: To identify the nucleotide sequences of B allele in suspected B subgroup Thai blood donors.

Methods: From the routine ABO typing using CAT, donor blood samples which MFA positive from the DiaClon ABO/D + Reverse Grouping card (Bio-Rad Laboratories, Switzerland) were collected for B allele analysis. After preparation of genomic DNAs, polymerase chain reaction (PCR) was performed using primers specific to exon 7 of the ABO gene. PCR products were fractioned on a 1% agarose gel and then gel purified. Sanger sequencing was carried out on ABI3730XL (Bio Basic Canada Inc., Markham, Canada). The consensus sequences were analyzed and mutation positions were compared to the ISBT 001 blood group allele table.

Results: In total, 7 unrelated donors were observed with red blood cell mixed-field agglutination. These samples supposed to be B_3 phenotype which showed weak B expression. From B allele analysis of exon 7 located at nucleotide (nt) 375-1065, different alleles were detected. One donor carried heterozygous ABO*BW.11 (c.695T>C) allele, one carried ABO*BW.33 (c.550G>A) allele, one carried the novel c.810C>G variant and the other four donors showed ABO*B.01 allele.

Summary/Conclusions: CAT is sensitive in MFA detection, however, observing MFA does not necessarily indicate the B_3 subgroup. Direct sequencing proved that ABO*BW alleles encode weak B antigen expression including MFA. Our study found

a novel variant of the B allele, c.810C>G, with an amino acid substitution from phenylalanine (F) to leucine (L) in position 270 of B-transferase enzyme. Further investigation is needed to determine the effect of amino acid change on the activity of transferase enzyme. Moreover, a whole ABO gene sequencing is needed to confirm the new variant as well as the 4 donor samples, which showed weak B antigen expression with CAT assay but did not indicate any mutations in exon 7.

P-538

Abstract has been withdrawn

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LONG RANGE HAPLOTYPE ANALYSIS OF THE MALARIA PARASITE RECEPTOR GENE ACKR1 IN AN EAST–AFRICAN POPULATION

Q Yin[1], K Srivastava[1], A Gebremedhin[2], A Makuria[1,3] and W Flegel[1]

[1]Department of Transfusion Medicine, NIH, Bethesda, United States [2]Medical Faculty, Addis Ababa University, Addis Ababa, Ethiopia [3]Food and Drug Administration, Wheaton, United States

Background: The human atypical chemokine receptor 1 (ACKR1) gene encodes a glycoprotein expressing the Duffy blood group antigens (Fy). The Duffy protein acts as a receptor for distinct pro-inflammatory cytokines and malaria parasites Plasmodium vivax and Plasmodium knowlesi. Only 1 study has systematically analyzed the ACKR1 gene at the haplotype level, and no long range ACKR1 haplotype has been confirmed in malaria endemic area. The population in Gambela is endogenous to the southwestern region of Ethiopia and exposed to malaria for many generations.

Aims: We aimed to identify long range alleles (confirmed haplotypes) and their variations of the ACKR1 gene, possibly including regulatory elements, without ambiguity in an autochthonous population in a malaria endemic area.

Methods: We collected blood samples from 60 healthy volunteers in Ethiopia's southwestern low altitude tropical region. An assay was devised to amplify the ACKR1 gene as a single amplicon and determine its genomic sequence. All haplotypes were resolved at 5,178 nucleotides each, covering the ACKR1 gene and its 5' and 3' flanking region. When necessary, allele-specific PCR with nucleotide sequencing or length polymorphism analysis was applied.

Results: Among the 120 chromosomes analyzed, 18 ACKR1 alleles were confirmed without ambiguity. All alleles carried the SNP at c.125G>A found in the common Fy (b+) phenotype. However, 16 out of these 18 alleles were also compatible with the clinically relevant FY*02N.01 allele, which is Duffy protein negative as defined by a GATA box mutation at c.-67T>C. The other 2 alleles represented a FY*02 allele of the Fy(b+) and a FY*02W.01 allele of the Fy(b+w) phenotypes, respectively. Among the 310,680 nucleotides sequenced, we found 18 single nucleotide polymorphisms (SNPs); only 1 SNP was novel. 4 SNPs occurred in the exons, 5 in 5'-flanking region, 1 in 3'-flanking region, 5 in 5'-UTR and 3 in the intron 1. The 2 SNPs rs12075 and rs17838198 were non-polymorphic in our Ethiopian samples, all other substitutions at the 16 remaining polymorphic sites followed the Hardy-Weinberg equilibrium. No SNP, other than c.-67T>C, indicative of a non-functional allele was detected.

Summary/Conclusions: We described haplotypes of the ACKR1 gene in an autochthonous East-African population and found 18 distinct ACKR1 alleles. The high frequency of FY*02N.01 allele (95%) in this study is similar to other studies conducted in western, central and south-eastern African regions from Gambia to Mozambique (95% - 100%).The long range alleles determined without ambiguity are useful as templates to phase and analyze next generation sequencing data, thus enhancing the reliability of clinical diagnostics.

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ALTERED FY^B EXPRESSION IN THE PRESENCE OF FY C.298G>A POLYMORPHISM

M St-Louis[1], G Laflamme[1], J Lavoie[1] and C Éthier[2]

[1]Affaires médicales et innovation [2]Laboratoire de référence et de cellules souches, Héma-Québec, Québec (Québec), Canada

Background: Molecular analyses have been slowly implemented in transfusion medicine more than two decades ago. Knowledge identifying genes involved in

blood groups and progress in technology permitted to perform those analyses. The Duffy blood group (ISBT 008), although simple with five antigens and a two-exon gene, presents several genetic variants. The Fy^a/Fy^b polymorphism was reported by several groups in 1995 (c.125G>A, Gly42Asp). Some variants are particular to specific populations, for example FY*01N.01 (c.−67T>C) prevalent in African descent individuals encoding Fy(a−b−) phenotype. In Caucasians, FY*X is more often observed. Two variants are responsible for this Fy^x phenotype or more accurately Fy (b+^{w}): FY*02W.01 (c.265C>T, c.298G>A) and FY*02W.02 (c.145G>T, c.265C>T, c.298G>A). The c.298G>A (Ala100Thr) polymorphism alone was described in several samples without impacting the antigen expression, since it is predicted to occur in the second membrane-spanning domain of the protein.

Aims: In 2013, a first blood sample was referred to the Immunohematology Reference Laboratory (IRL) for a weak Fy^b expression. Three additional samples were later found with similar results.

Methods: Phenotype was repeated twice with two different sources of anti-Fy^b. ACKR1 (DARC or FY) sequencing was performed. Cloning was done to confirm on which allele the heterozygous polymorphisms were in cis or trans.

Results: The Fy^b expression was weaker than positive controls (tested in tube, saline at 37°C, IAT; 0 to 3 +). Sequencing analyses showed the presence of c.125G>A and c.298G>A polymorphisms both in heterozygous form, and normal polymorphisms at positions c.145G>T, c.266G>A and c.901C>T (other polymorphisms associated with weak phenotype, ISBT's Website). Allele cloning confirmed the presence of the c.298A in cis with c.125A (Fy^b antigen). No anti-Fy3, -Fy5 nor -Fy6 reagents/sera were available for testing.

Summary/Conclusions: Human polyclonal reagents (pools of human sera) were used by different groups in the past. Similar anti-Fy^b was used for the four cases described here (three different lot numbers). However the results showed weaker reactions compared to controls. This difference compared to previous publications might be caused by the fact that sera from different immunized donors were used to prepare the different reagent lots. Although the Fy^b was weakly expressed, none of the four cases reported here developed an anti-Fy^b.

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A NOVEL FY*02 SILENT ALLELE CAUSED BY A NUCLEOTIDE DELETION MECHANISM AND RESPONSIBLE FOR A FY NULL PHENOTYPE IN AN ALGERIAN PATIENT WITH STRONG ANTI–FY3 IMMUNIZATION

J Babinet[1], S Ramelet[1], G Laiguillon[1], A Raneri[1], L Mannessier[2], C Vrignaud[1,3,4] and T Peyrard[1,3,4]

[1]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine, Paris [2]Etablissement Français du Sang, Lille [3]Laboratoire d'Excellence GR-Ex [4]UMR_S1134, Inserm/Université Paris Diderot, Paris, France

Background: The Duffy (FY) system includes three major antigensFy^a, Fy^b and Fy3. The molecular basis of the Fy^a/Fy^b polymorphism corresponds to the c.125A>G SNP (p.Asp42Gly) in exon 2 of the FY gene (DARC or ACKR1). The Duffy protein is found on red blood cells (RBCs) and other tissues. The Fy(a-b-) type is frequently encountered in people of African origin, due to a c.-67t>c mutation in the promoter of the FY*B allele (FY*02N.01). This mutation abolishes the expression of the Duffy protein in RBCs only. Other much rarer mutations in the open reading frame sequence (missense, nonsense, insertion or deletion, frameshift) may abolish its expression in all tissues; they are reported either on a FY*A (n = 7) or FY*B (n = 5) backgrounds. People being homozygous for this second kind of mutations are mostly discovered when alloimmunized against the whole FY protein (anti-Fy3). Finally, there are weakened FY variants, the most common corresponding to very weakened Fy^b and Fy3 antigens, called the Fy^x phenotype (FY*02W.01 or FY*X allele), difficult to detect with most anti-Fy^b reagents.

Aims: A patient with a Fy(a-b-) phenotype originating from Algeria (North Africa) was subject to an in-depth serological study in 1977 in our laboratory, for an anti-Fy3 alloimmunization occurring after a transfusion. Recently, this plasma was re-evaluated with current laboratory techniques and a study of the FY gene was performed.

Methods: The RBC antibody screening/identification/titration were carried out by indirect antiglobulin test (gel-test, Bio-Rad) on native RBCs. FY genotyping was performed on DNA-chips (BeadChip HEA v1.2, Immucor). FY sequencing was carried out on genomic DNA.

Results: The serological study showed the presence of anti-E and confirmed the high potency of anti-Fy3, with a titer of 16,000 on Fy(a+b+) RBCs, and 4,000 on Fy (a-b+^{w}) RBCs with a FY*02N.01/FY*02W.01 genotype. The antibody was non-reactive on all E-, Fy(a-b-) RBCs of African origin (n = 6). Genotyping showed a homozygous FY*B allele with no c.-67t> c mutation. FY sequencing confirmed the

absence of a mutation in the gene promoter and the presence, in the homozygous state, of a novel FY*B allele showing a deletion of one nucleotide at position 400 in exon 2 (c.400delT). This deletion is predicted to cause a frameshift and generation of a premature stop codon at position 147 (p.Cys134Valfs*14).

Summary/Conclusions: We report here the case of a patient from North Africa who developed a potent anti-Fy3 initially discovered 40 years ago, able to strongly agglutinate RBCs with a weakened Fy^b/Fy3 expression. Due to his African origin, no molecular study had been conducted so far, on the assumption that he would be FY*02N.01/ FY*02N.01. FY sequencing revealed a homozygous deletion of one nucleotide (c.400delT) in a FY*B allele, supposed to abolish the expression of the Duffy protein, both in RBCs and other tissues. We suggest this new allele to be named FY*02N.07, subject to the agreement of the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology. Our case is similar to those exceptionally reported in the literature, where the complete absence of Duffy protein exposed to a severe anti-Fy3 immunization after transfusion.

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GENETIC ANALYSIS OF VEL BLOOD GROUP IN XINJIANG AREA OF CHINA

T Liu, Y Liu, R Zhang, L Shi and F Zhao

Jiangsu Province Blood Center, Nanjing, China

Background: Vel is one of the most difficult blood types to supply in many countries. But there are little studies and data on Vel blood group in China at present. Our team has reported the frequency of SMIM1 c.64_80del allele of Han population in Nanjing of China, which is significantly lower than that of other countries that have been reported. Now, we performed a detailed genetic analysis of Vel blood group in Xinjiang area of China, which demonstrated strong regional and ethnic characteristics.

Aims: Molecular screening of Vel− blood donors and give a detailed genetic analysis of Vel blood group in Xinjiang area of China.

Methods: Two pairs of primers respectively specific for SMIM1 wild-type (named "+p") and c.64_80del alleles (named "−p") were designed. Genomic DNAs of 3328 healthy blood donors randomly selected from Yili Blood Center in Xinjiang Province were combined into 832 pools of four samples. DNA pools were amplified by "−p". Samples from positive pool were further individually amplified by "−p" and "+p". Sanger sequencing were performed to verify the genotype of the one with c.64_80del mutation.

Results: We identified 14 individuals heterozygous for SMIM1 c.64_80del allele in 3328 blood donors, which are from Han population and 23 ethnic minorities. Seven of them were Uygur (total Uygur donor: 864), four were Kazakh (total Kazakh donor: 580), two of them were Han (total Han donor: 846), and one was Mongolian (total Mongolian: 97). That's to say, the allelic frequency of c.64_80del among the donors tested in Xinjiang area of China was 0.21% (14/6656). The frequency of c.64_80del allele of Han population in Xinjiang is 0.12% (2/1692), which is significantly higher than that of Han population in Nanjing (0.0049%;Liu,2017). The allelic frequency of c.64_80del among Uygur, Kazakh and Mongolian were 0.41%, 0.34% and 0.52%, respectively.

Summary/Conclusions: The allelic frequency of c.64_80del in Xinjiang area is significantly higher than that of Nanjing. Han population from Xinjiang and Nanjing are quite different on c.64_80del allelic frequency. The allelic frequencies of different ethnic minorities in Xinjiang area also showed much difference. Together, the distribution of the Vel blood group shows strong regional and ethnic characteristics.

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CHARACTERIZATION OF A NOVEL HIGH–PREVALENCE ANTIGEN IN THE CROMER BLOOD GROUP SYSTEM

C Vrignaud[1,2,3], J Chiaroni[4,5], C Landré[1], E Durieux-Roussel[5], B Peres[5], Y Colin[3,6], O Hermine[3,7], C Le Van Kim[3,6], S Azouzi[1,2,3] and T Peyrard[1,2,3]

[1]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine [2]UMR_S1134, Inserm/Université Paris Diderot [3]Laboratoire d'Excellence GR-Ex, Paris [4]Aix Marseille Université, CNRS, EFS, ADES, "Biologie des groupes sanguins" [5]Etablissement Français du Sang PACA Corse, Marseille [6]UMR_S1134, Inserm Université Paris Diderot Institut National de la Transfusion Sanguine [7]Institut Imagine, UMR_S1163 Université Paris Descartes, Paris, France

Background: The Cromer blood group system consists of 19 antigens carried on a GPI-linked glycoprotein (DAF or CD55), with 16 high-prevalence and 3 low-

prevalence antigens reported to date. All Cromer antigens are absent in the exceptional Inab phenotype (Cromer-null). DAF contributes to the regulation of the complement system on the red cell surface. Except for one Cromer-null allele, the molecular background of all Cromer antigens corresponds to a single nucleotide mutation in CD55 gene (consensus sequence NM_000574).

Aims: We describe here a novel high-prevalence antigen in the Cromer blood group system.

Methods: Blood samples were referred to our laboratory for investigation of a pan-agglutinating antibody. Antibody identification (gel-test IAT, Bio-Rad) was performed on native, papain-treated (Diagast) and trypsin-treated (Sigma) RBCs. Genomic DNA was extracted from peripheral blood cells. Exome capture was carried out on genomic DNA as recommended by the manufacturer, using the SureSelect Exon kit V5 (Agilent Technologies). Sequencing data were analyzed by an in-house software package (PolyWeb, Institut Imagine, Paris).

Results: The proband was a 103-year-old female patient of French Corsican origin (island in the Mediterranean Sea), group O, R_2R_2, K-. She had one pregnancy in 1949 and a positive inconclusive antibody identification in 2002. In 2011, she was hospitalized for anemia and samples were sent to our laboratory for investigation of a pan-agglutination occurring after transfusion of 2 RBC units. The antibody reacted 1 + on all native and enzyme-treated reagent RBCs (negative autocontrols), but its specificity could not be assessed despite an in-depth workup. A probable HTLA antibody was concluded. New blood samples were referred in 2016 in an anemia context, but the serological investigation remained inconclusive. We then decided to extract DNA samples of the proband and her son (serologically incompatible) to perform exome sequencing. This revealed in the proband the presence of a homozygous mutation in exon 6 of the CD55 gene, c.713G>A, predicted to cause a p.Gly238Glu amino acid change. Her son was found to be heterozygous for the same mutation. The c.713G>A mutation has not been reported to date in any previous sequencing project (e.g. 1000 Genomes). The Cromer specificity of the antibody was further confirmed after finding no reactivity of the patient's eluate with our single source of Cromer-null RBCs that happened to become available in 2017 when discovering an Inab phenotype in a 8-year-old patient (CROM*01N.04/CROM*01N.04 genotype).

Summary/Conclusions: The so-called Next Generation Sequencing approach allowed us here to indirectly resolve this complex and challenging serological case and to characterize the molecular basis of a novel high-frequency antigen in the Cromer blood group system. The exome sequencing method not only made us able to find a novel CD55 allele but also, and most importantly, to identify the specificity of the patient's antibody and to provide for a possible transfusion strategy. We suggest this novel allele to be provisionally named CROM*01.-20, and the new CROM20 antigen to be called CORS (from the Corsican origin of the patient), subject to the formal agreement of the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology.

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THREE NOVEL JK ALLELES RESPONSIBLE FOR A JK NULL PHENOTYPE WITH ANTI–JK3 ALLOIMMUNIZATION

C Vrignaud[1,2,3], S Martin-Blanc[3], S Ramelet[3], C Jeannequin[3], A Binet[3], C Landré[3] and T Peyrard[1,2,3]

[1]Laboratoire d'Excellence GR-Ex [2]UMR_S1134, Inserm/Université Paris Diderot [3]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine, Paris, France

Background: The Kidd blood group system comprises three antigens Jk[a], Jk[b] and Jk3. The molecular basis of the Jk[a]/Jk[b] polymorphism corresponds to a mutation in the JK (SLC14A1 or HUT11A) gene in exon 9, c.838A>G (p.Asn280Asp). Besides, the Jk[b] antigen is associated with a synonymous mutation in exon 7, c.588A>G (rs2298718). Jk3 is a high-prevalence antigen, absent in the rare Jk(a-b-) phenotype, also known as Jk[null]. Several molecular backgrounds have been reported for Jk[null], either on a JK*01 or JK*02 allele basis (homozygous or compound heterozygous inactivating mutations).

Aims: We report here the serological and molecular investigation of three unrelated Jk(a-b-) patients.

Methods: Blood samples were referred to our laboratory for RBC antibody investigation and confirmation of a rare Jk(a-b-) phenotype. Antibody identification (IAT, gel-test Bio-Rad) was performed on native, papain-treated (Diagast) and trypsin-treated (Sigma) RBCs. The Kidd phenotype was determined by standard hemagglutination techniques with two commercial reagents (Bio-Rad/polyclonal and monoclonal). Genomic DNA sequencing for the JK gene (consensus sequence NM_015865) was performed as previously described by Horn et al, Transfusion, 2012.

Results: The first proband was a 64-year-old female patient from Bosnia. Blood samples were referred in 2009 for confirmation of a Jk[null] phenotype and study of a pan-agglutinating antibody. The patient's serum reacted with all native and enzyme-treated reagent RBCs, but no reactivity was observed on Jk(a-b-) RBCs, being consistent with an anti-Jk3 alloimmunization. The second case was a 68-year-old female patient referred in 2013 for confirmation of a Jk(a-b-) rare type and suspicion of an anti-Jk[a] reactivity; this antibody was concluded to be an anti-Jk3 in our laboratory. The third individual, a 26-year-old woman, was subject to an antibody screening in 2017 prior to a gastric surgery. The presence of anti-Jk3 was confirmed, as well as an anti-Jk[b] after allogeneic adsorption on homologous RBCs. Genomic DNA sequencing revealed in the first patient the presence, on a JK*01 allele basis, of a mutation in exon 5 at position 191 (c.191G>A), expected to cause the p.Arg64Gln amino acid change. For the second proband, the mutation c.376G>A (p.Ala126Thr) was found in exon 6 at homozygous state. JK sequencing revealed, in the last patient, the presence of an insertion of one nucleotide in exon 7 at position 584 (c.584insA), at homozygous state, responsible for a frameshift and premature stop codon (p.Asn195Lysfs*22). Those two last mutations were found on a JK*02 allele basis, associated with the c.588A>G synonymous change.

Summary/Conclusions: We characterized here three novel silent JK alleles, JK*01 (191A), JK*02(376A,588G) and JK*02(584insA,588G). All of these novel mutations were predicted to be deleterious according to the respective scores of the PolyPhen and SIFT tools. Furthermore, the c.191G>A mutation was reported in numerous genome sequencing projects (rs114362217) and observed in both European and African populations. The second mutation was described in the ExAC project (rs775752379) and found in Europeans. However, the c.ins584A insertion has never been reported to date. After the JK*02(588G,830insC) allele recently reported by our team (Vox Sang 2017;112(Suppl1):229), JK*02(584insA,588G) is only the second case of a silent JK allele caused by a nucleotide insertion mechanism.

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NOVEL SPLICE SITE MUTATIONS CREATING THE ST[A] ANTIGEN

N Watanabe-Okochi[1], H Tsuneyama[1], K Isa[2], K Sasaki[2], Y Suzuki[1], R Yabe[1], K Ogasawara[2], M Uchikawa[1], N Tsuno[1] and K Nakajima[1]

[1]Kanto-Koshinetsu Block Blood Center, Japanese Red Cross [2]Central Blood Institute, Japanese Red Cross,, Tokyo, Japan

Background: The low incidence antigen St[a] in MNS system is commonly associated with various hybrid molecules between Glycophorin B (GPB) and Glycophorin A (GPA). The GP(B-A) hybrid with N antigen at their N-terminal, known as GP.Sch, is predominant in the St(a+) individuals. In a few St(a+) individuals, GP(A-A) hybrid with trypsin resistant M antigen has been found. The St[a] with resistant M antigen is encoded by GYP*(A-ψB-A) (GYP*Zan), GYP*(A-ψE-A) (GYP*Mar), and GYP*A (GYP*EBH).

Aims: By analyzing the genomic DNA isolated from Japanese St(a+) individuals, we confirmed novel alleles encoding the St[a] specific glycophorin with trypsin-resistant M antigen.

Methods: Blood samples were derived from blood donors of the Kanto Koshinetsu block blood center. Written informed consents were obtained from all blood donors before blood sampling. Screening with monoclonal anti-M against bromelain treated RBC were performed with an automated blood grouping analyzer (PK7300, Beckman Coulter). When the positive reaction was observed, the St[a], M, N, S and s antigens were examined by the tube method using untreated RBCs with anti-St[a] (in house), anti-M (CBC-1 + CBC-2, in house), anti-N (HIRO-29, in house), anti-S and anti-s (Ortho Clinical Diagnostics, Japan). Positive reaction of trypsin-treated RBC with anti-M was also confirmed by tube method. Genomic DNA samples of St(a+) with trypsin resistant M antigen were extracted from white blood cells in peripheral blood. To identify the molecular mechanism of St[a] antigen, the extracellular domain exon 2 to 4 of GYP*A was amplified by PCR. The PCR products were subsequently sequenced.

Results: We confirmed novel alleles of the St[a] gene with trypsin-resistant M antigen. One of the new molecular mechanisms is the 9 bp deletion including the GT motif of the donor splice site at 5′ end of intron 3 of GYP*A. As the donor splice site is essential in the mRNA processing, exon 3 is spliced out and then exon 2 directly ligates to exon 4. The exon 3 skipping is a critical event for the St[a] formation. We also found a novel GYP*(A-ψB-A) hybrid gene containing the pseudoexon 3 of GYP*B. The 5′ proximal breakpoint is c.178 - c.203 in exon 3 and the 3′ proximal breakpoint is c.232 + 307–489 in intron 3. As another variant, a rare hybrid formation comprising GYP*E and GYP*A was identified. The 3′ proximal breakpoint of this GP(E-A) variant is c.232 + 706–763 in intron 3. We confirmed that the

sequence data of the GP(E-A) variant matched to the reference sequence of GYP*E from c.38-390 in intron 1 to the 3′ breakpoint. The pseudoexon 3 of GYP*E is spliced out by the defective donor splice site and exon 2 of GYP*E is directly ligated to exon 4 of GYP*A. The 5′ proximal breakpoint is not identified yet, since GYP*E has highly sequence similarity with GYP*A.

Summary/Conclusions: We analyzed 193,009 Japanese individuals, and identified that 29 individuals with resistant M had the St^a antigen (0.02%). Based on nucleotide sequences, 10 of the 29 St(a+) individuals revealed a novel splice site mutation such as 9 bp deletion including the donor splice site at 5′ end of intron 3 of GYP*A. Five individuals had GYP*(A-ψB-A) hybrid allele. Nine had a novel GP(E-A) variant. The remaining 5 individuals are still unknown.

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TWO PREVALENT GYPB DELETIONS ARE CAUSATIVE OF MNS BLOOD GROUP U NEGATIVITY IN BLACK AFRICANS

C Gassner[1], G Denomme[2], C Portmann[1], S Meyer[1], N Trost[1], C Jungbauer[3], B Just[4], J Storry[5], M Forster[6], A Franke[6] and B Frey[7]

[1]Molecular Diagnostics and Research & Development, Blood Transfusion Service Zurich, SRC, Zurich-Schlieren, Switzerland [2]Blood Research Institute, Versiti, Inc., Milwaukee, Wisconsin, United States [3]Blood Service for Vienna, Lower Austria and Burgenland, Austrian Red Cross, Vienna, Austria [4]German Red Cross Blood Donation Service West, Hagen, Germany [5]Department of Laboratory Medicine Lund University, Hematology & Transfusion Medicine, Lund, Sweden [6]Institute of Clinical Molecular Biology, Christian Albrechts University of Kiel, Kiel, Germany [7]Head Office, Blood Transfusion Service Zurich, SRC, Zurich-Schlieren, Switzerland

Background: The U antigen (MNS5) was originally described in 1953 and was characterized as a high-frequency-antigen that is absent in 1.2% of African Americans (Wiener, JAMA, 1953). In 1954, the association with the MNS blood group system and concurrent S–s– phenotype became evident (Greenwalt, PNAS, 1954), and was later postulated to be caused by a homozygous GYPB deletion (Huang, Blood, 1987). Until now however, lack of exact molecular definition of such deletions prohibited unequivocal interrogation of both parental haplotypes.

Aims: This study aimed for an exact molecular definition of GYPB deletions, causative of recessive negativity in phenotype S–s–U– Black Africans. Added to classical MNS genotyping, positive detection of such deletions should enable definitive GYPB genotyping.

Methods: Bioinformatical analysis of the publicly available 1000 Human Genomes (1000G) data revealed several hits for two distinct ~100 kb and one hit each for a ~32 kb and ~18 kb GYPB deletion, all identified among Black Africans. Sanger sequencing of analytical gap-PCRs bridging these deletions in predefined S–s–U– samples revealed the deletions' exact molecular positions and were used to design specific diagnostic PCRs using sequence-specific priming (PCR-SSP). Subsequent validation genotyping was performed in 23 samples of known S–s–U– phenotype and concomitant negativity for both GYPB*03 (S) and GYPB*04 (s), plus the 1000G samples of the Coriell Human Genetic Cell Repository, showing the ~32 and ~18 kb deletions.

Results: One 110.24 kb deletion stretched from 4.96 kb 5′ of the GYPB start codon until 8.51 kb 5′ of the GYPE start codon. The other 103.26 kb deletion started 16.42 kb 3′ of the GYPA stop codon and ended 4.58 kb 3′ of the GYPB stop codon. Both deletions encompassed the whole GYPB gene and involved highly paralogous intergenic sequences, suggesting unequal crossing-over as causal molecular origin for this variation. Of 23 validation samples, 13 genotyped as GYPB*05N(del110 kb) homozygotes, 6 GYPB*05N(del110 kb)/(del103 kb) heterozygotes, one GYPB*05N (del103 kb) homozygote and three were heterozygous for GYPB*05N(del110 kb) and a yet undefined, second parental GYPB-deletion. The originally expected ~32 kb deletion in one Coriell sample, was in fact GYPB*05N(del110 kb)/(del103 kb) heterozygous, displaying ~32 kb combined absence of GYPB sequences, rather than being a unique deletion. The suggested ~18 kb deletion was only observed in one Coriell sample. Of 46 haplotypes with a presumptive GYPB deletion analysed in total, 36 (78.2%) were GYPB*05N(del110 kb), 9(19.6%) were GYPB*05N(del103 kb), and 3(6.5%) remained unresolved. Overall haplotype-frequency was estimated to be 11.0%, considering the above mentioned 1.2% S–s–U– phenotype frequency in Black Africans.

Summary/Conclusions: This study describes the characterization of three causal GYPB deletions underlying the S–s–U– phenotype, and development of genotyping assays for detection of such individuals. Thus, these assays, when performed simultaneously with classical genotyping for S, s, and the rudimentary expressed Uvar alleles, allows for unequivocal results and correct phenotype predictions of all genotypes involved. With an observed 1.2% S–s–U– phenotype frequency, heterozygous

involvement of such GYPB deletions may be expected in about 19.5% of all Black Americans. Recent reports on the molecular nature and prevalence of GYPB deletional haplotypes and their contribution to a reduced risk for Malaria invasion, are further supportive of our independent findings (Leffler, Science, 2017).

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"A FAMILY STUDY REVEALS THE RED CELL S–S–U– PHENOTYPE: CHALLENGES PRESENTED WITH THE AUSTRALIAN DONOR DEMOGRAPHIC"

D Stern[1], Y Liew[2], E Schoeman[2], G Millard[2], G Lopez[2], E Roulis[2], C Knauth[2], R Flower[2], C Hyland[2] and G Kidson-Gerber[3,4]

[1]Blood Bank Prince of Wales Hospital, New South Wales Health Pathology, Randwick [2]Australian Red Cross Blood Service, Brisbane [3]New South Wales Health Pathology, Randwick [4]University of New South Wales, Randwick, Australia

Background: A 63y.o. male of Kenyan descent was admitted to Prince of Wales Hospital, Sydney, on his return from Africa to continue treatment for acute mixed phenotypic leukaemia. He was transfused 13 units of red cells before transfer. Blood samples were referred to the Australian Red Cross Blood Service Red Cell Reference Laboratory, Brisbane, for genotyping as phenotyping was not possible. The wife was Fy(a–b–), s+ or serological phenotype; the two daughters tested were both Fy(a–b–), S–s–U–. These samples were also referred for genotyping.

Aims: To elucidate the molecular basis for the observed S–s–U– phenotype and explain the pattern of inheritance for this family. We also discuss problems for matching such blood types.

Methods: Red cell phenotyping and SNP-array based genotyping was performed using standard procedures. Extended sequencing was performed by massively parallel sequencing (MPS) using TruSight One (TSO) sequencing panel (Illumina). Copy number variation analysis was performed by comparing normalised mean coverage for each GYPB exon to reference values to measure GYPB zygosity. To confirm TSO results, gene-specific long-range PCR amplicons of the complete GYPB were generated for each sample and for wildtype GYPB control and sequenced using NexteraXT kit (Illumina). Reference alignment of sequence reads (against Hg19) and variant detection was performed using CLC Genomics Workbench.

Results: Phenotyping and SNP-typing results showed all family members were homozygous for the FY*02N.01 allele frequent in the African population which results in the Fy(a–b–) red cell phenotype. It was also noted that genotyping showed that the patient and daughters were homozygous for a GYPB null allele in which either GYPB Exons 2 to 6 were absent (GYPB*01N) or in which Exons 1 to 6 were absent.

The patient's wife carried one copy of a GYPB null allele displaying the same genotyping pattern as her family and one copy of the wildtype GYPB*04 (GYPB*s) allele which predicts the s+ phenotype.

Summary/Conclusions: Patients with the Fy(a–b–) phenotype arising from the GATA1 mutation may be transfused with Fy(a–b+) red cells under current protocols. Extended genotyping here showed that the patient and two daughters are homozygous for a variant gene in the MNS blood group system that resulted in the S–s–U– phenotype. The precise boundaries defining where the nucleotide sequence changes occur await further investigation. This case is notable for a number of reasons: Firstly, this demonstrates the benefit of extended genotyping in the clinical setting. Secondly, had the patient been alloimmunised, a red cell match would have been difficult as the inventory for frozen S–s–U– phenotypes was limited (seven units in Australia) and one blood donor was registered on the Australian panel at that time. This patient received 15 units of red cells over 3 months in Australia with no evidence of alloimmunisation. Finally, the problem supporting such patients in the future needs consideration.

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GP.MOT, A NOVEL GLYCOPHORIN HYBRID MOLECULE WITH MILTENBERGER PHENOTYPE IN JAPANESE BLOOD DONOR

A Oda[1], Y Suzuki[1], K Isa[2], C Toyoda[1], K Ogasawara[2], M Uchikawa[1], R Yabe[1], N Tsuno[1] and K Nakajima[1]

[1]Kanto-Koshinetsu Block Blood Center, Japanese Red Cross [2]Central Blood Institute, Japanese Red Cross, Tokyo, Japan

Background: MNS blood group system consists of 49 antigens carried on glycophorin A (GPA), glycophorin B (GPB) or hybrid molecules composed of a portion of GPA and GPB. Miltenberger phenotypes are expressed on hybrid glycophorin molecules, GP (A-B), GP (B-A-B) and GP (A-B-A), formed by the genetic recombination of GYP*A and GYP*B. GP.Vw, GP.Hut, GP.Nob, GP.Joh and GP.Dane are encoded by GYP*(A-B-A) hybrid gene. GYP*(A-B-A) arise from gene conversions involving GYP*B and GYP*A as the donor and recipient, respectively. GP.Mur, GP.Hop, GP.Bun, GP.HF, and GP.Kip are encoded by GYP*(B-A-B) hybrid gene, and GP.Hil and GP.JL are encoded by GYP*(A-B) hybrid gene.

By screening Japanese donors using anti-Mi[a], we detected a Mi (a+) that could not be classified as the known Miltenberger phenotypes.

Aims: We report a novel GP (B-A) glycophorin hybrid molecule predicted to be encoded by GYP*(A-B-A) gene.

Methods: Genomic DNA was isolated from whole blood cells derived from the Japanese donor. Testing of MNS blood group system antigens on the RBCs was performed using standard serological tests with polyclonal and monoclonal antibodies. Flow-cytometry and immunoblotting analysis were performed with glycophorin-specific monoclonal antibodies. The nucleotide sequence of the glycophorin gene was analyzed using the direct sequencing.

Results: The MNS blood type of the propositus was M + N +[w] S − s + . Testing of antibodies against low-frequency antigens revealed positive with Mi[a], MUT, Mur, and Hop+Nob (Kip) and negative with Vw, Hil, Hop, and MINY. Flow-cytometric analysis of the patient's red cells revealed the fluorescence intensities of M and s antigens equivalent to that of M + N + and S − s +, respectively. The fluorescence intensity of N antigen was lower than that of the M + N + . Immunoblotting with the monoclonal antibodies to MUT, Mur, N and C-terminal domains of GPA showed an abnormal band of approximately M_r 43,000. Direct sequencing demonstrated a normal GYP*A[M], normal GYP*B[s] and a hybrid gene. Although the exact 5′ breakpoint was not identified, it was confirmed to be located at least upstream of IVS1-222, and the 3′ breakpoint was placed between c.209 and c.220. The replacement of GYP*A by homologous region of GYP*B, including exon 2, intron 2 and part of pseudoexon 3 of GYP*B, to generate a novel GYP*(A-B-A) gene, was identified. The hybrid nucleotide sequence contained the sequence motifs previously shown to be required for the expression of the Mi[a], Mur, MUT, Hop+Nob (Kip), which is consistent with our serological findings.

Summary/Conclusions: The GP.MOT phenotype can be predicted to be produced by a hybrid GP (B-A) protein caused by a DNA insertion of GYP*B into GYP*A, GYP* (A-B-A). The composition of the hybrid protein is GPB (20-45)-GPψB (46-70)-GPA (71-149).

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PREDICTED MNS 3 AND MNS4 PHENOTYPES FROM GENOTYPING RESULTS AMONG THAI POPULATIONS TO PREVENT TRANSFUSION-INDUCED ALLOIMMUNIZATION RISKS

O Nathalang[1], R Ang[2], B Kurin[3], S Limprasert[3], S Mitundee[4], N Leetrakool[5] and K Intharanut[1]

[1]Graduate Program, Faculty of Allied Health Sciences, Thammasat University, Pathumtani, Thailand [2]Department of Medical Technology, Faculty of Pharmacy, University of Santo Tomas, Manila, Philippines [3]Department of Medical Technology, Faculty of Allied Health Sciences, Thammasat University, Pathumtani [4]Regional Blood Centre 12th Songkhla, Thai Red Cross Society, Songkhla [5]Blood Bank Section, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Background: MNS3 (S) and MNS4 (s) antigens of the MNS system are of clinical importance because alloanti-S and -s have usually caused delayed hemolytic transfusion reactions and hemolytic disease of the fetus and newborn (HDFN). Difficulties in test interpretation by serological techniques may be found in cases of transfusion-dependent patients and fetal risk for HDFN. Various red cell genotyping has been established to predict the phenotypes to solve serological test limitations.

Aims: This study aimed to determine GYPB*S and GYPB*s genotype frequencies leading to predicted S and s phenotypes and to estimate the alloimmunization risks among central, northern and southern Thai populations.

Methods: Altogether, 1,237 blood samples from Thai blood donors were included. Only 150 samples were tested with anti-S and anti-s by indirect antiglobulin test. All samples were genotyped for GYPB*S and GYPB*s alleles using in-house PCR with sequence-specific primer. Additionally, the allele frequencies were used to estimate alloimmunization risks and compare with other populations.

Results: The phenotyping and genotyping results in 150 samples were in 100% concordance. The allele frequencies of GYPB*S in central, northern and southern Thais were 0.061, 0.040 and 0.097, and GYPB*s were 0.939, 0.960 and 0.903, respectively. The frequencies among central Thais were similar to those among northern Thai and Korean populations (P > 0.05) but significantly differed from those of Asian, Caucasian African American and Hispanic populations (P < 0.05). In addition, the risk of S alloimmunization among southern Thais (0.1566) was higher than those among central (0.1038) and northern Thais (0.0736).

Summary/Conclusions: This was the first study to report S and s predicted phenotypes and estimate alloimmunization risks among Thais, which is beneficial to prevent transfusion-induced alloimmunization among donors and patients.

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A MOLECULAR MECHANISM UNDERLYING THE P_1/P_2 PHENOTYPES: ALLELE-SELECTIVE RUNX1 BINDING REGULATES P1 BLOOD GROUP STATUS BY TRANSCRIPTIONAL CONTROL OF A4GALT

L Stenfelt[1], J Westman[1], K Vidovic[1], M Möller[1], Á Hellberg[2], S Kjellström[3,4] and ML Olsson[1,2]

[1]Laboratory Medicine, Lund University [2]Clinical Immunology and Transfusion medicine, Office of Medical Services [3]Department of Chemistry [4]Excellence in Biological and Medical Mass Spectrometry (CEBMMS), Lund University, Lund, Sweden

Background: P1 and P[k] are glycosphingolipids in the P1PK blood group system, synthesized by the A4GALT-encoded α1,4-galactosyltransferase, which utilizes paragloboside and lactosylceramide as acceptor substrates, respectively. In addition to the compatibility aspects of these molecules, both constitute receptors for microbes and toxins. P1 status on erythrocytes determines the common P_1 (P1 + P[k]+) and P_2 (P1−P[k]+[weak]) phenotypes. A4GALT transcript levels are higher in P_1 individuals and single nucleotide polymorphisms (SNPs) in non-coding regions of A4GALT, particularly rs5751348, correlate with P_1/P_2 status. Interestingly, the In(Lu) phenotype is caused by KLF1 haploinsufficiency and shows decreased P1 levels on erythrocytes.

Aims: Despite the above findings, molecular mechanisms underlying P1 expression remain elusive. We aimed to resolve this longstanding question and hypothesized KLF1 and/or other transcription factors (TFs) to regulate A4GALT in a P^1-allele-specific manner.

Methods: The genomic region surrounding rs5751348 was examined for TF-binding sites using JASPAR (http://jaspar.genereg.net/) and other databases. Electrophoretic mobility-shift assay (EMSA) was performed using nuclear extracts from HEL cells or recombinant KLF1, anti-KLF1 for supershift and anti-RUNX1 for shift-blocking assay. Three P^1- and two P^2-specific, biotinylated oligonucleotide probes of different lengths were synthesized and used for EMSA and protein pull-down experiments, following incubation with HEL nuclear extracts. The probe-protein complexes were immobilized onto magnetic beads and subjected to Western blot or LC-MS/MS analysis. Possible interactions between candidate TFs and all detected proteins that bound only to the P^1 probe were queried by STRING analysis (https://string-db.org). HEL and MEG-01 cells were transfected with siRNA targeting KLF1 and RUNX1. Transcript levels of the targeted genes and A4GALT were determined with qPCR and normalized to beta-actin levels. GAPDH and siRNA without human gene targets served as positive and negative controls, respectively. Experiments were performed in technical triplicates and statistics analyzed using the Mann-Whitney U-test.

Results: The P^1-specific motif around rs5751348 revealed putative binding sites for several hematopoietic TFs, including KLF1, EGR1 and RUNX1. All three displayed predicted decreases of binding energy scores with the P^2-specific variant of rs5751348. To investigate potential transcription factor binding to the implicated region, EMSA was performed. Intriguingly, a P^1-specific shift with nuclear extract was noted but no supershift with anti-KLF1. Neither KLF1 nor EGR1 were detected by Western blot of proteins bound to P^1 probes. Furthermore, efficient siRNA silencing of KLF1 did not affect A4GALT transcript levels. Instead, protein pull-down experiments with P^1 but not P^2 probes identified multiple peptides corresponding to the hematopoietic transcription factor RUNX1 by mass spectrometry. This finding

was confirmed by Western blot of proteins bound to P^1 but not P^2 probes, and also by an EMSA competition assay where increasing amounts of anti-RUNX1 weakened the P^1-specific shift bands. Knockdown of RUNX1 gave a 90% reduction of RUNX1 protein, which resulted in a significant 64% decrease of A4GALT transcripts.

Summary/Conclusions: These data indicate that RUNX1 regulates A4GALT and thereby the expression of P1 and P^k blood group antigens, implicated in transfusion incompatibility and host-pathogen interactions. Thus, the molecular mechanism determining P1 status involves RUNX1 binding at the P^1 vs. P^2-differentiating rs5751348 site.

P-551

A CASE OF ANTI–PP1P^K PRODUCED IN A COMPOUND HETEROZYGOTE WITH A NOVEL A4GALT NULL ALLELE

L Tilley[1], R Laundy[1], T Bui[2], Q Bach[2], T Hoang[2], T Pham[2], A Nguyen[2] and N Thornton[1]

[1]*International Blood Group Reference Laboratory, NHS Blood & Transplant, Bristol, United Kingdom* [2]*National Institute of Hematology and Blood Transfusion, Hanoi, Viet Nam*

Background: Red cells of the rare p phenotype lack P1, P^k, P and LKE antigens, carried on carbohydrate residues of red cell glycosphingolipids. The p phenotype results from homozygosity or compound heterozygosity for inactivating mutations in A4GALT, which encodes the enzyme responsible for converting lactosylceramide to P^k and paragloboside to P1. Individuals of p phenotype have an antibody, known as anti-PP1P^k, which agglutinates or haemolyses all red cells except those of the p phenotype and can cause severe haemolytic transfusion reactions. Anti-PP1P^k has also been implicated in early spontaneous abortion and women with the p phenotype have a significantly higher incidence of habitual abortion.

Aims: To present results from serological and molecular investigations of a case of anti-PP1P^k with a novel molecular background of the p phenotype, including a family study.

Methods: Samples from a 33 year old Vietnamese patient, with a diagnosis of thin endometrium and a history of five first trimester miscarriages, were investigated due to the presence of a strong alloantibody reacting with all cells except her own and those of her sister. Blood samples from the patient's brother, sister and mother were also tested. Serological investigations were performed by standard tube LISS IAT and direct agglutination techniques. Genomic DNA was extracted and PCR amplification and sequencing was carried out for exons 2a and 3 of the A4GALT gene.

Results: The patient and her sister were found to have the p phenotype (P1−, P−, P^k−) and both had strong anti-PP1P^k present in their plasma. Their samples were mutually compatible. Cells from their mother and brother were incompatible.

Sequencing of A4GALT exon 2a revealed all family members to be homozygous for 42C>T, associated with the P_2 phenotype. Sequencing of exon 3 revealed compound heterozygosity for two different deletions in both p individuals. The first c.241_243delTTC, resulting in p.Phe81del, corresponds to a known null allele, A4GALT*01N.01.01. The second appears to be a novel allele, carrying a deletion of 13 nucleotides between positions 809 and 821, resulting in a frameshift at amino acid position 270, and truncation at amino acid 345 (c.809_821del; p.Ser270Thr fs*75). Compound heterozygosity for both deleted alleles is predicted to result in non-functional A4GALT and a resulting p phenotype. The brother and mother were both revealed to carry the novel mutated allele in the heterozygous state, together with an A4GALT*P2 allele.

Summary/Conclusions: We have identified a novel null allele of A4GALT, found in a Vietnamese family. The novel allele, carried in a compound heterozygous state with a known null allele, A4GALT*01N.01.01, resulted in the p phenotype in the patient and her sister and anti-PP1P^k was identified in their plasma. The patient had a history of multiple first trimester spontaneous abortions, which is known to occur at a higher rate than normal in women with the p phenotype.

P-552

DEVELOPMENT OF A RENEWABLE REFERENCE PANEL FOR GENOTYPING OF RH BLOOD GROUP VARIANTS

EA Sippert[1], E Volkova[1], M Liu[1], T Mercado[1], O Illoh[1], Z Liu[1], G Denomme[2] and M Rios[1]

[1]*CBER/OBRR, U.S. Food and Drug Administration, Silver Spring* [2]*Versiti/Blood Research Institute, Milwaukee, United States*

Background: Patients who carry Rh blood group variants may develop clinically significant antibodies and require matched red blood cell transfusions. The availability of serological reagents for Rh variants is limited, making molecular genotyping assays essential for the management of transfusion for many of these patients. However, development of molecular assays has been hampered by the lack of reference reagents for RH variants needed to ensure their quality and performance. A renewable DNA panel covering many blood group alleles has recently been developed and validated by an international collaborative study.

Aims: To develop a renewable DNA panel for RH variants to complement the above-mentioned blood group panel.

Methods: Immortalized B-cell lines were generated from 53 whole blood donors. RHD and RHCE genes were characterized using a combination of multiplex PCR, RH-specific exon sequencing, Real-time PCR allelic discrimination and polymerase chain reaction-restriction fragment length polymorphism.

Results: High-resolution analysis of RHD and RHCE revealed that 16 of the 53 samples carried variant alleles, either for RHCE or RHD or for both. Of these 16 samples, 14 carried at least one of the following RHCE variant allelesRHCE*ce48C; RHCE*-ce48C, 1025T; RHCE*ce48C,733G; RHCE*ce48C,105T,733G; RHCE*ce254C; RHCE*-ce733G and RHCE*Ce122G; and 9 carried at least one of the following RHD variant allelesRHD*DIVa; RHD*DAU-0; RHD*DAU-5; RHD*DHMi; RHD*DIIIa and RHD*ψ. The remaining 37 samples carried conventional RHCE alleles (Ce, cE or ce) along with either conventional hemizygous or homozygous RHD or deleted RHD.

Summary/Conclusions: Comprehensive characterization of the RH locus on 53 donor samples resulted in the identification of 16 samples carrying RH variant alleles of potential interest to be included as a member of a panel for RH variant genotyping. We plan to perform collaborative studies to characterize the first RH variant panel and continue to screen for additional RH variants to be included in this panel.

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GENOTYPING PANEL DESIGNED TO IDENTIFY BLOOD DONORS LACKING HIGH PREVALENCE RH ANTIGENS

MA Keller, J Keller, D Thomas and T Horn

National Molecular Laboratory, American Red Cross, Philadelphia, United States

Background: Rh alloimmunization in patients with sickle cell disease can lead to challenges finding compatible blood donors. Rh variant antigen expression is common in individuals of African descent. In patients with anti-hr^B or anti-hr^S, insufficient decrease in sickle hemoglobin (HbS) % after exchange transfusion, hemolytic transfusion reactions and/or monocyte monolayer assay incompatibility has been reported. Such patients may benefit from RH allele-matched donors for transfusion. RH allele matching describes the process of selecting blood donors based on the RHCE and RHD alleles of the patient, using a tiered system (Keller MA et al. Transfusion 2013; 53(2S):174A).

Aims: Our blood center has routinely used RBC genotyping to screen blood donors since 2009. More than 160,000 donors have been screened since 2011. We recently developed an RHCE genotyping panel that utilizes multiplex dideoxynucleotide extension and analysis on the MassARRAY (Agena BioSciences). The assay includes markers that allow prediction of not only V, VS, hr^B and hr^S antigens but also STEM, JAL, CELO and CEAG. Donors were chosen based on the RHCE genotype results of the HemoID DQS genotyping panel (Agena BioSciences). The results of testing more than 900 donors is presented.

Methods: Genomic DNA was cherry-picked from 96-well plates tested by HemoID DQS using a QIAgility (QIAGEN). Donors who were predicted to be E- K- HbS negative and hr^B+^{vw}/- or negative or hr^S negative or E-e+^{weak} were tested. The genotyping panel tests for RHCE c.48G/C, c.254C/G, c.340C/T, c.667G/T, c.712A/G, c.733C/G, c.818C/T, c.916A/G, c.1006G/T, c.1025C/T.

Results: Of 10,948 donors tested by HemoID DQS, 926 (8.5%) were selected for additional RHCE genotyping. Of these, 290 (31.3%) were predicted to be hr^B+^{vw} due to the RHCE*ce733G allele, 31 (3.3%) were predicted to be hr^B- with 5 of these homozygous for RHCE*ce48C,733G,1006T. Only 5 (0.5%) of donors tested were predicted to be hr^S negative, being heterozygous for RHCE*ceMO and RHCE*ceAR. Eighty (8.6%) donors tested were C- with one or two copies of a RHCE*ceTI allele, associated with cross-reactivity with some anti-C reagents. Seventeen (1.8%) donors had weakened V antigen expression associated with the RHCE*ceAR allele. A small number of donors expressed low prevalence antigens STEM or JAL (0.3% each). Nearly half of donors tested (48.1%) were RHCE*ce48C homozygotes associated with partial e antigen expression.

Summary/Conclusions: An algorithm has been developed to select a subset of donors for testing on an in-house developed RHCE genotyping panel. RH genotyped donors were assigned RHCE alleles and their hr^B, hr^S, V and VS status can be definitively predicted. The frequency of E- hr^S- donors in this cohort of donors selected based on RH variants was very low, highlighting the difficulty in identifying such donors.

Approximately 50% of donors tested are candidates for the American Rare Donor Program. The selection of donors based on RHCE markers in an RBC genotyping panel and HbS status paired with a custom genotyping panel focused on e variants is useful at identifying rare donors for RH allele matching with Rh alloimmunized patients.

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SEROLOGICAL AND MOLECULAR CHARACTERIZATION OF RHD VARIANTS

S Manfroi[1], A De Filippo[1], S Pergolizzi[2], L Righini[1] and V Randi[2]

[1]Immunohematology and Transfusion Service Metropolitan Area of Bologna, S.Orsola-Malpighi Polyclinic [2]Immunohematology and Transfusion Service Metropolitan Area of Bologna, Maggiore Hospital, Bologna, Italy

Background: The characterization of RhD variants is essential both in blood donors and in patients, for adequate blood supply and appropriate use of anti-D immunoglobulin. Monoclonal anti-D reagents can help to differentiate between weak or partial RhD, but they rarely identify the specific RhD variant. Molecular techniques can resolve the major part of serological discrepancies and diagnose RhD variants at risk of immunization.
Aims: To evaluate the advantages of monoclonal anti-epitopes antisera and molecular methods in RhD variants investigation; to define a diagnostic algorithm as a guide for RhD variants characterization.
Methods: RhD variant results of 186 samples, analysed by serological [Extended Partial RhD Typing Set (Diamed, Switzerland); Advanced Partial RhD Typing Kit (Quotient, Alba Bioscience, USA)] and molecular [PCR-SSP D weak, PCR-SSP CDE, PCR-SSP DaddOn (Innotrain, Germany); PCR-SSP RH-TYPE (BAGene, Germany) e IDRHDXT (Progenika-Grifols, Spain)] methods, were retrospectively reviewed. Sensitivity and concordance between monoclonal panels and molecular typing results were evaluated on 104 evaluable samples. To overcome the small number of samples, an indicator of RhD variant concord was calculated for each test and named specific/generic ratio (=numbers of RhD variant specific results/ numbers of RhD variant generic results).
Results: Overall, Extended Partial RhD Typing Set had a 62.2% sensitivity rate for RhD variant (100% for partial RhD vs 49% for weak RhD) and a 35.1% specific/generic ratio (46.2% for partial RhD vs 16.7% for weak RhD). Advanced Partial RhD Typing Kit had a higher sensitivity both in partial and weak RhD variants (100% vs 95.2%) and a specific/generic ratio of 80% and 77.4% respectively.
PCR-SSP kits had the highest sensitivity in their own RhD variant group (100% in weak RhD and 78.3% in partial RhD, respectively), the overall specific/generic ratio was 100%. Sensitivity and specific/generic ratio of IDRHDXT were 100%.
Summary/Conclusions: As expected, monoclonal anti-epitopes panels had the better performance in the identification of RhD variants with amino acid changes outside of the membrane; however, the Advanced Partial RhD Typing Kit had the higher concordance with molecular results and a good sensitivity in weak D type 1 and 2 identification. Molecular typing results were conclusive and congruent with serological results in all cases, with the exception of 18 samples with unknown or not yet identified RhD variants. Even if serological RhD variants should be confirmed by molecular analysis, the early phase of serological analysis with monoclonal antibody panel allows to direct the following molecular characterization, especially to identify or exclude RhD variants (weak D types 1–3) that would be treated as RhD+ for transfusion and anti-D immunoglobulin administration. The results were used to define a diagnostic algorithm for RhD variant characterization (by serological and molecular methods) targeted on clinical context (urgent, routine, donor, patient, pregnancy).

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MOLECULAR CARACTERIZATION OF RHD GENE IN PATIENTS AND DONORS: TEN YEARS EXPERIENCE OF LOMBARDY IMMUNOHEMATOLOGY REFERENCE LABORATORY

C Paccapelo, G Spaltro, F Truglio, M Cosco, V Iemmolo, N Revelli, A Villa and D Prati

Immunohemathology Reference Laboratory, U.O.C. Centro Trasfusionale, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Milan, Italy

Background: The Rh antigens are encoded by two highly homologous genes, RHD and RHCE. The D antigen is the most clinically significant antigen of the Rh blood group system. Its extreme immunogenicity makes it one of the most important

antigen in transfusion medicine and pregnancy. A number of RHD alleles which are associated with weak D, partial D or D$_{el}$ phenotype have been identified. Among European subjects, about 0.2% to 1% carry aberrant RHD alleles. Serology cannot discriminate some of these alleles from normal D antigen and mistyping of these individuals may potentially lead to anti-D alloimmunization.
Aims: We reviewed the RHD alleles identified in individuals with weak D or VS+V+ by HEA BeadChip™ kit referred to Lombardy Immunohematology Reference Laboratory starting from 2007.
Methods: Genomic DNA was isolated from whole blood using the QIAamp DNA Blood Kit (QIAGEN, Germany) and the RHD genotype determined by RHD BeadChip™ kits (Immucor-BioArray Solution, Warren NJ, USA) and PCR-SSP kits (Weak D-TYPE, Partial D-TYPE BAGene, Germany; RBC-Ready Gene CDE, RBC-Ready Gene D weak Inno-Train, Germany).
Results: Out of 449 individuals analyzed, 192 were patients and 257 blood donors. RHD*weak D type 1 was identified in 46.1% (patients: 50.5%, n = 97; donors: 42.8%, n = 110). This allele, cumulatively with others RHD alleles causing a weak D phenotype not at risk of alloimmunization, RHD*weak D type 2 (patients: 8.33%, n = 16; donors: 3.11%, n = 8) and RHD*weak D type 3 (patients: 8.33%, n = 16; donors: 9.73%, n = 25), represent 60.6% of all aberrant RHD identified. We also identified many allelic variants that may cause anti-D immunization. Interestingly RHD*weak D type 11 that cause D$_{el}$ phenotype represented 10.24%, n = 46 (patients: 13.54%, n = 26; donors: 7.78%, n = 20) of all our cohort. Other RHD allelic variant arising a weak phenotype were: RHD*weak D type 4 (total: 8.69%, n = 39; patients: 4.17%, n = 8; donors: 12.06%, n = 31), RHD*weak D type 4.2 (total: 2.45%, n = 11; patients: 1.04%, n = 2; donors: 3.5%, n = 9), RHD*weak D type 5 (total: 3.12%, n = 14; patients: 4.17%, n = 8; donors: 2.33%, n = 6), RHD*weak D type 14 (donor: 0.22%, n = 1), RHD*weak D type 15 (total 0.45%; n = 1 patient; n = 1 donor). The DAU cluster was found in 7.13%, n = 32 of our cohort, but RHD*DAU0 is the most represented especially within our African donor population (total: 6.24%, n = 28; patients: 2.6%, n = 5; donors: 8.95%, n = 23). Other RHD partial alleles cumulatively concurred to 6.90% n = 31 within the total population (RHD*DIIIa, RHD*DIVa; RHD*DIV type3; RHD*DV or RHD*DBS; RHD*DVI RHD*DVII RHD*DHMi, RHD*DNB, RHD*DFR).
Summary/Conclusions: RHD genotype showed that RHD*weak D type 1 was the most frequent allele in our population in accordance with the results of frequency of weak D antigen in other European countries. According to transfusion clinical practice, the subjects carrying weak D Types 1, 2 and 3 are not at risk of anti-D alloimmunization, and in our patients population they represent 67.19%, n = 129. However, patients carrying aberrant RHD alleles are more than 30% and they have to be managed carefully for transfusion or during pregnancy.

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RHD AND RHCE ALLELES IN BRAZILIAN SICKLE CELL DISEASE PATIENTS WITH UNEXPLAINED RH ANTIBODIES

CL Dinardo[1], S Kelly[2], S Castilho[3], L Schimidt[4], M Oliveira[5], M Dezan[1], I Ribeiro[1], B Custer[6], E Sabino[7] and C Westhoff[8]

[1]Immunohematology, Fundação Pró-Sangue, São Paulo, Brazil [2]Blood Systems Research Institute, San Francisco, United States [3]Immunohematology, Fundação Hemorio, Rio de Janeiro [4]Immunohematology, Fundação Hemominas, Belo Horizonte [5]Immunohematology, Fundação Hemope, Recife [6]Blood Systems Research Institute, San Francisco [7]Institute of Tropical Medicine University of São Paulo, São Paulo, Brazil [8]New York Blood Center, New York, United States

Background: The RH system is complex and diverse RHD and RHCE alleles have been described primarily in populations of African descent, including patients with sickle cell disease (SCD) from Africa, Europe and the Americas. Studies evaluating RH variation in SCD patients from racially diverse populations, as well as the incidence of unexplained Rh antibodies, are incomplete.
Aims: To describe RH variation among SCD patients of mixed race with unexpected Rh-antibodies enrolled in the Recipient Evaluation and Donor Study (REDS)-III Brazil SCD cohort.
Methods: A large SCD cohort was established in six Brazilian cities (São Paulo, Rio de Janeiro, Recife, Belo Horizonte, Juiz de Fora, and Montes Claros). All patients with unexplained Rh antibodies (RBCs type antigen positive but patients have the corresponding antibody identified following transfusion) were RHD and RHCE genotyped by targeted next generation sequencing (NGS) using Ion Torrent platform.
Results: There were 2795 SCD patients enrolled between 2013–2015, including 1638 (58.7%) self-reported mixed race, 748 (26.8%) black, 299 (10.7%) white and 110 (3.9%) unknown/other. At time of enrollment, 367 were alloimmunized; 54 (14.7% of 367) had 66 unexplained Rh antibodies (39 anti-e, 12 anti-D, 12 anti-C, 2

anti-E and 1 anti-c) and were subjected to RH NGS sequencing. We identified 19/108 (17.6%) variant RHD and 40/108 (37%) variant RHCE. The most frequent altered RHD were RHD*DIIIa-CE(4–7)-D (n = 4) and RHD*Ψ (n = 2) encoding D-negative phenotypes, and RHD*DAR (n = 4) and DIIIa (n = 2) encoding D-partial phenotypes. Less frequently detected RHD alleles included RHD*DAU0, RHD*DIVa, RHD*DUC2, RHD*DVII, RHD*541T and RHD*DAU3 (1 case each).

RHCE*ce48C, encoding weak e; RHCE*ce733G, encoding partial c and e and RHD*ceS, encoding partial c, partial e and hrB- were the most prevalent variant RHCE alleles (n = 14, 7 and 5, respectively). In addition, we detected RHCE*48C,733G (n = 4); RHCE*ceAR (n = 2); RHCE*ceAG (n = 2); RHCE*ceTI (n = 2); RHCE*ce48C,733G,1006T (n = 1); RHCE*ceMO (n = 1); RHCE*Ce122G (n = 1) and RHCE*Ce733G (n = 1). RHCE allele distribution was homogeneous among the different centers, but the specific RHD variant alleles differed throughout the country. All RHD*DAR were concentrated in the Northeast, comprising 80% of RHD variants detected. Variants of the DAU cluster, common in other African cohorts of patients with SCD, were only observed in Rio de Janeiro and Montes Claros. One novel allele was identified: RHD*225T in trans to a wild-type RHD. A high percentage of conventional RHCE*Ce encoding conventional C+ phenotypes was found with an overall allele frequency of 24.6%. The highest frequency of the DCe haplotype was observed in the Northeast (frequency of 30.7%).

Summary/Conclusions: RHD*DAR, RHD*DIIIa, RHCE*ce48C, RHCE*ce733G and RHCE*ceS are the most prevalent RH alleles encoding variant antigens among SCD patients from a diverse Brazilian population whose RBCs type serologically D+ or e+, but exhibiting Rh antibodies with the same specificity. In contrast to African-American and African-Caribbean patients, the DAU cluster is underrepresented and the frequency of the DCe haplotype is higher; 24.6% in Brazil versus 12% in the others. These differences likely reflect the significant population admixture in Brazil and may account for the lower reported alloimmunization rates and have significance for antigen matching in these patients.

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RHD ALLELE HETEROGENEITY AMONG INDIGENOUS PEOPLES IN NORTHERN CANADA

G Denomme[1,2], W Flegel[3], K Bensing[1], T Lijewski[1] and J Hannon[4]

[1]Immunohematology Reference Laboratory [2]Blood Research Institute, Versiti/Blood Center of Wisconsin, Milwaukee [3]Department of Transfusion Medicine, NIH, Clinical Center, Bethesda, United States [4]Canadian Blood Services, Edmonton, Edmonton, Canada

Background: Rh D antigen status is routinely performed to select appropriate blood products for transfusion recipients and to provide Rh immune globulin appropriately in pregnancy. The current approach to Rh D antigen phenotyping is based on data that originated from information on people of European ancestry. Data has been collected on persons of African ancestry with some data beginning to be collated on other ethnic groups. Little is known about RHD diversity for the Indigenous peoples in Northern Canada, which represents a distinct population comprising 4.3% of Canadians. Evaluating the RHD alleles present among Indigenous peoples in Northern Canada would validate the phenotyping reagents used to determine transfusion practice and the administration of Rh immune globulin for this patient population.

Aims: The purpose of this study was to characterize the RHD alleles present among the Indigenous peoples in Northern Canada.

Methods: The study was approved by the Aurora Research Institute, NWT and the Canadian Blood Services research ethics boards. Pregnant women in Northern Canada who self-identified as an Indigenous person provided informed consent to participate in the study. Rh D, C, E, c, e phenotyping was collected from manual testing. Residual blood from EDTA anticoagulated samples were used to obtain genomic DNA and to sequence RHD exons by a Sanger dideoxy method using the BigDye Terminator v3.1 Cycle Sequencing Kit with complementary M13 primers. The results were aligned to RHD_NG_007494.1 using SeqScape software.

Results: A total of 74 samples (73 RhD+ and 1 RhD-) were submitted to the study. Complete RHD exon sequence data was obtained on 63 of 74 samples; No RHD exons were amplified for 1 Rh D-negative sample, 10 samples failed to amplify all RHD exons; none were consistent with known hybrid RHD/RHCE alleles. Exon and flanking intron nucleotide polymorphisms at positions c.8, c.149-131, c.149-129, c.801 + 85, c.809, c.1154-30, and c.1187 confirmed 2 copies of RHD for 23 samples. Three different weak D type alleles were observed: one of each weak D type 1 (CDe/CDe), weak D type 3 (CDe/cde) and weak D type 91 (CDe/cDE). The combined nucleotide polymorphisms detected 9 alleles: RHD consensus; RHD*01W.1; RHD*01W.3; RHD*01W.91; RHD*c.149-131t,-129c; RHD*c.149-129c; RHD*c.149-

129c, c.1154-30c; RHD*c.149-129c, c.801 + 85t or RHD*c.801 + 85t, c1154-30c; RHD*c.1154-30c.

Summary/Conclusions: At least 106 alleles are present among the 74 samples submitted for analysis. RHD alleles among Indigenous peoples in Northern Canada reflect those weak D types observed in other ethnicities. Notably, there was a paucity of partial D alleles, although failed exon amplifications may be an indication of hybrid RHD/RHCE alleles or additional intronic nucleotide polymorphisms affecting PCR amplification.

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THE MOLECULAR GENETIC VARIABILITY OF THE RH BLOOD GROUP SYSTEM FOUND AMONGST BLOOD DONORS AT THE SOUTH AFRICAN NATIONAL BLOOD SERVICES (SANBS)

L Govender[1], K Vather[2] and U Jentsch[2]

[1]Specialised Laboratory Services, South African National Blood Services, Durban
[2]Specialised Laboratory Services, South African National Blood Services, Constantia Kloof, South Africa

Background: Identification of the genes that code for red cell antigens using molecular genotyping methods was first introduced at the South African National Blood Service (SANBS) in late 2014. Prior to this limited red cell genotyping data existed for SANBS blood donors. This study was the first to describe the Rh genetic variability based on red cell genotyping amongst a subset of SANBS blood donors which will assist sourcing antigen negative or rare blood units for transfusion thus preventing cases of Haemolytic Disease of the Newborn (HDN) or transfusion reactions.

Aims: To describe the unique genetic variability of the Rh blood group system in a subset of South African blood donors.

Methods: Red cell genotyping of randomly selected donors was performed using the IDCORE[XT] assay on the Luminex 200IS instrument from January 2015 to August 2016. A retrospective comparative data analysis of the Rh system was completed on all valid red cell genotyping results. Indian and Coloured donors were excluded due to inadequate representation. Demographic information, serological phenotypes and red cell genotyping results were collated on a Business Intelligence IT database and reported.

Results: Of the 236 donors, 59% were males and the majority were White donors (58%, n = 136). There were more Rh positive donors 85% (n = 203) than Rh negative donors 15% (n = 42). Amongst 203 Rh positive genotypes, the distribution between Black (B) and White (W) donors were as follows: 73B:17W had RHCE*ce/ce (R₀), 14B:20W had RHCE*cE,*ce (R2r), 7B:11W had RHCE*cE,*cE (R2R2), 6B:26W had RHCE*Ce,*ce (R1r), 0B:16W had RHCE*Ce,*Ce (R1R1) and 0B:13W had RHCE*Ce,cE (R1R2). The rare RHCE*ceAR, RHCE*ce[712G] (hrS-) and RHCE*ce [733G,1006T], RHD*r's-RHCE*ce[733G,1006T] (hrB, Rh:-34) genotypes were found in 4 and 2 R₀ Black donors respectively. In comparison the Rh negative genotypes were most prevalent amongst White donors (n = 33) and distributed as follows: 25 RHCE*ce,*ce (rr), 4 RHCE*cE,*ce (r″r), 2 RHCE*Ce/cE (r′r″), 1 RHCE*Ce/*ce (r′r) and 1 RHCE*Ce/Ce (r′r′). There were only 3 Rh negative Black donors of which all 3 had the rare genotype RHCE*ce[733G,1006T], RHD*r's-RHCE*ce[733G,1006T] (rr, hrB-) phenotype.

Summary/Conclusions: Due to the high costs of the red cell genotyping assay compared to serology, only data for 236 donors were available. However genotyping based on molecular methods is critical as it overcomes the limitations of serological methods. Our analysis showed the main Rh genotypic variability between the White and Black donors to be the higher prevalence of RHCE*ce,*ce genotype in Rh positive Black donors. The Rh negative genotypes are more prevalent amongst White donors. Only Black donors displayed the r's haplotype associated with hrB- or RHCE*ceAR associated with hrS-. There were further clear associations of rare blood types to specific Rh subgroups. Based on the outcomes of this study, focused screening by molecular methods was implemented when searching for specific rare blood types. While the Rh system rare blood types are similar to those found amongst countries on the International Rare Donor Programme (IRDP), South Africa does have a larger pool of hrS- and hrB- donors having been first discovered amongst Black South Africans.

MOLECULAR TESTING OF SEROLOGIC RHD DISCREPANT FEMALES WITHIN CHILDBEARING AGE –A FACILITY'S EXPERIENCE

L Wlosinski and I Lopez-Plaza

Transfusion Medicine, Henry Ford Health System, Detroit, Michigan, United States of America

Background: The Rh system is very complex, and follows the ABO system in immunogenicity. The RhD protein is very multifaceted, and depending on a person's genetics, the way in which the RhD antigen is expressed on the red blood cell (RBC) membrane can vary. From this variation, patients can be classified as having a weak expression of the D antigen (formally Du) through serologic testing. Weak reactions with Anti-D can also be caused by a variant (part of the antigen is missing) RhD. Serologic testing, mostly automated, are available to help detect potential RhD discrepancies in patients. Automated testing using two different clones of monoclonal Anti-D reagent provide the ability to detect discrepancies in RhD patient samples. However, only molecular testing can differentiate the RHD gene as being fully expressed or having a variant expression.

Serologically detected RhD discrepancies pose the most concern for women of child bearing age (<50 years old). Depending on the RHD variant identified, these women have the potential to develop Anti-D if exposed to the RhD antigen during pregnancy. This facility developed a pilot program to identify the genetic RHD status of qualifying RhD discrepant patients. Determining the RHD status of women <50 years old will aid in accurately conserving Rh-negative RBCs and allow for the proper administration of RhIg prophylaxis in this patient population.

Aims: Identify women of child bearing age at risk of developing Anti-D due to the present of a variant RHD gene.

Methods: Beginning January 2015, patient samples showing inconclusive results with Anti-D through automated testing are subject to manual serologic investigation via tube testing. Patients who qualified for manual analysis had their RBCs tested with the Anti-D monoclonal reagent validated for tube testing: A) Women <50 years old with manual reactions of ≥2+ had samples sent for molecular RHD determination. Until results are known, these patients are classified as Rh-negative and will receive Rh-negative RBCs and will be candidates for RhIg prophylaxis evaluation; B) Women >50 years old and all men with manual reactions ≥2+ will be classified as Rh-positive and receive Rh-positive RBCs; C) All patients with manual reactions <2+ will be classified as Rh-negative and receive Rh-negative RBCs. Molecular testing results were interpreted for patient support as per molecular laboratory recommendations.

Results: As of February 2018, there have been 97 female patients of child bearing age evaluated for RhD testing discrepancy. Seven patients were classified as Rh-negative by manual serological testing. Molecular testing was performed on 90 patients: of which, 8 patients were identified as Rh-positive with no variant, and variant RHD was identified in 82 patients. Variant RHD was identified in 91% of qualified patient samples.

Summary/Conclusions: Serologic RhD discrepancies via automated methods is a good predictor for the presence of variant RHD, recommending follow-up and confirmation with molecular testing.

PREVALENCE OF D VARIANTS AMONG RHD NEGATIVE C/E+ BLOOD DONORS IN MOROCCO IN COMPARISON WITH OTHER ETHNIC GROUPS

H El Housse[1], M El Wafi[1], Z Ouabdelmoumene[1], F Zarati[2], N Nourichafi[2], K Bouisk[2], M Benajiba[3] and N Habti[1,3]

[1]laboratory of Hematology and Cellular and Genetic Engineering, faculty of medicine and pharmacy –Casablanca, Hassan II university [2]Regional blood transfusion center, Casablanca [3]National blood transfusion center, Rabat, Morocco

Background: The D antigen is the most immunogenic antigen in the Rh system. Determination of D variants is of critical importance in the field of both transfusion and obstetric medicine. Transfused D negative patients with RBCs carrying these variants may develop alloantibodies against the D antigen. The frequency of D variants varies significantly among different ethnic populations. However, D variants are more frequent among subjects D negative RhC and/or RhE positive.

Aims: The aim of this study is to evaluate the frequency of D variants in morocco and to compare it with data of other ethnic groups.

Methods: Blood samples with EDTA anticoagulant were collected from 544 blood donors phenotyped RhD negative using an automated analyzer (Olympus PK 7300,

Japan) in Regional Blood Transfusion Center of Casablanca. Collected blood samples were rephenotyped in our laboratory. Rhesus antigens (C, E, c and e) were determined using standard tube method and monoclonal according to the manufacturer's instructions (Diagast, France). Blood donors typed as RhC and/or RhE positive were tested for weak D using papain test, indirect antiglobulin test and adsorption elution technique with anti-D blend IgG and IgM (Fortress Diagnostics, UK). DNA of Samples positives with weak D tests were tested by multiplex PCR covering exons 3, 4, 5, 6, 7, 9 and 10.

Results: The results of sensitive serological tests showed that 12.7% blood donors were RhD+ of which 4 D type Del. PCR Multiplex revealed 9.5% of partial D variants and 3.1% of which is not determined. The frequency of RHD + in RHD-C/E + varies from one ethnic group to another, it is low in Europe (0.53%), similar within Germany (1.53%) and Denmark (1.71%) and higher in Tunisian population (8.89%).

Summary/Conclusions: The distribution of D variants among different races shows different findings. This has clinical significance in transfusion medicine and in hemolytic disease of fetus and newborn [HDFN].

Abstract has been withdrawn

ASSOCIATION BETWEEN THE RHD*01N.01 ALLELE AND A NEW RHCE*CEEK ALLELE WHICH DOES NOT HARBOR THE C.48 G>C NUCLEOTIDE CHANGE

M Deleers[1], V Thonier[2], V Claes[3], C Daelemans[4], T Peyrard[2] and H El Kenz[1]

[1]Department of Transfusion, LHUB-ULB, CHU Brugmann, Brussels, Belgium [2]Institut National de la Transfusion Sanguine (INTS), Centre National de Référence pour les Groupes Sanguins (CNRGS), Paris, France [3]Department of Transfusion, LHUB-ULB, Hôpital Erasme [4]Department of Obstetrics and Gynaecology, Hôpital Erasme, Brussels, Belgium

Background: The RHCE*ceEK allele (RHCE*01.05.01) is defined by 4 single nucleotide substitutions: c.48 G>C, c.712 A>G, c.787 A>G and c.800 T>A. When present at the homozygous state, it encodes the rare Hr- blood group (RH:-18). This allele is mostly encountered in people of African descent. Three other RHCE alleles have also been associated with the Hr- phenotype: RHCE*ceAR, RHCE*ceBI and RHCE*ceSM. Homozygous or compound heterozygous individuals could develop an anti-Hr (anti-RH18) which has been responsible for hemolytic transfusion reactions and hemolytic disease of the fetus and newborn. Until now, the RHCE*ceEK allele has only been reported to segregate with either RHD*01N.01, RHD*DAR1.02, RHD*DAR1.03 or RHD*DOL2.

Aims: To report a new RHCE*ceEK allele without the c.48 G>C which is linked to the RHD*01N01 allele.

Methods: ABO, Rh and Kell typing were performed with monoclonal reagents in two techniques: column-agglutination (Bio-Rad) and solid phase (Immucor). Antibodies identification was done using IAT-IgG on untreated, papain treated and trypsin treated RBCs. The Hr phenotype was determined with in-house reagents. RHD and RHCE genotyping were run with the RHD, RHCE Beadchip kits (BioArray Solutions, Immucor) or in house real-time PCR techniques.

Results: The phenotype of the patient (a 32-year-old tutsi pregnant woman) was group B, D+C-E-c+e+ with no weakened reactions. Her antibody identification showed a complex mixture of anti-E, anti-c, anti-Hr and anti-hr[S]. Genomic testing found this patient to be homozygous or hemizygous for RHD*01 and homozygous for RHCE*ceEK (c.712 A>G homozygous but c.48 G>C heterozygous). The patient was phenotyped as Hr-. At birth, her newborn was phenotyped as group B, D-C-E-c+e+. No signal was obtained on the RHD Beadchip kit concluding her genotype to be RHD*01N.01/RHD*01N.01. The molecular analysis of the RHCE gene was consistent with a RHCE*ceEK allele at the heterozygous state (c.712 A>G heterozygous but without the c.48 G>C nucleotide change).

Summary/Conclusions: According to the RHCE genotyping of the mother, it is likely that she harbors a conventional RHCE*ceEK and a new RHCE*ceEK allele that lacks the c.48 G>C nucleotide change. The molecular work performed on the newborn is proof of this new allele and its linkage with a RHD*01N.01 allele. This point is also interesting because the vast majority of RHCE*ceEK are defined as a haplotype with one of the following alleles RHD*DAR1.02 or RHD*DAR1.03. This family has to be investigated in more details because the results from the mother also

suggest a linkage between a RHCE*ceEK and a normal RHD gene, a situation which has never been described.

P-563

TWO NOVEL PARTIAL D ANTIGENS, CHARACTERIZED BY SINGLE MISSENSE NONTEMPLATED MUTATIONS CAUSING A SIGNIFICANT IMPACT ON RHD PROTEIN TERTIAL STRUCTURE AND D EPITOPES EXPRESSION

M Pisacka[1], J Kralova[1], K Fennell[2], R Hoffman[2], S Schneider[3] and Ž Sovová[4]

[1]Reference Laboratory for Immunohaematology, Institute of Haematology and Blood Transfusion, Prague 2, Czech Republic [2]Molecular Laboratory, Grifols Immunohematology Center, San Marcos, Texas, United States of america [3]Inno-train Diagnostik GmbH, Kronberg, Germany [4]Biochemistry Department, Institute of Haematology and Blood Transfusion, Prague 2, Czech Republic

Background: The clinically important D antigen of the Rh system is encoded by the RHD gene, which is one of most polymorphic blood group genes in humans with still increasing number of known allelic variations (to date around 500). These alleles encode the amino acid sequence of the primary structure, which is then folded and organized into secondary and tertiary structures of final RhD protein. Gene variations – point mutations and gene conversions – influence the RhD protein incorporation into the Rh complex of the red blood cell (RBC) membrane and its normal or altered exofacial expression. Monoclonal anti-D antibodies recognize multiple epitopes on the surface of the D antigen. Individuals with lack of one or more epitopes are referred to partial D antigen and can produce allo-anti-D. Amino acid changes in partial D antigens are usually located in six exofacial loops of the polypeptide chain and in the extracellular part of the RhD protein vestibule with several exceptions when the critical amino acid residue is located in one of twelve transmembranous segments and influence through the general protein conformation the expression of exofacial epitope(s).

Aims: Investigation was prompted by finding RBCs with suspect partial D antigens in two Czech pregnant women (serology testing revealed clearcut significant loss of D epitopes) with no explanatory results of conventional genotyping assays. RHD sequences were then determined from genomic DNA and D epitope patterns were studied with commercial and workshop anti-D panels and compared to other mutations in the same region.

Methods: Serology testing was done by column agglutination (Biorad Neutral/IgM/ and Cooms /IgG/) using monoclonal anti-D antibodies (Partial D kit Biorad, D_Screen kit Diagast, Nantes and Paris MoAb workshops). Routine Partial and Weak D genotyping was performed by PCR-SSP (Inno-train: FluoGene), sequencing in Inno-train and Grifols IH Center. Homology modeling was performed in Modeller using crystal structure 3HD6 (human rhesus glycoprotein RhCG) as a template. The best of 10 models was chosen according to its stereochemical properties determined with Procheck.

Results: Routine RhD typing showed weakened D expression in conventional ABO RhD gel cards and R1r phenotype in both cases. Commercial Partial D kit (6 anti-D) revealed patterns not fitting for known D variants (3+ reactions vs. one negative in the first and three negatives in second case). Commercial PCR-SSP kits for Partial D and for Weak D provided normal result (no variant detection). Sequencing found so far not reported mutations with predicted amino acid changes in the RhD protein vestibule in one case (683T>C coding the Leu228Pro substitution, proposed name RHD(L228P)) and deep in the twelfth transmembranous helix in the other (1105G>A coding Gly368Lys substitution, proposed name RHD(G368K)). Epitope mapping found in D228P lacking D-Eps 1.2, 5.1, 5.3, 6.6, 8.2, 8.3 and 11.1 and sub-splitting D-Eps 1.1, 5.4, 6.3 and 8.1; in D368K lacking D-Eps 1.2, 2.2, 5.1, 5.3, 6.5, 6.6, 6.7, 8.2, 8.3 and 11.1 and sub-splitting D-Eps 5.4, 6.1, 6.3, 6.4 and 8.1.

Summary/Conclusions: Two novel mutations causing partial D phenotype are interesting from the point of view their impact on known D epitopes. The amino acid substitution in RHD(L228P) is located in the D protein vestibular part and allow to compare the effect of neighbouring amino acid substitutions on D epitopes expression. The variant RHD(G368K) is predicted to have substitution in last transmembranous part of the D protein but affect substantially the exofacial epitopes expression.

P-564

Abstract has been withdrawn

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A NEW RHD VARIANT ALLELE (RHD G339V) SHOWS WEAKENED D EXPRESSION COMPARED TO RHD G339E AND G339R MUTANTS

S Chun[1], S Choi[2], Y Lim[3], H Koo[4] and D Cho[2]

[1]Laboratory Medicine, Chonnam National University Medical School, Gwangju [2]Laboratory Medicine, Samsung Medical Center, Seoul [3]Pediatrics, Pusan National University Children's Hospital, Yangsan [4]Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: We report a new RHD variant allele (RHD 1016G>T, G339V) that was discovered in a Korean male hepatocellular carcinoma patient, performed an epitope mapping of the D-antigen, and analyzed the expected effect of this variation with comparison to two other D-weak expressing variants with amino acid change in the same position.

Aims: To identify a novel RHD variant and its effect on the expression of D-antigens, including epitope expression.

Methods: Serologic testing of the D antigen was done and all ten RHD exons were sequenced to full length. Epitope mapping was studied on 9 sites of the D antigen, and its epitope expression was examined.

Results: RHD 1016G>T (G339V) was observed to have no reaction on routine D testing and weak D tests. Further evaluation with multiple clones of anti-D reagents (Anti-D TOTEM, Diagast, Loos, France) showed positive to a fraction of the tested reagents. In silico analysis with methods provided by SDM - a server for predicting effects of mutations on protein stability and malfunction was done in comparison with other variants that resulted in amino acid change at position a.339 (weak D type 7; G339E and weak D type 39; G339R). We suspect the intensity of D antigen of new allele found in this report was the weakest, followed by type 39 and type 7. Although the antigen strength of type 39 and type 7 cannot be compared parallel, both report as 'weak D', while G339V observed in our case only showed trace of reactivity in weak D testing, suggesting that in silico analysis is in concordance with actual phenotypic results.

Summary/Conclusions: We have discovered a novel variation with amino acid change within the transmembrane region of the RHD-protein. Identification of the location of the single nucleotide variation predicting the intensity of D antigen expression by in silico analysis can be helpful in predicting the characteristics of the changed RHD-protein.

P-566

Abstract has been withdrawn

P-567

RHD GENOTYPING IS SUITABLE FOR ALL PATIENTS WITH WEAKENED D PHENOTYPES – A CASE WITH COEXISTENCE OF WEAK D AND ASIA TYPE DEL ALLELES RESULTING IN COMPLETE EXPRESSION OF D-ANTIGEN

S Chun[1], S Choi[2], Y Lim[3], H Koo[4] and D Cho[2]

[1]Laboratory Medicine, Chonnam National University Medical School, Gwangju [2]Laboratory Medicine, Samsung Medical Center, Seoul [3]Pediatrics, Pusan National University Children's Hospital, Yangsan [4]Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Background

We have recently experienced a case with coexistence of a weak D type 25 (RHD 341G>A) allele and an Asia type DEL (RHD 1227G>A) allele, and revealed that the D-epitope expression of these individuals can suggest the possibility for D-positive blood transfusion in such individuals.

Aims: To identify the effect of the coexistence of an Asia type DEL allele with a weak D allele with serologic studies targeted on various epitopes of the D antigen.

Methods: Serologic testing of the D antigen was done and all ten RHD exons were sequenced to full length. Epitope mapping was studied on 9 sites of the D antigen, and its epitope expression was examined.

Results: Blood grouping was done by manual tube methods with two anti-D reagents. Routine D testing showed negative, and weak D testing with indirect antiglobulin test (IAT) showed 3+ positive reaction. Extended Rh phenotype was CeEe. Full sequencing of all exons and adjacent introns of the RHD gene was done. We observed heterozygous of G and A nucleotides at position 341 (NM_016124.4:

c.341G>A, weak D type 25) and 1227 (NM_016124.4:c.1227G>A, RHD*DEL1, Asia type DEL), indicating the presence of two RHD alleles. Investigation of D-antigen epitopes was done with IAT and an additional adsorption and elution study when IAT results were negative. Reagents for evaluation of epitopes was done with anti-D reagents from the D-SCREEN kit (Diagast, Loos, France). IAT results were positive to reagents targeted at epitope 2.1, 3.1, 5.4, 6.4 (identical to typical weak D type 25), and with anti-D reagents negative to IAT, adsorption and elution tests showed positive for the remaining epitopes.

Summary/Conclusions: The serologic investigation of this study is reminiscent to the epitope mapping by Guo et al, done on 154 Asia type DEL case. We suggest that RHD genotyping is to be extended to all D-variant cases in the Asian population - to detect the presence of the Asia type D allele, which can result in subjects being omitted for Rho(D) immune globulin administration, and candidates for D-positive blood transfusion.

P-568

RHCE VARIANTS DETECTED IN SAMPLES WITH WEAK AND/OR DISCREPANT RESULTS IN ROUTINE RH TYPING: A SEVEN YEAR-EXPERIENCE OF AN IMMUNOHEMATOLOGY REFERENCE LABORATORY

N Nogués, C González, N Boto, M Salgado, M Ibañez, C Canals and E Muñiz-Diaz
Immunohematology, Banc de Sang i Teixits, Barcelona, Spain

Background: Many studies have been conducted in different populations with the aim to identify RHD variants associated with altered D antigen expression. As expected, due to the similarity of RHD and RHCE genes, an increasing number of RHCE variants have also been identified when investigating weak or altered expression of RhCE antigens. However, the clinical importance of RHCE variants is less well known and most studies have focused on populations of African ancestry.

Aims: The aim of the present study was to characterize the RHCE variants present in a collection of samples referred to our Immunohematology Reference Laboratory because of weak and/or discrepant results in routine Rh typing.

Methods: During a 7 years period (2011–2017), samples with suspected RHCE variants have been comprehensively analyzed at serological and molecular level. MoAbs used for expression analysis were: Anti-C (MS24), anti-c (MS33 and H48), anti-E (MS260) and anti-e (MS21,MS63 and MS16). RHD gene exon scanning and RHCE genotyping was performed by PCR-SSP. All RHCE exons were amplified with RHCE-specific primers and sequenced.

Results: A total of 19 samples, corresponding to blood donors (n = 10) and patients (n = 9) have been studied. Among these, three samples had discrepant results in RhE typing and were identified as carrying the RHCE*cE.04 allele (RHCE*cEIV) in two cases and the RHCE*cE.01 (RHCE*cEEW) in one case. Four additional samples were studied because of discrepant results in Rhc typing, three of which were identified as carrying the RHCE*ceVS.07 (RHCE*ceJAL) variant. The RHCE*ce allele detected in the remaining sample carried the 48G>C and 733C>G changes with an additional 299A>G change in exon 2. This allele has apparently not been described yet and is associated with altered Rhc expression. Besides, two samples with weak RhC and Rhe expression have been found to carry the RHCE*Ce.25 (RHCE*Ce1007T) variant in one case, and a novel RHCe variant with a 1190-1191ATdel in exon 9, in the other case. A novel RHcE allele, carrying a microdeletion (c.-1_3delGATG) affecting the ATG start codon has also been identified in a sample with weak Rhc and RhE expression. Apart of this, three other samples carrying the rare D– phenotype were also analyzed at the molecular level. The hybrid allele RHCE(1-2)-D(3-9)-CE(10) was identified in two of these samples. The third one, though, was heterozygous and carried a silent RHCE*03N.02 (RHCE*cE907delC) allele together with an apparently normal RHCE*Ce allele. Despite further pursuing the analysis of this sample, we have not been able to identify any alterations silencing the expression of this allele. Other samples studied include blood donors (n = 4) with abnormal results in RhD typing, which ended up identified as RHCE*ceSL carriers and two clinical samples carrying the hybrid DHAR allele and the RHCE*ceCF variant, respectively, all of them known to express D epitopes in the RhCE protein.

Summary/Conclusions: The comprehensive analysis of the samples included in this study has allowed us to gain insight into the RHCE variants present in our population. Despite most of the encountered RHCE variants had already been described, some novel RHCE alleles have also been identified. Overall, the molecular alterations detected in RHCE alleles correlated well with the weak, partial or null expression of the encoded RhCE antigens. However, in one sample of D– phenotype, we could not find any alterations in an unexpressed RHCe allele, indicating there are other mechanisms involved in RHCE gene silencing not identified by the current methodology.

P-569

RHCE ALLELES DETECTED AFTER WEAK AND/OR DISCREPANT RESULTS IN AUTOMATED RH BLOOD GROUPING OF BLOOD DONORS IN MOROCCO

H El Housse[1], M El Wafi[1], Y Fichou[2], Z Ouabdelmoumene[1], F Zarati[3], N Nourichafi[3], K Bouisk[3], M Benajiba[4], C Ferec[2] and N Habti[1,4]

[1]*Laboratory of Hematology and Cellular and Genetic Engineering, faculty of medicine and pharmacy –Casablanca, Hassan II university, Casablanca, Morocco*
[2]*Etablissement Français du Sang, Bretagne, France* [3]*Regional Blood Transfusion Center, Casablanca* [4]*National Blood Transfusion Center, Rabat, Morocco*

Background: More than 170 variants (weak or partial RHD alleles) are currently known. A similar heterogeneity of RHCE alleles may be anticipated. Individuals carrying a variant are at risk to develop alloantibodies in response to mismatched pregnancy or transfusion. The prevalence of RHCE variants in Morocco remains unknown.

Aims: The aim of this study is to determine variants of RHCE allele in blood donors of regional blood transfusion center of Casablanca.

Methods: Totally 4,458 Samples from blood donors were routinely analyzed for RhCE phenotype using the Qwalys analyzer with monoclonal anti-C, -c, -E, and -e reagents. Samples with weakened and/or discrepant serologic reaction patterns of the C, c, E, or e antigens in automated testing and/or by tube and column agglutination techniques were analyzed by QMPSF and all 10 RHCE exons were sequenced.

Results: We identified 17 samples (0.38%) with weak expression of one or two major RhCE antigens by serologic tests. Molecular analysis of this 17 samples revealed 11 different RHCE alleles: one has not been published before (novel allele: RHCE*cE 499G), ceVS.01, ceVS.05, ce.06, ce.01, ce.07.01, ce.30, CE(48C, 150T, 178A, 201G, 201G, 203G, 307T, 676G), ce(48C, 105T, 733G, 744C, 1025T) and two RHCE-D-CE hybrid alleles: RHce-D(9)-ce and RHCe-D(4)-Ce.

Summary/Conclusions: These results show the importance of RHCE molecular analysis of any sample showing an aberrant phenotype, discrepant, weak, or unclear results for any of the antigens CcEe in order to allow better donor and recipient matching based not only on phenotypically matched red blood cell units, but also on units that are genetically matched.

P-570

WEAKENED EXPRESSION OF RH3 AND RH4 ANTIGENS CAUSED BY A NOVEL RHCE VARIANT WITH A DELETED START CODON

S Martin-Blanc[1], C Vrignaud[1,2,3], M Roussel[1], S Ramelet[1], C Narboux[4], M Hennion[4] and T Peyrard[1,2,3]

[1]*Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine* [2]*UMR_S1134, INSERM/Université Paris Diderot* [3]*Laboratoire d'Excellence GR-Ex, Paris* [4]*Etablissement Français du Sang Nord de France, Lille, France*

Background: Rh is a complex blood group system encoded by the paralogous RHD and RHCE genes that currently includes 55 antigens officially recognized by the International Society of Blood Transfusion (ISBT). The RHCE gene encodes four alleles: Ce, cE, ce and CE. The decreased expression of both C and e is not rare in the Caucasian population, whereas the weakened expression of both E and c is quite uncommon.

Aims: We describe here a novel RHCE*cE allele with a deleted start codon that codes for a decreased expression of the E (RH3) and c (RH4) antigens.

Methods: Blood samples of 24 unrelated patients of Caucasian origin were referred to our reference laboratory for the following reasons: (i) weak E and/or c reactivity; (ii) reagent vigilance procedure. Phenotype investigation was carried out by standard hemagglutination techniques. Genomic DNA was isolated from WBCs by a fully automated method followed by RHCE exon and flanking intron region sequencing (consensus sequence NM_020485).

Results: Among the 24 blood samples referred to our national immunohematology reference laboratory, 16 were referred for suspicion of both c and E variants and eight for a weak E antigen expression only. All were confirmed to be weakly reactive in our two routine techniques (Ortho BioVue System/monoclonal and Bio-Rad ID-System/polyclonal). A panel of monoclonal antibodies showed negative reactions with clones MS258, MS80 (anti-E) and c370 2A8 (anti-c) but positive with all other tested reagents. RHCE sequencing revealed the presence of the same deletion, at heterozygous state and partly covering the beginning of exon 1, c.-1_3del (deletion of four nucleotides), causing the loss of the conventional start codon of the gene.

Summary/Conclusions: We report here a novel mutation in a RHCE*cE allele, c.-1_3del. It could have been expected that the critical localization of this deletion

could have fully abolished the RHCE protein expression. However, the E and c antigens are unambiguously detected here on the RBC membrane with common monoclonal reagents. We speculate that another AUG sequence in 5′ UTR, at position c.-43, may be used as a replacement initiation codon. The encoded protein would be in such a case 13 amino acids longer at N-terminus, while globally preserving the RHCE quaternary structure. The weakened antigenic expression could be either due to an altered trafficking to the plasma membrane or deficient anchoring at the RBC surface. This hypothesis would need to be confirmed by protein analysis techniques. As a precaution, we consider individuals expressing this allele as being partial E and partial c and recommend antigen-negative RBC units especially for women of child-bearing age to be transfused.

We propose that this novel RHCE*cE allelic variant should be assigned a reference number by the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology in the official list of alleles of the Rh blood group system.

P-571

DEFINITION OF A STRATEGY TO OPTIMIZE THE SELECTION OF DONORS WITH RHCE VARIANT ALLELES IN AN ADMIXED POPULATION

T Vendrame[1], C Arnoni[1], R Person[1], A Cortez[1], F Latini[1] and L Castilho[2]
[1]Colsan, São Paulo [2]Unicamp, Campinas, Brazil

Background: RH genes are highly polymorphic and more than 120 variant RHCE alleles have already been described. RHCE alleles considered clinically significant are almost exclusively found in people of African descent and are those that code for partial Rh antigens and most of the time for a protein lacking a high-prevalence antigen. It is not easy to find compatible donors to fulfill the needs of the patients with RHCE variants, in special the alloimmunized patients with Sickle Cell Disease (SCD).
Aims: In order to provide a better transfusion support to SCD patients presenting RHCE variants, our aim was to define a strategy to facilitate the selection of donors with the most common RHCE variants in a country with increased miscegenation.
Methods: We selected three groups of blood donors: 104 African Brazilian Donors (ABD) which were characterized by genetic markers; 307 Self Declared African Descendant Donors (SDA); and 583 Donors typed as D-negative but C-positive (D-C+). The samples of ABD and SDA were submitted to molecular tests for analyses of 712A>G, 254C>G, 667G>T and 733C>G polymorphisms. According to the results, we performed another analysis using a flowchart previously described (Arnoni et al, Immunohematology, 2015). D-C+ RBC samples with a negative result in a specific PCR for RHD intron 4 and exon 7 and also for RHDΨ, were submitted to a specific PCR for RHD exon 9. Those with positive results were genotyped (SSP-PCR) for RHCE 733C>G and 1006G>T polymorphisms and confirmed with a multiplex PCR to D-CE hybrid exon 3, characterizing the presence of the (C)ce[S] haplotype.
Results: The frequency of RHCE variant alleles was 27.88% in the ABD group and 36.16% in the SDA group, being RHCE*ceVS.02 and RHCE*ceVS.01 the most frequent alleles found, respectively. In SDA group we also found 9 samples homozygous for RHCE variant alleles, leading to partial c, partial e and the hrB- phenotype, while in the ABD group all the variant alleles were associated with a conventional Ce or cE allelic forms. Additionally, from 583 samples of the D-C+ group studied, 45.8% had the exon 9 of RHD and all of them presented at least one hybrid D-CE-D[S] haplotype. Four of them were homozygous for the (C)ce[S] haplotype and 10 were compound heterozygous with other RHCE variant alleles.
Summary/Conclusions: Our results suggest that in an admixed population as the Brazilians, it is easier to find RHCE variant alleles in donors self-declared as African descendent than in donors with the African ancestry defined by molecular markers. In addition, the strategy to identify the (C)ce[s] haplotype in donors typed as D-C+ can also help to find donors with rare RhCE phenotypes.

P-572

RHD ALLELES IN SEROLOGICALLY D NEGATIVE BLOOD DONORS

K Bensing[1], G Denomme[1,2], M Schanen[1], C Piefer[1] and W Anani[1,2,3]
[1]Immunohematology Reference Laboratory [2]Blood Research Institute, Versiti/BloodCenter of Wisconsin [3]Department of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin, United States of America

Background: Over 70,000 BloodCenter of Wisconsin donors of all ethnicities (self-identified) have been genotyped since 2010. The RHD455 single nucleotide polymorphism (SNP) is routinely to detect the presence of a partial RHD allele and as a marker to ensure accuracy of high throughput genotyping by verifying the presence or absence of the RHD allele in serologically D+ and D- blood donors respectively. Rarely, a discrepancy between genotype and serology occurs that must be investigated.
Aims: The purpose of this study was to investigate the presence and determine the frequency of RHD alleles in serologically D- blood donors.
Methods: Automated RhD phenotyping was performed using EDTA-anticoagulated blood. RhCE phenotyping was performed using anti-C, anti-E, anti-c and anti-e reagents. High-throughput red cell genotyping was performed using Taqman primer/probe endpoint assays. Weak D and Partial D analysis was performed using single specific primer polymerase chain reaction (SSP-PCR). RHD exons were polymerase chain reaction (PCR)-amplified from genomic DNA using allele-specific flanking intronic primers containing 5′ M13 sense/antisense sequences. PCR-amplified fragments were sequenced by Sanger dideoxy method using the BigDye Terminator v3.1 Cycle Sequencing Kit with complementary M13 primers. The results were aligned to RHD_NG_007494.1 using SeqScape software. Donors with RHD*08N.01 (RHD*Pseudogene) and RHD*03N.01 (RHD*DIIIa-CEVS(4-7)-D) alleles were excluded from the analysis.
Results: Twenty-eight (0.04%) blood donors having an RHD phenotype/genotype discrepancy were investigated for the presence of variant RHD alleles: 20 Caucasian (CA), 3 Asian (AS), 3 Hispanic (HI), 1 African American (AA) and 1 Other (OT). RhCE phenotyping performed on these samples revealed 17 C+, 8 E+, 1 C+E+ and 2 C-E-. Results obtained on 24 donors were divided into 4 categories: Weak D (n = 3): RHD*01W.10 (CA; RHCE*Ce), RHD*01W.17 (CA; RHCE*cE), RHD*01W.28 (CA; RHCE*cE); Partial D (n = 4): RHD*11 (2 CA and 1 OT; RHCE*Ce) RHD*06.02 (CA; linked to RHCE*cE, not RHCE*Ce); Nonfunctional D (n = 10): RHD*01N.02 (CA; RHCE*ce), RHD*01N.07 (3 CA, 2 related; RHCE*cE), RHD*01N.08 (CA; RHCE*Ce), RHD*01N.41 (CA; RHCE*Ce), RHD*01N.69 variant (no c.1136G>T) with RHD Exon 2 deleted (HI; RHCE*Ce), RHD*01N.81 (CA; RHCE*Ce), novel RHD*01N c.221G>A P.Trp74Ter (AA and HI; RHCE*Ce) and DEL (n = 7): RHD*DEL1 (3 AS; 1 RHCE*Ce/RHCE*cE; 2 RHCE*Ce), RHD*DEL8 (CA; RHCE*Ce), RHD*DEL11 (3 CA, 2 related; RHCE*Ce).
Four donors had inconclusive results. All showed the presence of RHD exons when SSP-PCR analysis was performed and were missing at least 1 RHD Exon using Sanger sequencing suggesting the presence of intronic polymorphisms or a nonfunctional allele.
Summary/Conclusions: Although a very small fraction of the population (0.04%), the presence of an RHD allele in a serologically D- blood donor may be a significant finding in terms of transfusion and anti-D alloimmunization. RHD sequencing revealed 3 variants previously not described. The presence of the RHD455 SNP along with RHCE*Ce or RHCE*cE is an indicator of a variant RHD allele in a D- blood donor.

P-573

Abstract has been withdrawn

P-574

FREQUENCY AND CHARACTERIZATION OF RHD VARIANT ALLELES IN SEROLOGICALLY D–NEGATIVE PREGNANT SURINAMESE WOMEN

R Zonneveld[1,2], H Kanhai[3,4], I Waas[5], A Javadi[6], B Veldhuisen[6], M Lamers[7], A Brand[8], W Zijlmans[1,3,9], C van der Schoot[6] and H Schonewille[6]
[1]Scientific Research Center Suriname [2]Department of Pediatrics, Academic Hospital Paramaribo [3]Faculty of Medical Sciences, Anton the Kom University of Suriname, Parimaribo, Suriname [4]Department of Obstetrics, Leiden University Medical Center, Leiden [5]Hogeschool In Holland [6]Experimental Immunohematology, Sanquin Research, Amsterdam [7]Faculty of Medicine, Radboud University, Nijmegen [8]Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, Netherlands [9]Department of Pediatrics, Diakonessen Hospital, Parimaribo, Suriname

Background: The D antigen is highly polymorphic and over 250 RHD variants have been described. Next to the normal D+ expression, three types of variant D expression exist: weak D, Del and partial D. Individuals with partial D variants express D antigens that lack one or several of the 30 D-epitopes, which can have an effect on D antigen expression, hampering detection by routine serology. Characterization of RHD alleles, especially in ethnic groups with limited access to preventive measures

is of practical clinical importance. In Suriname, the D phenotype of transfusion recipients, pregnant women and newborns is only serologically determined, and anti-D prophylaxis for women at risk for D immunization is not routine. The population of Suriname is a mixture of different ethnic groups, of which Hindustani, Maroons, Creoles, and Javanese represent the four most common. Our previous studies revealed 4.3% serological D negativity and anti-D in 12% of multigravida D- women in Suriname (Zonneveld, Transfusion, 2016 and 2017).

Aims: Determine the frequency and characterization of RHD variant alleles in Surinamese serologically D- pregnant women from different ethnic groups.

Methods: A cross-sectional study, in D- pregnant women, who visited one of the four hospitals (Academic Hospital Paramaribo, Diakonessen Hospital, 's Lands Hospital and Sint Vincentius Hospital) in Paramaribo Suriname for routine pregnancy care, was performed. In Suriname, pregnant women are routinely tested once for the D blood group using a conventional serologic slide direct agglutination test with a single monoclonal antibody. From D- women who participated in the RheSuN study, residual blood was separated into plasma and remainder cells (DNA) and shipped to the Netherlands, for RHD variant allele testing, using qPCR targeting RHD exons 5 and 7 and RH-Multiplex Ligation-dependent Probe Amplification (RH-MLPA) after DNA extraction. Samples with either exon 5 or 7 present or with discrepancies between molecular and serological D were further analyzed with RH-MLPA as single samples. The remainder (i.e. both exons absent) were tested with RH-MLPA in batches of 5–6 DNA samples.

Results: From a total of 214 pregnant women included in the RheSuN study, 91 samples were available for RHD variant allele testing. Of these, in 39 samples either exon 5 or 7 was present and in 52 both exons were absent. RH-MLPA revealed 127 RHD deletions (RHD*01N.01). A total of 47 variant alleles were detected; 21 RHD*DIIIa-CEVS(4-7)-D (RHD*03N.01), 18 RHD*Pseudogenes (RHD*08N.01), two RHD*807G (RHD*01.18), two RHD*DAR6 (RHD*09.06), one RHD*DAU0 (RHD*10.00), one Del (RHD*01EL.01) and for two alleles the variant is currently unknown. Six samples showed, despite D- serology, an apparently normal RHD allele and are also under further investigation. Anti-D was only found in eleven women with D negative variant RHD genes (RHD deletions, RHD*DIIIa-CEVS(4-7)-D and RHD*Pseudogenes)

Summary/Conclusions: The frequency of variant RH alleles in a cohort of 91 Surinamese serologically D- pregnant women was 26% (47/182), with RHD*03N.01 and RHD*08N.01 representing 87% of variant alleles. D antibodies were only present in women with genotypes commonly known to be at risk for anti-D.

On behalf of the Rhesus in Surinamese Neonates (RheSuN) study group.

P-575

Abstract has been withdrawn

P-576

DEL PHENOTYPING AND GENOTYPING ANALYSIS IN CHINESE PREGNANT WOMEN WITH A PRIMARY D NEGATIVE PHENOTYPE

Y Ji, Z Wang, S Jia, J Chen, R Zhang, J Wen, L Wei and G Luo
Institute of clinical blood transfusion, Guangzhou Blood Center, Guangzhou, China

Background: DEL is a very weak form of D antigen, which is very rare in Caucasian and Black ethic groups, but more common in East Asian population. DEL individuals are commonly mistyped as D- phenotype for low density of D antigen expression on the surface of red cell. Adsorption-elution test is the only way for DEL testing serologically, which is not routinely performed in most of clinical laboratories. So far, more than 40 alleles have been reported accounting for DEL phenotype. RHD*01EL.01 (RHD*1227A) is most prevalent in East Asian DEL individuals, so which was called as "Asia type" DEL.

Aims: To conduct phenotyping and genotyping analysis of DEL in the Chinese Southern Han pregnant women with a primary D– phenotype.

Methods: From October 2015 to January 2018, peripheral blood samples of 1098 Chinese pregnant women with a primary D– phenotype were tested. D antigen was firstly tested again using another blend anti-D reagent (Clone TH-28/MS-26, IgM/IgG). Then, adsorption-elution test for DEL phenotyping was conducted in the samples with primary D– phenotype. A high-resolution melting (HRM) method was developed for "Asia type" DEL genotyping using one pair of RHD specific primers to amplify Exon 9 of RHD gene covering the synonymous mutation (c.1227G>A). The zygosity of RHD gene predicted by HRM analysis was confirmed by hybrid rhesus

box PCR with PstI digestion. The samples with the inconsistent RHD genotype were further analyzed by MLPA genotyping and/or RHD gene sequencing. Meanwhile, serological RhCE typing and antibody screening were performed.

Results: Twenty-four pregnant women were identified having D variant phenotype. In the rest of 1074 samples with primary D– phenotype, a total of 272 pregnant women (272/1074, 25.33%) were identified with DEL phenotype. And eight different kinds of genotypes were identified including RHD*01EL.01/01N.01 (n = 222, involving Ccee phenotype (n = 208), CCee (n = 11) and CcEe (n = 3)), RHD*01EL.01/01EL.01 (n = 30, all of them having CCee phenotype), RHD*01EL.01/01N.03 (n = 15, all of them having CCee phenotype), RHD*01EL.01/D-CE(3-10) (n = 1, CCEe), RHD*01EL.01/DVI.3 (n = 1, CCEe), RHD*01EL.01/weak D type 25 (n = 1, CcEe), RHD*01EL.01/01N.16 (n = 1, CCEe) and one novel RHD*761T/01N.01 genotype (n = 1, Ccee). Among the 1042 pregnant women except for 32 pregnant women who had received anti-D prophylaxis prior to DEL testing, 264 pregnant women were identified with "Asia type" DEL phenotype and no one of them was detected to produce alloanti-D. In the rest of 778 pregnant women with true D– phenotype, 50 of them (50/778, 6.43%) were detected to produce alloanti-D with a titer from 1:2 to 1:4096. The guidance of no need to receive anti-D prophylaxis was provided to the 264 "Asia type" DEL pregnant women.

Summary/Conclusions: "Asia type" DEL pregnant women cannot produce alloanti-D after exposure to D+ blood of fetus. The developed HRM genotyping method is fit for routine testing of "Asia type" DEL, which is really relevant to avoid the unnecessary anti-D prophylaxis for "Asia type" DEL pregnant women as the phenotype is so common in the Chinese population and anti-D immunoglobulin is also still not available in the mainland of China.

P-577

ASSOCIATION BETWEEN ANTI–D IMMUNOGLOBULIN DEVELOPMENT IN IMMUNISED BLOOD DONORS AND THE RED BLOOD CELL PHENOTYPE

J Tan[1,2], J Wong[3], R Flower[1,2] and W Dyer[1,2]
[1]Research and Development, Australian Red Cross Blood Service, Alexandria [2]Sydney Medical School, University of Sydney, Camperdown [3]Medical Services, Australian Red Cross Blood Service, Alexandria, Australia

Background: Cases of haemolytic disease of the foetus and newborn have declined significantly since the introduction of successful routine administration of prophylactic anti-D immunoglobulin (Ig) to susceptible RhD-negative pregnant women. The Blood Service conducts an Anti-D Program to actively immunise selected RhD-negative blood donors with small volumes of RhD-positive red blood cells (RBCs) to stimulate anti-D Ig production. Approximately 50% of primarily immunised donors develop serum anti-D Ig concentrations >1 IU/ml and are assigned a 'Responder' profile. We have previously sought to examine the donor genetic factors associated with the donor responder profile (Tan, Molecular Immunology, 2015).

Aims: We hypothesise that the RhD-positive RBCs phenotype could also influence the donor responder profile.

Methods: The immunisation record for 218 anti-D donors was collected and analysed. We further examined a subset of 154 anti-D donors who were immunised with RhD-positive RBCs belonging to only one haplotype: either R0 (Dce), R1 (DCe), R2 (DcE) or RZ (DCE).

Results: We determined that 71% of n = 42 female anti-D donors and 52% of n = 176 male anti-D donors were Responder donors (p value = 0.025). We found that Non-Responder donors were unlikely to develop anti-D antibodies with additional booster injections. We found that 59% of donors immunised with R2 only and 60% of donors immunised with R1 only RhD-positive RBCs developed anti-D Ig, as opposed to donors immunised with R0 only (41%) or RZ only (39%) RhD-positive RBCs. Responder anti-D donors also developed antibodies to RBC antigens to which we did not match when selecting RBCs for immunisation.

Summary/Conclusions: Further data collection and analysis will allow us to determine if the red blood cell phenotype can influence an anti-D donor's ability to develop anti-D antibodies.

P-578

Abstract has been withdrawn

P-579

CONFIRMATION OF A COMPOUND HETEROZYGOUS STATUS FOR THE RHAG GENE IN A RH NULL SUBJECT OF THE REGULATOR TYPE

C Vrignaud[1,2,3], S Ramelet[1], J Cartron[4] and T Peyrard[1,2,3]

[1]Centre National de Référence pour les Groupes Sanguins, Institut National de la Transfusion Sanguine [2]UMR_S1134, Inserm/Université Paris Diderot [3]Laboratoire d'Excellence GR-Ex [4]Institut National de la Transfusion Sanguine, Paris, France

Background: The Rh-associated glycoprotein (RhAG or CD241, formerly known as Rh50 glycoprotein; human blood group system #30) is known to form a complex on the red blood cell surface with the RhD and RhCE proteins and is essential for the expression of all Rh antigens. The gene encoding RhAG (chromosome 6) is very similar to that of RHD and RHCE (chromosome 1). Molecular alterations of the RHAG gene may cause a global decreased expression of the Rh protein, inducing the so-called Rh_{mod} phenotype or can lead to the exceptional Rh_{null} of the regulator type when the RHAG mutations are deleterious.

The first cases of nonfunctional RHAG allelic variants were described by Chérif-Zahar et al (Nature Genetics, 1996) in five Rh_{null} people, through genomic DNA and cDNA studies. A deletion of the c.1086A nucleotide in RHAG was detected in one Rh_{null} patient, named "T.B.". However, this deletion was surprisingly found in heterozygous state and all attempts to amplify the product of the second RHAG allele were unsuccessful. The c.1086delA allele was subsequently referred to as RHAG*01N.02 in the ISBT allele database. Since the discovery of his exceptional blood type, "T.B." became a repeat blood donor for the French National Rare Blood Bank.

Aims: We describe here the complementary investigation of the "T.B." proband with the currently available genomic tools, in order to find the full molecular basis of his Rh_{null} phenotype.

Methods: Genomic DNA was extracted from peripheral blood cells by a fully automated device. Whole exome sequencing was performed with Illumina technology by Eurofins Genomics. The 10 RHAG exons were amplified with specific primers and sequenced.

Results: "T.B.", a 54-year-old male donor, is known to be of blood group A_2, Rh_{null}, K-. He had no transfusion history and did not make anti-Rh29. The exome study confirmed the presence of the previously characterized c.1086delA mutation in the RHAG gene (predicted to cause a frameshift after Ala362) and revealed the presence in exon 3 of another deletion, c.543delT, in the heterozygous state. This mutation is predicted to result in a frameshift after the codon encoding phenylalanine at position 181. This c.543delT mutation was further confirmed by conventional Sanger sequencing of the RHAG gene.

Summary/Conclusions: "T.B." belongs to those exceptional individuals with a so-called Rh_{null} of regulator type and was initially reported in 1996 to unexpectedly demonstrate only one inactivating mutation in the RHAG gene. As "T.B." samples were readily available from our cryobank, this prompted us to investigate this case again. The genomic DNA sequencing with two different approaches allowed us to find a novel silent RHAG allele with a c.543delT mutation (p.Phe181Leufs*5) and to definitely explain at the same time the Rh_{null} phenotype of the proband. We suggest to update the current databases with this newly reported silent RHAG allele, which could be named RHAG*01N.19, subject to the agreement of the ISBT Working Party on Red Cell Immunogenetics and Blood Group Terminology. This case highlights the fact that reinvestigation of some unexplained former immunohematology cases may be relevant and successful with the currently available molecular techniques.

P-580

A SOMATIC MOSAICISM INVOLVING THE RH ANTIGEN IN THE PROGRESSION OF PRIMARY MYELOFIBROSIS

S Joshi[1], S Bakdash[2] and N Quraishy[2]

[1]Section of Transfusion Medicine, Robert Tomsich Pathology and Laboratory Medicine Institute, The Cleveland Clinic [2]Section of Transfusion Medicine, Robert Tomsich Pathology and Laboratory Medicine Institute, The Cleveland Clinic, Cleveland, Ohio, United States of America

Background: Approximately 11% of patients with primary myelofibrosis (PMF) carry somatic, myeloid-restricted, activating MPL mutations that may arise from copy neutral (CN) loss of heterozygosity (LOH) on chromosome 1. This LOH may involve neighboring RHD/RHCE gene loci resulting in a phenotypic change in expression of the Rh antigen and Rh type discrepancy, and may impact the transfusion support of such patients.

Aims: To describe the immunohematological features, molecular findings and clinical progression of a patient with PMF.

Methods: A literature review describing clonal changes in patients with progressive myeloid malignancies based on a case review of a patient with PMF.

Results: A 64-year-old female with a longstanding history of a myeloproliferative disease, managed conservatively with no prior transfusions, was scheduled for an elective red cell transfusion for symptomatic anemia. Pre-transfusion ABO-Rh typing by gel hemagglutination showed a mixed-field reaction on Rh-D typing in contrast to her historic type of O-Rh (D) positive from as recently as a month prior. The discrepancy was attributed to PMF progression. On bone marrow exam, a previously hypocellular, slightly fibrotic marrow now showed prominent osteosclerosis amidst increased fibrosis, and stained positive for pSTAT5. Bone marrow cytogenetics (G banding) demonstrated a normal karyotype. JAK2 V617F mutation was negative. Chromosomal SNP microarray detected a copy number loss in the long arm of chromosome 13, which includes the Rb1 tumor suppressor gene, in 100% cells counted. Approximately 20–30% of cells contained a large CN-LOH in the short arm of chromosome 1 involving most of 1p, including the RHD/RHCE loci (1p36.2 to p34). Next Generation Sequencing confirmed the presence of a pathogenic MPL W515L mutation on chromosome 1(1p34.2). The patient received infrequent O, Rh-positive RBC transfusions over the next two years. Although she did not make anti-D, she developed anti-C and anti-Jk (b) against corresponding Rh and Kidd blood group system antigens, respectively.

Summary/Conclusions: The incidence of Rh discrepancies in myeloproliferative neoplasms (MPNs) is probably underreported considering the frequency of chromosome 1 aberrations in these disorders. This report of a patient with acquired Rh antigen mosaicism secondary to a clonal MPN, with somatic loss of the Rb1 tumor suppressor gene followed by CN-LOH of chromosome 1, underscores the diverse molecular pathways and multistep pathogenesis that is involved in the evolution of their phenotype. The mutational events described suggest an initial non-phenotypic mutation followed by a mutation with a detectable hematological phenotype. Phenotypic evidence of clonal evolution may impact transfusion in patients with MPNs.

P-581

COMPLETE NEXT GENERATION SEQUENCING FOR RH GENES: ESTABLISHMENT OF REFERENCE RHD AND RHCE ALLELES

W A Tounsi, T Madgett and N Avent

School of Biomedical and Healthcare Sciences, Plymouth University, Plymouth, United Kingdom

Background: The Rh blood group system (ISBT004) is the second most important blood group after ABO. Two closely related genes, RHD and RHCE, encode 55 different antigens. Recombination, deletion, and point mutations in these two genes generate Rh allelic diversity and generate the eight most common Rh haplotypes which include: R_1 (DCe), R_2 (DcE), R_0 (Dce), R_z (DCE), r (dce), r_y (dCE), r' (dCe), and r'' (dcE). Blood group genotyping could decrease Rh mistyping and eventually minimise the adverse reactions following blood transfusion, especially for blood transfusion dependent patients. Previous studies have used exome sequencing to identify Rh variation but the high homology between the RHD and RHCE genes could make it challenging to analyse data, especially exons 8 and 10, where there are no amino acid differences between the two genes.

Aims: We aimed to use LR-PCR to amplify the Rh genes to get a full sequence including promoter, introns and all exons. We focused on establishing reference alleles for the RHD and RHCE genes by studying intronic SNPs in both genes and their relationship to specific Rh haplotypes.

Methods: Genomic DNA samples (n = 92) from blood donors and the ISBT 1996 workshop of different phenotypes were sequenced using the Ion Personal Genome Machine™ (PGM™). The RHD gene was sequenced from all samples and the RHCE gene was sequenced from blood donor samples. Data was then mapped to the hg38 reference sequence and analyzed using the CLC Workbench 9.5.

Results: Multiple exonic SNPs were detected that encode 12 RHD alleles which include RHD*01W.1, RHD*01W.02, RHD*01W.3, RHD*03.01, RHD*25, RHD*04.04, RHD*06.01, RHD*03.01, RHD*07.01, RHD*17.01, and RHD*17.02. One novel allele was identified, in which one RHD hemizygous sample showed SNP L110P that encodes RHD*07.01 and RHD-RHCE(4)-RHD that encodes RHD*17.02, which means that this RHD allele is a hybrid between two variant RHD alleles. Due to RHD*DAU0 (RHD*10.00) being the hg38 reference sequence for the RHD gene, 21 homozygous SNPs were detected in all samples which are thought to be specific to the reference allele. Compared to the reference sequence, multiple intronic SNPs were detected that are suspected to be a haplotype specific. 23 SNPs were homozygous SNPs in all samples with the R_2 haplotype and 15 SNPs were homozygous in all samples with

R$_1$ haplotype. Intronic SNP analysis of the RHCE gene revealed over 100 intronic SNPs in intron 2 and confirmed the presence of the 109 bp insertion in intron 2 in samples with the R$_1$ haplotype. More than 50 intronic SNPs were detected in all R$_2$ and r samples.

Summary/Conclusions: In this research, 92 samples were sequenced for the RHD gene and the RHCE gene to study different alleles present in the population to establish reference allele sequences by utilising the analysis of intronic SNPs and their correlation to a specific Rh haplotype. Intronic SNPs are suspected to be related to a specific haplotype, which may represent novel diagnostic approaches to investigate known and novel variants of both genes.

P-582

COMPARING SEQUENCING OF THE RHD GENE BETWEEN THE ION PERSONAL GENOME MACHINETM AND MINION

T E Madgett, W Tounsi, G Farnham and N Avent

School of Biomedical and Healthcare Sciences, University of Plymouth, Plymouth, United Kingdom

Background: With high homology between the RHD and RHCE genes in the Rh blood group system (ISBT004) and high allelic diversity of the Rh alleles, DNA sequencing offers huge opportunities for complete blood group genotyping. Previous studies have used second generation methods of sequencing such as Ion Personal Genome Machine™ (PGM™) but the complexity of the Rh system makes it prime for single molecule sequencing.

Aims: We aimed to compare our LR-PCR/Ion PGM™ sequencing with MinION sequencing for the RHD gene. We focused on establishing whether MinION sequencing could be used to achieve allele phasing and accurate variant calls.

Methods: Genomic DNA samples (n = 3, R$_1$R$_1$, R$_2$R$_z$, R$_1$R$_2$) from blood donors were sequenced using the MinION for the RHD gene. LR-PCR products (9.8–13.7 kb) were sequenced using the SQK-LSK108 kit and SpotON flow cells (PK.1). The MinION was run for 2–6 h, followed by base calling with ONT Albacore software. Reads were extracted with poretools and mapped to the hg38 reference sequence, before analysis using BWA-MEM with ONT settings. Variants and phasing of alleles were called using Nanopolish software. The data was then compared to sequencing data for the same samples from the Ion PGM™.

Results: The MinIon generated ~90,000 reads in a two hour sequencing run, which gave coverage that ranged up to 8,000×. We were able to call variants and phase different alleles and compare results between the MinION and the Ion PGM™. For one R$_2$R$_z$ sample that was sequenced for RHD on the Ion PGM™, there were no amino acid changes detected, despite this sample being serologically phenotyped as weak D. From zygosity testing, the R$_1$R$_1$ sample showed discrepancy between hemizygous RHD exon 5 and homozygous RHD exon 7, indicating deletion of exon 5 in one of the RHD alleles. The Ion PGM™ was unable to detect the absence of RHD exon 5 on one of the alleles due to the presence of the wild type allele Intronic SNPs were detected in all samples sequenced on the MinION. Intronic SNPs had been shown to correlate with specific haplotypes from the Ion PGM™. LR-PCR amplicons were sequenced on both platforms but fragmentation was necessary with the Ion PGM™. It was challenging to map the short reads to the hg38 reference sequence, due to shorter reads sometimes aligning to different regions in the gene. In contrast, the MinION produced reads covering the entire LR-PCR amplicons (9.8–13.7 kb). Allele phasing using Ion PGM™ data is not feasible, unlike the MinION in which longer reads are generated.

Summary/Conclusions: This research has shown the potential of using the MinION single molecule sequencing platform for blood group genotyping. With the advantage of allele phasing, complicated genetic structures such as exist for the RHD/RHCE genes (for example, hybrids) can be more easily assessed. The platform is straightforward to use and cost-effective. Work is ongoing optimising barcoding sequencing on the MinION to allow sequencing of multiple samples in the same run for the RHD gene. This work opens up possibilities of studying variation in other blood group genes using the MinION.

P-583

RHD TYPING AMBIGUITIES IN MERGING SEROLOGICAL AND MOLECULAR DATA – THE DETERMINING CONTRIBUTION OF GENE SEQUENICING

A Matteocci[1], T Mancuso[2], F Pirelli[1], T Hutchinson[3], G Nespoli[1], R Borgogno[4], G De Rosa[5], C D'Amico[6], K Castagna[1], A Collaretti[1], L Rogai[1] and L Pierelli[1]

[1]Transfusion Medicine Unit, San Camillo Forlanini Hospital, Rome [2]Mktg, Immucor Italia S.p.A., Milan, Italy [3]BioArray Solutions, Immucor, Warren, New Jersy, United States of America [4]RPVE-OIRM, Ospedale S.Anna, Turin [5]Ospedale G.B.Grassi, Ostia (RM) [6]Ospedale Spaziani, Frosinone, Italy

Background: The introduction of RHD genotyping in the routine of transfusion laboratory allows the resolution of most RhD discrepancies found with serological standard methods. Nevertheless, diagnostic platforms still show large limitations in detecting RhD variants, and the use of RHD gene sequencing is sometimes crucial in clearly defining the RhD status of patients and donors, especially when molecular and serological techniques present typing ambiguities due to the lack of specific markers for some RhD variants in the commercially available kits.

Aims: The present study was aimed at evaluating how frequent – and how determining – was the turning to RHD sequencing analyses. In order to do this, we took as an example the amount of RHD genotyping assays performed in 2017.

Methods: RhD serological typing was carried out in microplate direct agglutination tests (NEO, Immucor) by using 2 different anti-D IgM clones (Clone 1, DVI+: LDM1 + ESD1M; Clone 2, DVI-: RUM-1, TH28) and 2 different anti-D IgG clones (Clone 1: MS26; Clone 2: D415 1E4). In 2017, 440 samples were found to be discrepant with this approach, therefore they were addressed to RHD genotyping with the RHD BeadChip kit (Immucor): 14 samples (3.2%) still showed inconclusive results due to a full-length gene, wild-type result, in conjunction to weak agglutination scores or higher and/or discordant scores (3 + /4 +). These samples were further analyzed by bidirectional sequencing analysis of the whole RHD coding region.

Results: Over 14 samples analyzed by RHD sequencing – 5 males, 9 females, median age 34.5 years. (25 to 71 years) – 8 had a Weak D variant (4 Weak D type 100, 1 Weak D type 12, 1 Weak D type 16, 1 Weak D type 27, and 1 Weak D type 126), 4 had a Partial D (3 Weak D type 45, 1 DNU), and 2 showed a Weak D type 61, which is categorized under the DEL variants. The subject with Weak D type 12 was of African descent, while all the others were Caucasians. The patient bearing a DNU variant also showed the presence of anti-D alloantibodies in her serum.

Summary/Conclusions: The contribution of RHD sequencing has been pivotal in resolving RhD typing ambiguities in our experience. Although we only considered a relatively short period of time (1 year), sequencing analyses allowed us to identify 3 cases with Weak D type 45 (women of childbearing age) and 2 with Weak D type 61 (blood donors); these are respectively grouped under the Partial D and DEL categories by the ISBT committee, with important implications in the practice of immunoprophylaxis and transfusion therapy.

P-584

UTILITY OF RED BLOOD CELL GENOTYPING OF BLOOD DONORS

M A Keller, J Keller and T Horn

Molecular Laboratory, American Red Cross, Philadelphia, Pennsylvania, United States of America

Background: Red blood cell (RBC) Genotyping can be a cost-effective and efficient means of identifying donors lacking high prevalence antigens or multiple common blood group antigens. Units from such donors are used for transfusion to patients with alloantibodies, or in the case of patients with sickle cell disease, for prophylactic phenotype matching to avoid alloimmunization.

Aims: Our blood center has routinely used RBC genotyping to screen blood donors since 2009, having screened more than 160,000 predominantly African American donors since 2011. We recently transitioned from Immucor PreciseType HEA Molecular BeadChip to Agena BioScience HemoID DQS. We describe the CY2017 results of genotyping ~25,000 mostly ethnically diverse donors using HemoID DQS which includes 42 antigens in 12 blood group systems as well as HbA, S and C.

Methods: Donors were selected based on self-declared AA ethnicity, or based on historic serologic types. Blood tubes from red cell donors were transported from regional sites to a centralized molecular testing laboratory. Genomic DNA was extracted from 200uL of whole blood using an automated extractor. DNA was subjected to 2 multiplex PCR reactions. Following dephosphorylation of unincorporated dNTPs, assay probes were extended into polymorphic sites by single nucleotide

extension with acyclo-NTP termination and analyzed by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) spectrometry on a MassARRAY (Agena BioScience). RareFinder, an R-based script (Agena BioScience), was used to tally specific predicted phenotypes.

Results: Of the 25,205 genomic DNA samples, 343 (1.4%) yielded no result for one or both wells of the genotyping assay. Of the 24,862 samples with complete predicted phenotypes, 97 (0.4%) were S-s-U-, 162 (0.65%) were Js(a-), 58 (0.2%) were Jo(a-), 53 (0.2%) were Hy-, 29 (0.12%) were Lu(b-), 2 (0.0008%) were Co(a-). No donors were identified to be Di(a-), Sc:-1 or LW(a-). Enriched in AA, the cohort included 11,813 donors (47.5%) who were C-E-K- and 7272 donors (29.2%) who were C-E-K-Fy(a-b-). 18 donors (0.07%) were predicted to RH:43 (CF+) and 164 donors (0.6%) were Fyb+w. Sickle trait was identified in 5.4% of donors tested. RHCE c.48C, c.712, c.733 and c.1006 single nucleotide polymorphism were used to identify 664 (2.7%) E- donors predicted to be hr^{B+vw}/- and 125 (0.5%) E- donors predicted to be hr^B-. Though 71 (0.3%) were heterozygous for RHCE c.712A, no donors were predicted to be E- hr^S- based on homozygosity for this marker.

Summary/Conclusions: High-throughput RBC genotyping is an efficient means of identifying antigen negative blood donors. In addition, RBC genotyping identifies donors who carry variants associated with antigen typing discrepancies, including RH:46 and Fy^b. If the frequency of donors with predicted phenotypes of E- hr^B- and E- hr^{B+vw}/- are combined, the resulting 3.2% is close to the 3% hr^B- reported in blacks (Reid ME et al. The Blood Group Antigen FactsBook, 2012). The failure to identify donors homozygous for RHCE c.712A in nearly 25,000 predominantly African American donors highlights the rarity of the E- hr^S- phenotype in the US.

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THIRD-GENERATION (LONG READ) SEQUENCING OF BLOOD GROUP GENES: PRELIMINARY DATA AND FUTURE APPLICATIONS

Y Fichou[1], C Le Maréchal[2] and C Férec[2]

[1]UMR1078, Inserm, EFS, UBO, Ibsam [2]UMR1078, Inserm, EFS, UBO, IBSAM, CHU Brest, Brest, France

Background: While conventional next-generation sequencing (or second-generation sequencing) has proven efficient and powerful for sequencing blood group genes, phasing still remains a challenging issue due to short read sequencing data and/or absence of closely-linked polymorphic markers. For the past few years, third-generation sequencing, including the PacBio technology, has emerged as a potent tool to investigate several kilobases (kb) in a single read.

Aims: We thought to test the PacBio sequencing technology to investigate the full locus of genes involved in the expression of blood group antigens, i.e. ACKR1 and RHD, involved respectively in the Duffy and Rh blood group systems.

Methods: Primer sets were designed to generate large amplicons in the ACKR1 (1 product; 3.0 kb) and RHD (3 overlapping products; 22.8, 23.6, and 22.7 kb) genes by long-range PCR amplifications. Two different pools were made. First, ten genomic DNA (gDNA) samples (external quality control) with known genotypes were used to amplify the ACKR1 target, and the purified products were barcoded and mixed together at equimolar ratio. Second, the three RHD products were generated by using gDNA extracted from the K562 cell line and pooled together. Both libraries were sequenced individually with the Sequel System (Pacific Biosciences, CA, USA) by using the Single Molecule, Real-Time (SMRT) Sequencing technology.

Results: In the ACKR1 gene, all 20 alleles were identified and their genotype was in full accordance with those obtained by alternative means (i.e. microarray and Sanger sequencing). In the RHD gene, the full sequence of the gene locus, i.e. approximately 60 kb, could be reconstituted successfully.

Summary/Conclusions: For the first time to our knowledge, genomic sequences of blood group genes have been specifically generated by the PacBio technology. We are currently in the process of extending our study to other blood group genes, including RHCE (Rh blood group), GYPA/GYPB (MNS), KEL (Kell), SLC14A1 (Kidd), and ART4 (Dombrock). Although routine diagnostics by those means is not recommended due to its cost, determination of reference gene/allele sequences, which are insufficiently documented in this field of research, is a typical application of this technology, resulting in the production of valuable datasets for blood group genotyping. Another convenient application is the resolution of complex genomic rearrangements and hybrid genes that are commonly observed in blood group genes, more specifically in those encoding the Rh and MNS antigens. Overall our preliminary results pave the way to the use of third-generation sequencing in the field of blood group genomics.

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MULTICENTER CLINICAL STUDY OF ID CORE XT: COMPARISON WITH IMMUCOR PRECISETYPE HEA ASSAY, FDA–LICENSED SEROLOGY AND BI–DIRECTIONAL SEQUENCING

M López[1], I Hormaeche[2], N Rapun[3], M Stef[4], M Keller[5], M Kalvelage[6], K Billingsley[6], G Teramura[7], M Delaney[8], C Westhoff[9], S Vege[9], M Chee[10], P Shi[10], Y Du[10], L Gardner[10], A Ramans[10], M Blunk[10] and D Tejedor[2]

[1]R&D, Progenika Biopharma, a Grifols company, Derios [2]Technical Department [3]Product Development & Support, Progenika Biopharma, a Grifols company, Derio, Spain [4]CLIA Laboratory, Progenika Inc., a Grifols Company, San Marcos, Texas [5]Hematology, American Red Cross, Philadelphia, Pennsylvania [6]Hematology, LifeShare Blood Center, Shreveport, Louisiana [7]Hematology, Bloodworks Northwest, Seattle, Washington [8]Hematology, Children's National Health System, Washington, DC [9]Hematology, New York Blood Center, Long Island, New York [10]Clinical Affairs, Grifols Diagnostic Solutions, Emeryville, California, United States of America

Background: DNA-based molecular technologies are increasingly being implemented by immunohematology laboratories to improve extended blood group antigen matching in transfusion medicine. ID CORE XT is a qualitative, PCR and hybridization-based genotyping test (Luminex xMAP technology) for the simultaneous identification of multiple alleles encoding red blood cell antigens in genomic DNA. This test is used to genotype 29 polymorphisms targeting 53 alleles to predict 37 antigens in ten blood group systems Rh (C^W, C, c, E, e, V, VS, hr^B and hr^S), Kell (K, k, Kpa, Kp^b, Js^a, Js^b), Kidd (Jk^a, Jk^b), Duffy (Fy^a, Fy^b), MNS (M, N, S, s, U, Mi^a), Diego (Di^a, Di^b), Dombrock (Do^a, Do^b, Hy, Jo^a), Colton (Co^a, Co^b), Cartwright (Yt^a, Yt^b) and Lutheran (Lu^a, Lu^b).

Aims: The objective of this clinical study was to evaluate the performance of ID CORE XT in comparison with well-established reference methods for clinical determination of blood group antigens.

Methods: Whole blood samples were collected in EDTA tubes from blood donors at three reference blood centers in the United States. Genomic DNA samples were extracted and tested with ID CORE XT, Immucor PreciseType™ HEA Molecular Bead-Chip and Bi-Directional-Sequencing (BDS). Commercial tests were performed according to the manufacturer instructions. The ID CORE XT predicted phenotypes were compared to PreciseType HEA and FDA-licensed serology tests. The antigens not tested by PreciseType HEA and with no FDA-licensed serology available (C^W, hr^S, hr^B, Mi^a, Yt^a and Yt^b) were compared to BDS results. Since the polymorphism and predicted allele genotypes interrogated by ID CORE XT are not reported by PreciseType HEA, the genotypes were compared to BDS, as the gold-standard method.

Results: A total of 1,026 blood donors were included in this evaluation. The valid run and valid test rates of ID CORE XT obtained in the study were 96.87% (due to a protocol deviation) and 100%, respectively. The discrepancies were resolved by a referral reference laboratory: i) Comparison with PreciseType HEA: Five samples showed discrepant predicted phenotypes. Four samples with RHCE (C, V and VS) due to limitations of PreciseType HEA, and one false M negative result by ID CORE XT; ii) Comparison with serology: One sample gave a false negative for Lu^b antigen by serology; iii) Comparison with BDS: Four samples gave discrepant genotypes with ID CORE XT. Three discrepancies were resolved as DNA sample mix-up by BDS. One discrepancy was due to an allele-drop out by BDS. The concordance of ID CORE XT with the reference methods was 100%, with the exception of GYPA:c.[59C>T] genotype and the corresponding antigen, M, which was 99.9%. The lower bound of the one-sided 95% CI for the concordance was greater than 99% for each of the polymorphisms, allele genotypes and antigens.

Summary/Conclusions: ID CORE XT is an accurate testing system for the prediction of 37 red blood cell antigens and for the determination of 29 polymorphism genotypes and the associated predicted alleles in ten Blood Group Systems. From the clinical trial results, the ID CORE XT can be implemented for genotyping in routine of the immunohematology laboratories.

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GENOTYPING OF BLOOD GROUP VARIANTS IN THE DUTCH PATIENT AND DONOR POPULATION

B Veldhuisen[1,2], P Ligthart[2], J Koster[2], R Jonkers[2], R Schreuder[2], S van den Bovenkamp-Jansen[2], I Dengerink[2], S de Jong[2], A Tissoudali[2], C Folman[2], M de Haas[2,3] and C van der Schoot[1]

[1]Experimental Immunohematology [2]Diagnostic Immunohematology, Sanquin, Amsterdam [3]Immunohematology, Leiden University Medical Center, Leiden, Netherlands

Background: Blood group typing of patients and donors is performed to prevent allo-immunisation and transfusion reactions or in the case of pregnant women to prevent hemolytic disease of the fetus and newborn. Genotyping methods are used when serological methods are not possible or not conclusive guide prophylaxis. To be able to reliably predict the phenotype from the genotype it is important that reference laboratories report on rare blood group alleles that they have encountered in their daily practice. In 2017 at the reference laboratory of Sanquin, a total of 1114 individuals were genotyped to determine their blood group antigens, variants of blood group antigens, chimerism or RHD zygosity. Here we report on the phenotypic and genotypic characterisation of rare alleles which were observed among these samples.

Aims: To characterise rare blood group alleles for which molecular typing was needed because serology could not provide a conclusive result.

Methods: In a diagnostic setting we have used three different genotyping assays. Allelic discrimination assays were used to type common blood group antigens, a Multiplex Ligation-dependent Probe Amplification (MLPA) assay to determine antigens of 18 different blood group systems, including the D-variants and zygosity, and finally Sanger sequencing to determine variants which could not be determined by MLPA. DNA was extracted from 200 µl EDTA blood using either a Qiasymphony or Chemagic instrument.

Results: Eight novel alleles in the RH, KEL and JK blood group systems have been detected. A new allele in the DAU cluster (c.602C>G; c.998G>A; c.1136C>T) with extremely weak expression using several anti-D reagents lacks epitopes 1 (LHM70), 5 (HIRO-6) and 8 (HIMA-36). Another novel allele (c.17C>T; c.520G>A; c.916G>A; c.932A>G) lacks the same epitopes. Two patients negative for epitopes 1; 2 (5C8) and 8 have a DFR-like allele with an additional mutation similar to weak D type 45 (c.505A>C; 509T>G; c.514A>T; c.1195G>T). A novel mutation in exon 2 of RHD (c.225C>A; p.S75R) causes a weak expression of RHD. An RHCE variant was found containing RHD exons 2 to 4 and part of exon 5, which is serologically comparable to an RHCE*CeRN variant. Two novel mutations in the KEL gene (c.1736T>G and c.1704–2A>G) cause loss of expression of KEL*02. Finally, a mutation in exon 5 of the SLC14A1 gene (c.191G>A; p.R64Q) causes loss of JK*02 expression.

Summary/Conclusions: Eight novel rare blood group alleles were detected by genotyping donors and patients for which serology could not provide a conclusive result. An expanding database of all blood group alleles with corresponding serology should support the prediction of the blood group phenotypes from genotypes.

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IDENTIFICATION OF BLOOD DONORS WITH RARE RED BLOOD CELL PHENOTYPES USING LOW-COST PROTOCOLS

K Guz[1], A Orzińska[1], M Pelc-Kłopotowska[1], M Krzemienowska[1], P Bartoszewicz[1], J Duda[1], A Walaszczyk[2], A Żmudzin[3], A Szelążek[4], M Lewicka[5], A Lipińska[6], W Żurawska[7], J Wróbel[8], B Michalewska[1] and E Brojer[1]

[1]Department of Immunohematology, Institute of Hematology and Transfusion Medicine [2]Regional Blood Transfusion Centre, Warsaw [3]Regional Blood Transfusion Centre, Radom [4]Regional Blood Transfusion Centre, Wałbrzych [5]Regional Blood Transfusion Centre, Poznań [6]Regional Blood Transfusion Centre, Szczecin [7]Regional Blood Transfusion Centre, Słupsk [8]Regional Blood Transfusion Centre, Białystok, Poland

Background: Patients immunized to high prevalent erythrocyte antigens require compatible transfusion from donors with no such antigens. Identification of the donors with rare blood group - antigen-negative - at low cost is possible using high throughput genotyping methods.

Aims: Identification of Yt[a/b], Kp[a/b], Do[a/b], Di[a/b], Co[a/b], LW[a/b], Lu[a/b], Kn[a/b] i Vel (+)/(-), LAN (c.574C>T) polymorphisms encoding rare antigens and determination of the frequency of such alleles in a group of Polish blood donors.

Methods: DNA from 948 blood donors from Regional Blood Transfusion Centres was isolated automatically using Chemagic DNA Blood Kit LH (Chemagen) with Janus pipettor (Perkin-Elmer). Allelic discrimination of 10 polymorphisms was performed automatically in 96-well format by real-time PCR (LightCycler 480, Roche) according to standardized home-made protocols.

Results: Among 948 blood donors six donors with YT*B/B genotype and one with homozygous LAN (c.574C>T) genotype were identified. The estimated frequency of tested rare alleles in Polish population is as follows: YT*A 0.932/YT*B 0.068; KP*A 0.006/KP*B 0.994; DO*A 0.319/DO*B 0.681; DI*A 0.002/DI*B 0.998; CO*A 0.945/CO*B 0.055; LW*A 0.978/LW*B 0.022; LU*A 0.019/LU*B 0.981, KN*A 0.979/KN*B 0.021, VEL(+) 0.986/VEL(-) 0.014, LAN(+) 0.989/LAN(-) 0.011.

Summary/Conclusions: (1) Donors identified with unique rare antigens Yt[a]-negative and Lan-negative have extended the Polish rare blood donor registry and are valuable for diagnostic purposes and transfusion in patients with anti-Yt[a] and anti-Lan antibodies.

(2) The estimated frequency of alleles indicates that identification of homozygous donors in the remaining rare antigens requires testing of at least 10,000 donors.

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THE IMPACT OF MOLECULAR MATCHING ON RED CELL ALLOIMMUNIZATION IN TRANSFUSION-DEPENDENT PATIENTS

L Castilho, S Menegati, T Delfino, M Macedo and S Gilli

Hemocentro, Unicamp, Campinas, Brazil

Background: Red cell alloimmunization is a serious problem in chronically transfused patients. Routine phenotyping of blood recipients and the use of phenotype-matched blood units for transfusion has been useful to lower the occurrence of red cell alloantibodies in those patients but extensive phenotyping is expensive, laborious and cannot be performed in certain situations. The molecular understanding of blood groups has enabled the design of assays that are being used to better guide matched red blood cell transfusions and to maintain an inventory of units DNA typed.

Aims: Based on this, our aim was to evaluate the impact of molecular matching on the incidence of red cell alloimmunization in transfused patients with Sickle Cell Disease (SCD), thalassemia and with myelodysplastic syndrome (MDS).

Methods: Blood group genotypes were determined in 67 DNA samples from chronically transfused patients with SCD, in 65 patients with thalassemia, in 43 patients with MDS and in 5000 DNA samples from blood donors. Laboratory developed tests (LDTs), HEA BeadChip™, RHD BeadChip™, RHCE BeadChip™, and sequencing were used to determine the genotypes among patients and donors. Molecular matching was performed in 3 levels: (1) RH and K matching; (2) extended matching and (3) extended matching including RH variants. We considered the total of red blood cell units requested for each patient and a number of 2 donations per year for the compatible donors.

Results: According to the patients needs we performed molecular matching for 100% of our MDS patients and 70% of our thalassemic patients at level 1, 90% for SCD patients and 30% for patients with thalassemia at level 2 and 30% for patients with SCD at level 3. The patients were transfused with a median of 36.4 RBC units. After five years of molecular matching, the overall incidence of RBC

alloimmunization decreased from 36.8% to 10.5% in the patients with MDS, from 38.5% to 16.7% in the patients with thalassemia and from 52.4% to 25.6% in the patients with SCD.

Summary/Conclusions: Molecular matching has shown clinical benefits to our transfusion-dependent patients, contributing significantly to reduce the rates of alloimmunization with Rh and K matching in the MDS and thalassemic patients and with extended matching in SCD patients. Improvements in the clinical outcomes of the patients with SCD receiving extended molecular matching blood including RH variants have also been observed as shown by an increase in their Hb levels and reduction in the % of HbS, better in vivo RBC survival and diminished frequency of transfusions.

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APPLICATION OF MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION (MLPA) ASSAY FOR HIGH-THROUGHPUT GENOTYPING OF CHINESE DONORS

Y Ying, X Xu, X Hong, K Ma, J He, F Zhu and W Hu

Zhejiang provincial Key Laboratory of Blood Safety Research, Blood Center of Zhejiang Province, Binjiang, Hangzhou, Zhejiang, China

Background: Genotyping of common red blood cell (RBC) antigens have been successfully applied in some routine testing, such as discrepantly serologic results, lack of commercial antibodies, screening of rare blood group donors, and so on. It is a more effective and accurate method than traditionally serologic assay. Many molecular techniques (AS-PCR, PCR-RFLP, real-time PCR, etc.) have been developed base on single nucleotide polymorphisms (SNP) between antithetical alleles and detected only single blood group system for one test. Thus, they are almost low-throughput and have limitation for some routine testing.

Aims: To overcome the limitation of conventional serology and establish a high-throughput and low costs assay, a High-throughput genotyping assay based on multiplex ligation-dependent probe amplification (MLPA) technology was applied in Chinese population.

Methods: Three different probe combinations, including 104 sites were used to detect the samples. The MLPA reaction was performed on a thermocycler (ABI 9700, Applied Biosystems) according to the manufacturer's instructions (MRC-Holland). MLPA probes were hybridized and ligated with the DNA. The ligation products were PCR amplified using fluorescence-labeled universal primers, and the PCR products were electrophoretically analyzed in POP-7 polymer on a DNA analyzer (ABI 3730, Applied Biosystems). A computer program (coffalyser, MRC Holland) was used to analyze the raw data. Also, the copy numbers of some alleles, such as RHD, were determined by MLPA.

Results: Three multiplex PCR systems were able to simultaneous analysis 104 sites, including 18 red blood cell groups (RH, Colton, Cromer, Diego, Dombrock, Duffy, Gerbich, Indian, Kell, Kidd, Knops, LW, Lutheran, Lewis, MNS, Ok, Scianna, Yt) and two platelet antigen systems(HPA-1and HPA-2). The clear and typical peak positions and fluorescence peaks of the amplified fragments were clearly discernible. Eighteen blood group and two platelet antigen systems genotypes of each sample were obtained after analysis by software. The position of the peak is related to the length of the amplified fragment, and the position of the mutation and the blood group antigen can be determined according to the position of the peak. The height of the fluorescence peak is related to the amount of the amplified product, and the copy number of the template can be quantitatively determined according to the peak of fluorescence. The results were found to be concordant with direct DNA sequencing completely and additional experiment (Hybrid Rhesus box test).

Summary/Conclusions: The blood-MLPA assay could easily and simultaneously identify the common blood-group alleles and correctly predicted phenotype in the Chinese population. It can provide a simple and high-throughput tool for DNA genotyping in the Chinese donor screening.

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ABO AND RH PHENOTYPE DISCREPANCIES DUE TO CHIMERISM AS A RESULT OF TWIN HEMATOPOIESIS

C Bub[1], L Santos[1], E Bastos[1], T Costa[1], M Aravechia[1], M Torres[2], L Castilho[3] and J Kutner[1]

[1]Hemotherapy e Cell Therapy [2]Clinical Pathology, Hospital Israelita Albert Einstein, São Paulo [3]Blood Bank, University of Campinas, Campinas, Brazil

Background: Blood group chimerism is a rare phenomenon occurring either congenital or acquired, and few cases are described in the literature. Since these cases do not present major clinical manifestations and are usually recognized at the time of blood group typing by mixed-field agglutination or discrepancies of cell typing / serum typing, it requires further evaluation.

Aims: We herein describe a case of female twins with ABO and Rh antigens permanent chimerism detected during routine ABO and Rh typing.

Methods: ABO and Rh typing were performed by hemagglutination in gel cards while ABO genotyping was performed by PCR-RFLP. Salive studies were performed by inhibition of hemagglutination in tube. A 21 short tandem repeat (STR) loci with the PowerPlex Fusion PCR Amplification Kit (Promega Corporation, USA) and ChimerMarker software (SoftGenetics) was used to verify the presence of chimerism.

Results: A 21-year old female donor was found to have mixed-field reactions in both ABO forward typing and Rhc typing. Mixed-field reactions in gel test with anti-A, anti-B and anti-c reagents ranging from 1 to 2 + were found during a donor typing routine. On reverse ABO grouping, donor plasma was nonreactive with group A and B RBCs. This donor was asked for a new blood collection, together with her relatives (father, mother and a twin sister). RBC and salive samples were collected from all of them. Father sample typed as B RhD-positive while mother sample typed as A RhD-positive without discrepancies in ABO typing. Both twins samples reproduced the same results initially detected in ABO typing and salive studies showed secretion of A and B substances. Mother, father and the twins typed as D+C+c+E-e+ (R_1r), however a mixed-field reaction was observed in the c antigen typing of the twins. ABO genotyping analysis performed by PCR-RFLP demonstrated an apparent ABO*A2.01/O.01.01 genotype. Twenty one short tandem repeat (STR) loci performed on genomic DNA extracted from twins' peripheral blood showed one or two additional peaks besides, the main tall STR peaks in at least six loci (D16S539, D18S51, D2S1338, vWA, TPOX, D8S1179), which were consistent with the presence of the chimerism.

Summary/Conclusions: This is a rare case of an ABO and Rh discrepancy that was found during routine donor typing in a donor with a twin sister. Although an uncommon occurrence, this is a permanent chimerism involving twins and two blood group systems with the presence of O, AB, c + and c – phenotypes. Despite being a rare phenomenon, diagnostic suspicion for the presence of a chimera is necessary in order to resolve typing discrepancies and to provide compatible blood for transfusion.

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STUDY OF ANTIBODY STRUCTURE SUITABLE FOR HEMAGGLUTINATION REACTION

R Tobita, Y Matsumoto, M Uchikawa, N Tsuno and K Nakajima

Kanto-Koshinetsu Block Blood Center, Japanese Red Cross, Tokyo, Japan

Background: The erythrocyte agglutination reaction in the saline test is dependent on the ability of the antibodies to form bridges across adjacent erythrocytes. Except for some IgG antibodies against some blood group antigens, most of the IgG antibodies are not able to induce erythrocyte agglutination in the saline test. It has been reported that the ability of some IgG antibodies to induce hemagglutination is dependent on the different length of the hinge region of the antibody.

Aims: We aimed to produce IgG antibody with the ability to induce direct hemagglutination in the saline test by changing the length of the linker between the scFvD and the hG.

Methods: Variable regions of heavy (VH) and light (VL) chains of the monoclonal anti-RhD antibody synthesized by anti-D producing hybridoma cells were amplified by PCR using the extracted cDNA, and the 3 'side of the VH and the 5′ side of the VL were ligated to a Linker (Gly-Gly-Gly-Gly-Ser)$_3$ to make a scFvD. Flexible Linkers (FL) were composed of (Gly-Gly-Gly-Gly-Ser) n as one unit, and prepared as a joint between the scFvD and the human IgG H chain constant region (hG). By adjusting the copy number "n", the length of FL suitable for the induction of hemagglutination was examined.

Results: Each of the obtained antibodies showed the ability to induce direct agglutination of D-positive red blood cells in the saline test. The antibody titers required to induce hemagglutination of R_1R_1 cells in the saline test at room temperature were

32 (agglutination score: 52) for scFvD(FL0_hG), 64 (67) for scFvD(FL3_hG), 32 (62) for scFvD(FL5_hG), 128 (79) for scFvD(FL7_hG) and 32 (66) for scFvD(FL9_hG).

Summary/Conclusions: All the produced antibodies were able to induce hemagglutination of antigen-positive red cells in the saline test. Although the molecular size of the produced monoclonals was similar to that of IgG molecules, the scFvD (FL0_hG), in particular, was able to induce strong direct hemagglutination in the saline test. Elimination of the constant region of the light chain may have improved flexibility of the IgG molecule, resulting in the ability to form bridges across adjacent erythrocytes. In addition, in this experiment, FL_7 of (Gly-Gly-Gly-Gly-Ser)$_7$ yielded the highest antibody titer, so we concluded that it has the most suitable length and flexibility for crosslinking erythrocytes. This genetically engineered monoclonal antibody may be useful for application in the laboratory testing of red cells especially in tube test and gel column testing without need of additional reagents.

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ANTIBODY FORMATION PREDICTION IN TRANSFUSION–DEPENDENT PATIENTS

J Tan[1,2], G Kidson-Gerber[3] and P Mondy[4]

[1]*Sydney Medical School, University of Sydney, Camperdown* [2]*Research and Development, Australian Red Cross Blood Service, Alexandria,* [3]*Department of Haematology, Prince of Wales Hospital, Randwick* [4]*Medical Services, Australian Red Cross Blood Service, Alexandria, Australia*

Background: A collection of single nucleotide polymorphisms (SNPs) within immunological genes and signalling pathways derived from gene chip screening proved useful in predicting anti-D immunoglobulin production for RhD-immunised healthy blood donors (Tan, Molecular Immunology, 2015). It is uncertain whether these same SNPs could have predictive value for patients that may receive antigen-incompatible blood transfusion.

Aims: We hypothesise that these identified genetic factors could be useful for predicting alloantibody formation in transfusion-dependent patients. Opportunities to conduct such studies are limited; patients are not deliberately transfused with non-self antigens. However, in the course of transfusion support to patients requiring red cells, they may receive phenotype mismatched units.

Methods: Regular transfusion patients (n = 46) at a Sydney metropolitan hospital were assigned as either a Responder or a Non-Responder profile based on their alloantibody/autoantibody status. DNA was extracted from thalassaemia patient blood samples (n = 42) and genotyped for target SNPs and their predicted Responder profile generated using our predictive model.

Results: Twenty nine percent of thalassaemia patients and 75% of sickle cell disease patients had formed antibodies. Older thalassaemia patients were more likely to have developed antibodies than their younger counterparts (P value = 0.033). Responder thalassaemia patients were significantly associated with two SNPs (BLNK, P value = 0.005; TSLP, P value = 0.05). The predictive model predicted 17 thalassaemia patients currently assigned as a Non-Responder based on their alloantibody/autoantibody status as likely to be Responders.

Summary/Conclusions: Findings from this predictive model indicate that the 17 thalassaemia patients classified as Responders may have a higher propensity to develop alloantibodies, and should continue to receive fully matched phenotyped red blood cell transfusions. Longitudinal follow up of these patients is required to determine if the predictive model was accurate.

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STORED RED BLOOD CELLS SUPPRESS ANTIGEN PRESENTATION FUNCTION OF DENDRITIC CELLS

X Wang, M Zhao, Q Zhou and L Zhan

Beijing, Peking, China

Background: A complex array of physicochemical changes happen to red blood cells (RBCs) during storage leading to post-transfusion enhanced clearance. Dendritic cells (DCs) play a crucial role in the engulfment of aged RBCs, however, it still lacks evidences on how stored RBCs (sRBCs) modulate their responses to the inflammatory stimuli, homing and antigen presentation ability.

Aims: To study interactions between stored RBCs and DCs, the inflammation responses initiated by stored RBC, migration and antigen presentation ability of DCs after co-incubation were monitored as indicators to shed light on the specific correlations.

Methods: We used C57BL/6J mice fresh RBC, stored RBC and PBS separately stimulated imDCs derived from mouse bone marrow at 37°C for 10 h with a low dose of LPS ex vivo. Co-culture supernatants were collected for batch analysis of cytokines and chemokine secretions by ELISA. DCs were then collected for phenotype analysis by FACS and the in vivo distribution and migration dynamics by bioluminescence imaging after adoptive transfusion, and the proliferation and activation of antigen-specific CD8 + T cells elicited by DCs were also detected.

Results: More sRBCs were internalized by DCs compared with the fresh ones, and blocking the CD47-SIRPα interaction significantly decreased the engraftment. The accumulation of sRBCs significantly promoted the expression of allostimulatory molecules as well as the secretion of Th1 type cytokines in the presence of LPS.In particular, the lymphoid-tissue homing ability of transfused DCs treated by sRBCs was also significantly higher than its fresh counterparts. An elevation of CCR7 and more well-organized cytoskeletons were measured in sRBCs treated DCs (sRBCs-DCs), with Rho/ROCK, PI3K/Akt and NF-κB pathways involved. On the contrary, the proliferation, activation and IFNγ secretion of antigen-specific CD8 + T cells in the stored RBC group. We demonstrated the opposite regulatory effects of the DCs' ability to prime the suppression of antigen-specific T lymphocytes by stored RBCs. The inhibition of antigen presentation in stored RBCs treated DCs was not mediated by alterations of antigen engulfment or MHCI/peptide TCR interaction but was probably associated with down-regulation of intracellular levels of immunoproteasome responsible for antigens processing in DCs.

Summary/Conclusions: Although stored RBCs are capable of promoting DCs to home to T cell abundant region, it does not mean that the sRBCs threw themselves into increasing DCs ability to initiate the downstream immune responses, which is maybe partly responsible for the immunosuppressive effects of stored RBCs transfusion.

Platelet Immunology

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MATERNAL ANTI–ALPHAIIB ANTIBODIES MAY LEAD TO MISCARRIAGE AND PANCYTOPENIA IN FNAIT BY TARGETING FETAL HEMATOPOIETIC STEM CELLS

B Oswald[1,2,3], J Sullivan[1,2], J Li[1,2,3,4], B Vadasz[1,2], P Chen[4,5], M Poncz[6,7], J Freedman[1,2,3,8] and H Ni[1,2,3,4,8,9]

[1]*Laboratory Medicine and Pathobiology, University of Toronto* [2]*Laboratory Medicine, Keenan Research Centre for Biomedical Sciences, St. Michael's Hospital* [3]*Toronto Platelet Immunobiology Group, St. Michael's Hospital and The Hospital for Sick Children* [4]*Research and Innovation, Canadian Blood Services* [5]*Laboratory Medicine, Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Toronto, Canada* [6]*Pediatrics, The Perelman School of Medicine at the University of Pennsylvania* [7]*Division of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States of America* [8]*Medicine* [9]*Physiology, University of Toronto, Toronto, Canada*

Background: Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a disorder caused by maternal immune responses against paternally inherited platelet antigens, characterized by severe bleeding including intracranial hemorrhage (ICH), intrauterine growth restriction, and death. FNAIT occurs in 0.5–1.5/1000 liveborn neonates, however this may be underestimated due to miscarriage. αIIbβ3 integrin is the most commonly targeted protein, and although the number of polymorphisms in the αIIb and β3 subunits are similar, the reported incidence of β3-mediated FNAIT is 20–30× greater. We previously demonstrated that the β3 subunit of αVβ3 on endothelial cells can be targeted in FNAIT leading to ICH and placental vascular pathologies (Journal of Clinical Investigation 2015, Nature Communications 2017). αIIb, although mainly expressed by platelets, is now known one of the earliest markers of hematopoietic commitment and expressed by populations of hematopoietic stem cells (HSCs). HSCs are generated in yolk sac and aorta-gonadal-mesonephros region, and migrate to the placenta, fetal liver and finally bone marrow.

Aims: We tested the hypothesis that miscarriage is prevalent in anti-αIIb mediated FNAIT and that maternal anti-αIIb antibodies target HSCs resulting in decreased blood cell counts, increased bleeding and fetal death.

Methods: Our active FNAIT model was established by immunizing female αIIb$^{-/-}$ mice with 10^8 wild-type (WT) platelets and breeding them with WT males. Non-immunized (naïve) αIIb$^{-/-}$ females were bred with WT males as controls. Sera was collected prior to breeding and ultrasound, a loss of >1 g/day, or delivery of dead pups were used to detect miscarriage. Mice were sacrificed at E14.5 and fetuses, placentas and fetal livers were weighed. These tissues, bone marrow, and blood were

prepared as single cell suspensions and analyzed with flow cytometry. Fluorescent markers were used to identify HSCs (Lin⁻/CD34⁺/c-kit⁺) or T cells (CD3⁺/CD4⁺/CD8⁺), B cells (CD19⁺) cells, myeloid lineage cells (CD11b⁺) and megakaryocytes (GPIbα⁺).
Results: Immunizing mice generated a significant anti-αIIb immune response. E14.5 FNAIT fetuses had reduced body and liver weight and bleeding diathesis, and post natal day 1 neonates had low platelet counts. Ultrasound revealed miscarriage mainly occurred at E14.5 of FNAIT pregnancies, and the rate of miscarriage was significantly higher than our β3-mediated model. Sera from immunized mice was able to bind fetal liver HSCs in vitro, suggesting that maternal anti-αIIb antibodies target fetal HSCs in vivo. FNAIT fetuses had reduced overall HSCs and αIIb⁺ HSCs in the placenta, liver and yolk sac. Blood analysis showed reduced T cell and megakaryocyte populations.
Summary/Conclusions: We established an anti-αIIb mouse model of FNAIT and revealed a high rate of miscarriage, which may explain the paucity of reported human cases. Further experiments are in progress to elucidate the mechanisms, and our results currently indicate maternal anti-αIIb antibodies bind and may target fetal HSCs during embryonic development, contributing significantly to impaired placental and fetal liver development, and miscarriage. Studying the destruction of early αIIb+ HSC progenitors may explain the decrease in total HSCs and account for other cytopenias in FNAIT fetuses as well as enrich our general knowledge of HSC development, migration, and differentiation.

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A CASE OF RECURRENT FETAL NEONATAL ALLO-IMMUNE THROMBOCYTOPENIA WITH INTRACRANIAL HEMORRHAGE AND AN ELUSIVE ANTI HPA-5B

G Clarke[1,2], L Beaudin[3], R Leung[4], T Petraszko[5,6] and A Skoll[4,6]

[1]Canadian Blood Services [2]Laboratory medicine and pathology, University of Alberta, Edmonton [3]Canadian Blood Services, Winnipeg [4]Maternal Fetal Medicine, BC Women's Hospital [5]Canadian Blood Services [6]University of British Columbia, Vancouver, Canada

Background: A 35 year- old G1P0 patient presented for perinatal care and was found to have a fetal intra-cerebral hemorrhage (ICH). Serological investigations for HLA and HPA antibodies were negative and genetic studies including whole genome sequencing identified no definitive etiology for the ICH. Maternal and paternal Human Platelet antigen (HPA) mismatch was noted with the maternal genotype HPA-5a/5a and the paternal type HPA-5a/5b. The pregnancy ended in fetal demise. No definitive cause for the ICH was identified. During her second pregnancy, fetal ICH occurred once again.
Aims: To identify emerging anti platelet (or anti-HLA) antibodies that may explain the ICH and determine if treatment for fetal/neonatal allo-immune thrombocytopenia (FNAIT) is warranted.
Methods: Early fetal ultrasound and clinical monitoring was instituted with ICH detected at 21 weeks gestation. Maternal and Paternal HPA genotyping for HPA-1–9, 11 and 15 were performed using the BeadChip BioArray (Immucor). Anti-HPA and anti-HLA antibody investigation was performed by Luminex method on a maternal plasma sample. Follow up testing by ELISA (MAIPA) and maternal plasma/paternal platelet crossmatch confirmed findings. Repeat testing on the same sample confirmed reproducible results. Additional testing by the same methods on a new maternal plasma sample followed one month later.
Results: Maternal and Paternal HPA genotyping confirmed a single HPA mismatch with maternal HPA-5a/5a genotype and paternal HPA-5a/5b genotype. Review of whole genome sequencing data on the fetus from the first pregnancy revealed an HPA-5a/5b genotype. Initial Luminex antibody screen was negative for anti-HPA antibodies and positive for HLA antibodies. Retesting of serum from the first pregnancy was performed and no anti-HLA antibodies were detected. Initial ELISA (MAIPA) revealed no positive results, however the HPA-5b containing test well and the maternal plasma/paternal platelet crossmatch showed higher OD readings than the wells containing HPA-5a platelets. Additional MAIPA testing was performed on the initial sample revealing a weak Anti-HPA-5b antibody by ELISA (MAIPA) and weak reactivity in paternal crossmatch. Repeat sample (sent in 1 month from the first collection) had grown stronger in the screen ELISA(MAIPA) methods and in the crossmatch
Summary/Conclusions: IVIG therapy (2 g/kg per week) was started and continued to the week of delivery. HPA matched platelet donors were identified and one booked for peripartum donation. The ICH remained stable through the remainder of the pregnancy. The baby was delivered by elective C/S at 35 + 2 weeks. Neonatal scan confirmed ICH. The cord platelet count was 287 × 10*9/l, higher than expected in treated FNAIT. Platelets were not transfused. The neonatal platelet genotype was

confirmed as HPA5a/5b. Repeat testing over time may be necessary to identify weak, but clinically significant antibodies. The presence of a maternal/paternal HPA mismatch in the setting of bleeding may be enough to institute therapy in the context of an otherwise un explained ICH. Given the unexpectedly high cord blood platelet count the possibility that the ICH was due to an alternate, as -yet un identified cause must be considered.

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MANAGEMENT OF SUBSEQUENT PREGNANCY AT RISK OF HPA-9B ALLOIMMUNIZATION WITH ADDITIONAL INCOMPATIBILITIES IN HPA-1, -3 AND -15 SYSTEMS

H Brouk, D Bennouar, A Amireche and H Ouelaa

Service of Hemobiology and Blood Transfusion, University hospital center, Faculty of Medicine, University of Badji Mokhtar, Annaba, Algeria

Background: Fetal and Neonatal alloimmune thrombocytopenia (FNAIT) is one of the most frequent causes of both severe thrombocytopenia and intracranial hemorrhage (ICH) in fetuses and term neonates. The diagnosis is established by demonstrating antibodies against human platelet antigens (HPA) and discordance in platelet antigen typing between parents or between the mother and neonate. FNAIT tends to be more severe in infants born subsequently to a mother who previously gave birth to an infant with this condition.
Aims: To report the management of subsequent pregnancy of previous severe NAIT due to the HPA-9b (Max(a)) antibody with additional risks of alloimmunization against HPA-1a, -3b and -15a antigens.
Methods: Noninvasive methods to estimate the severity of FNAIT during pregnancy were used. A platelet Antigen Monoclonal Antibody Immobilization Test (MAIPA) was performed every four to six weeks during pregnancy to test the mother's serum for the strength of anti-HPA antibodies, and for serological crossmatches with paternal platelets to detect rare HPA specificities. Platelet genotyping by PCR-SSP (HPA Ready Gene plus Inno-train Diagnostik GmbH) for HPA -1,-2,-3,-4,-5,-6,-9 and -15 and for HLA (HLA-Ready Gene DR Inno-train Diagnostik GmbH) were performed to detect HPA incompatibilities and to study immunization against HPA-1a antigen. The biological investigations were carried out at the Hemobiology and Blood Transfusion service of the University Hospital Center of Annaba (Algeria).
Results: Platelet genotyping revealed four incompatibilities between parents in HPA-1, -3, -9 and -15 systems. The father was heterozygous for the HPA-9 system and the future infant has a 50% chance of possessing the implicated antigen (HPA-9b). HLA DRB3*01:01 antigen was not found and this could be correlated with the lack of immunization against HPA-1a antigen. No detection of maternal allo-antibodies was observed by the MAIPA test, but low positivities were noted for crossmatches (GPIIb/IIIa) with paternal platelet in favor of anti-HPA-9b alloimmunization. Although there was no increase in crossmatches densities, IVIG treatment has been indicated as a preventive measure from 22 weeks of gestation with a posology of 1 g/kg/week.
Summary/Conclusions: Maternal immunization against HPA-9b is an important cause of FNAIT and should be considered in cases of apparent FNAIT not resolved on the basis of maternal-fetal incompatibility for "common" platelet antigens. Close monitoring during pregnancy can provide proper medical support to this condition and reduce the incidence of neurological sequelae in the fetus and newborn.

P-602

THE CD36 ANTIBODY MAY BE THE PRIMARY PLATELET IMMUNIZATION IN CHINESE

X Xu, S Chen, Y Ying, Y Liu, X Hong, J He, F Zhu and W Hu
Blood Center of Zhejiang Province, Hangzhou, China

Background: Platelet antigens and antibodies play important roles in immune thrombocytopenia. The most important antibody form besides HLA antibody in Caucasian is anti-HPA-1a. However, in Chinese it is not anti-HPA-1a because HPA-1a-negative phenotype is very rare. It is not clear which antibody has the most clinical significance in Chinese.
Aims: The aim of the study was to deduce the prevalence of CD36 antibody and evaluate its importance in the Chinese population.
Methods: The antigen frequencies of CD36 and other HPAs were analyzed and compared according to the data from Immuno Polymorphism Database of EMBL-EBI site and our previous reports. The antigenic mismatching possibility (MMP) of CD36 and HPAs was calculated using corresponding antigen frequency in Chinese and

Caucasian. The prevalence and constituent ratio (%) of antibodies against CD36 and HPAs in Caucasian were reviewed and statistically analyzed according to previous reports. The prevalence and constituent ratio of antibodies in Chinese were estimated using the equation: Ab(Chinese) = Ab(Caucasian) × MMP(Chinese)/MMP(Caucasian). The antibody prevalence and clinical significance were compared between CD36 and other HPAs in both Chinese and Caucasian. The work was supported by National Natural Science Foundation of China (81570170) and Zhejiang High-Level Innovative Health Talents.

Results: The frequency of CD36 wild-type allele and CD36 antigen in Caucasian was 0.9827 and 0.9997, respectively. The corresponding frequency was 0.9452 and 0.9970 in Chinese. So the MMP of CD36 antigen in Chinese was 10 times that in Caucasian (0.003 vs 0.0003). However, the MMP of HPA-1a in Chinese was only about 1/1000 of that in Caucasian (0.000023 vs 0.025). In Caucasian, the antibody with the highest prevalence was anti-HPA-1a (i.e. prevalence: 0.0025, and constituent ratio: 66.5%), followed by anti-HPA-5b, 1b and 5a. The prevalence of CD36 antibody was the same as that of HPA-5a antibody. But the antibody prevalence in Chinese derived from the above equation was completely different from that in Caucasian. The antibody with the highest prevalence in Chinese was CD36 antibody (i.e. prevalence: 0.0007, and constituent ratio: 54.0%), followed by anti-HPA-4a, 5b and 3a. While the calculated prevalence of anti-HPA-1a, along with 5a and 2a in Chinese, was almost the lowest among common platelet antibodies.

Summary/Conclusions: The profile of platelet antibodies between Chinese and Caucasian was completely different due to ethnic and genetic diversity. The major platelet immune antigens in Caucasian were HPA-1a and 5b, while CD36 was in a relatively minor role. On the contrary, CD36, rather than HPA-1a, may be the most clinically significant of platelet antigens in Chinese. Therefore, the primary task in China is to develop sensitive and specific techniques to identify CD36 antibody, and establish CD36-deficiency donor databases.

P-603
INVESTIGATION ON PLATELETS APOPTOSIS INDUCED BY ANTI-CD36 ANTIBODIES

Y Zhou, G Wu, F Lu, Z Zhong and J Lin
Nanning Institute of Transfusion Medicine, Nanning, China

Background: CD36 is broadly expressed on platelets, monocytes, endothelial cells etc. The incidence of CD36 deficiency is 4.13% in Guangxi, China. Antibodies against CD36 developed in CD36 deficiency people are frequently reported in the cases of Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT) and Platelet Transfusion Refractoriness (PTR) in Asian population . The role of programmed platelet death (apoptosis) in thrombocytopenia caused by anti-CD36 antibodies has been relatively under-investigated. Therefore, further detailed should get more attention.

Aims: To investigate the impact of anti-CD36 antibodies on platelets apoptosis and its contribution to platelet dysfunction that compares with anti-HPA-3a antibodies.

Methods: Platelets samples from twenty healthy blood donors were incubated with anti-CD36 antisera and CD36 monoclonal antibodies (Mabs, Clone FA6-152, GPIV), anti-HPA-3a antisera and CD41 Mab (Clone P2, GPIIb), respectively. Meanwhile, platelets were incubated with AB sera and PBS as control groups. The apoptotic events on platelets were detected by JC-1 and Annexin V staining, which analyzed the mitochondrial transmembrane potential (ΔΨm) depolarization and phosphatidylserine (PS) exposure, respectively .

Results: Compared to the percentage of apoptosis in control group (shown as mean ± standard deviation, 30.27 ± 11.89), anti-CD36 antisera(46.51 ± 12.29) and anti-HPA-3a (68.42 ± 14.62) antisera can markedly induce the apoptosis of platelets from healthy blood donors, but the role of anti-CD36 antisera was weaker than that of anti-HPA-3a antisera. The results of Mabs were consistent with the antisera, which CD41 can demonstrate greater platelets apoptosis for the ΔΨm depolarization as well as PS exposure.

Summary/Conclusions: These findings showed that normal platelets were incurred apoptosis by both of anti-CD36 and anti-HPA-3a antisera from thrombocytopenia patients. All the antisera and Mabs can induce the apoptosis of platelets from healthy blood donors, but the effect of CD36 was weaker than HPA. Compared with anti-HPA-3a antibody, it might be related to the less severe clinical manifestations of the newborn with FNAIT caused by anti-CD36 antibody.

P-604
IS IT RELEVANT TO GENOTYPE HUMAN PLATELET ANTIGENS IN OTHER SYSTEMS THAN HPA-1, 3, 5 AND 15?

C Chenet, J Quesne, F Bianchi, S Philippe, N Ferre, C Casale, Y Mammasse, V Jallu, C Martageix and R Petermann
Platelet Immunology, INTS, Paris, France

Background: Human platelet antigens (HPAs) are caused by allele polymorphisms located on 6 genes encoding the main platelet membrane glycoprotein complexes (GPIaIIa, GPIIbIIIa, GPIbIX) and CD109. Platelet genotyping is routinely performed in platelet immunology laboratories by different PCR-based techniques such as SSP, RFLP, RT, beadchip technology or NGS. The panel of antigens used can vary from lab to lab in the same country and is depending on allele frequencies according to ethnic populations under analysis.

Aims: The goal of this study was to determine whether the panel of antigens used in our lab for platelet genotyping was adequate according to our activity focused on fetal and neonatal alloimmune thrombocytopenia (FNAIT) and post-transfusion allo immunisation. Indeed, most of people studied are caucasians. However, because of the mix ethnic populations in Paris and different origin of samples (French overseas departments and territories), it is relevant to use a large panel of antigens for platelet genotyping.

Methods: In this study, platelet genotyping was performed routinely by HPA Bead-chip genotyping kit (CE-IVD BioArray Solutions, Immucor, Warren, NJ), HPA-Ready-Gene kit (CE-IVD, Inno-train Diagnostik GmbH, Germany) and in house SSP-PCR for other rare or private HPA systems. All data between 2015 and 2017 were collected using the Laboratory Information Management System of our institution.

Results: We analyzed the results obtained during the 3 last years (more than 2600 HPA genotyping). Most were done in a context of NAIT. We highlighted the involvement of 4 rare HPA systems in 22 people: HPA-4b (n = 2), HPA-6bw (n = 2), HPA-7bw (n = 1), HPA-9 bw (n = 17) which were detected in the following context: i) HPA-4b in one NAIT, ii) HPA-6bw in one miscarriage and in a prenatal diagnosis done in a background of known anti HPA-6b alloantibody, iii) HPA-7bw was found by chance during thrombocytopenia prospection and iv) HPA-9bw in 2 intracranial hemorrhage explorations and in 8 NAIT studies including one case with the discovery of an anti HPA-9b alloantibody. Moreover, 81 and 87 platelet genotyping analysis for less frequent or private HPA systems such as HPA-12 and HPA-27 respectively, were performed. One HPA-27bw and one HPA-12bw have also been identified, both of them were found in a NAIT context in the absence of detectable antibody in maternal sera. In FNAIT, we also found three individuals in the same family (father plus 2 children) genotyped as HPA-31bw the first HPA antigen (system) located on GPIX.

Summary/Conclusions: In the context of FNAIT or NAIT, the use of a large panel of antigens for platelet genotyping, including some rare and private HPA, makes sense regarding ethnical mixture of the population, particularly in situation where no HPA incompatibility was identified despite a very evocative clinical context. This strategy increases further the possibility of identifying HPA incompatibilities and might guide serological investigation to identify potential alloantibody.

P-605
ADENOSINE DIPHOSPHATE RECEPTOR GENE (P2Y12) SEQUENCE VARIANTS AMONG SWEDISH, PALESTINIANS AND CONGOLESE

MY Asees[1], C Hesse[2] and R Abu Saier[3]
[1]*Laboratory, PMC, Ramallah, Palestinian Territory* [2]*Transfusion medicine, Gothenburg University, Gothenburg, Sweden* [3]*Medical Lab Science, Al-Quds University, Ramallah, Palestinian Territory*

Background: $P2Y_{12}$ receptor plays a central role in platelet aggregation and thrombus formation. Recently, inter-individual variations in platelet response of healthy untreated individuals were established which was explained by genetic variations in $P2Y_{12}$ receptor gene. Several single nucleotide polymorphisms (SNPs) in $P2Y_{12}$ receptor have been associated with increased platelet reactivity and risk of cardiovascular diseases.

Aims: This study aimed to evaluate the pathological H2 haplotype (using G52T as a tag-SNP) and 18C>T polymorphisms in three different ethnic groups; Palestinians, Swedish and Congolese

Methods: The H2 haplotype and 18C>T SNPs were determined in conveniently selected healthy individuals from different ethnic groups (n = 254). The whole exon-3 of $P2Y_{12}$ was sequenced and analyzed by used ABI PRISM 310 Genetic Analyzer. The major and the minor allele frequencies of the $P2Y_{12}$ SNPs were determined in the study population and the genetic differences between ethnic groups in $P2Y_{12}$

were elucidated. In addition, the frequency of the genotypes was calculated among the ethnic groups.

Results: In this study, five benign single nucleotide polymorphisms (SNPs) were genotyped and identified; 18C>T, 36G>T, 162G>T, 546C>T and 989A>G. The overall frequencies of each SNP in all study population (n = 254) was 21.9, 10, 0.4, 0.6 and 0.4%, respectively. The frequency of H2 haplotype among Swedish (n = 55), Congolese (n = 54) and Palestinian (n = 145) was 23.6, 12, and 4.1%, respectively, while the frequency of 18C>T was 20%, 6.5% and 28.3%, respectively. There were significant differences in frequency of H2 haplotype and 18C>T among the ethnic groups (P < 0.001). In regard to the pathological SNPs, all of the study participants were negative.

Summary/Conclusions: There are significant differences in the frequencies of the genetic variants of the $P2Y_{12}$ exon-3 between the study ethnic groups. Further studies should be performed to study the effect of the genetic variations on ADP or TRAP- induced platelet aggregation.

P-606

ESTABLISHMENT OF A MULTIPLEX POLYMERASE CHAIN REACTION SEQUENCE–BASED TYPE METHOD FOR HUMAN PLATELET ANTIGEN SYSTEM 1 TO 6, 15 AND 21

S Chen, X Hong, K Ma, Q Wu, C Chen, J He, F Zhu and W Hu

Blood centre of Zhejiang Province, Hangzhou, China

Background: Human platelet antigen system(HPA) is associated with fetal/neonatal alloimmune thrombocytopenia(FNAIT)and platelet transfusion refractoriness. HPA genotyping by DNA methods is helpful to confirm the specificity of HPA antibodies and for prenatal typing of fetuses in suspected cases of FNAIT. The polymorphism of HPAs was only found in HPA-1 to 6, 15 and 21 systems in Chinese population. There were many polymerase chain reaction sequence-based type(PCR-SBT) methods for HPA, but multiplex PCR-SBT for them was rarely reported.

Aims: The aim of this study was to establish a multiplex PCR-SBT for simple, quick and accurate genotyping of HPA-1 to 6, 15 and 21 systems and estimate their distribution in Chinese Han population.

Methods: 1060 blood samples were collected from random platelet donors after informed consent. The genomic DNA were extracted and genotyped for HPA-1 to 6, 15 and 21 systems. Sixteen specific amplification primers(eight primer pairs) were designed by Primer 3 (v. 0.4.0) software based on the polymorphism sites obtained from the Immuno Polymorphism Database. All the 5′ end of these primers were added different specific adaptors. The eight primer pairs were divided into two groups. One group contained the primers for HPA-(8,11,21,23), HPA-15, HPA-(1,10), HPA-5. The other group consisted of HPA-2, HPA-(3,9,27), HPA-(4,16,19) and HPA-6,7. The amplification parameters were optimized. The primer pairs in the same groups were amplified in one tube. The amplicons were analyzed by electrophoresis and sequenced bidirectionally by four universal sequencing primer pairs designed according to the different specific adaptors in the amplification primers. This work was sponsored by National Science Foundation of China (81371905, 81570170) and the Medical Science Research Foundation of Zhejiang Province (2013KYB077).

Results: The obviously specific bands were observed in the electrophoresis of amplification products and the length of them was consistent with the expected value. The sequencing chromatograms were clear and the genotyping of ten samples from Platelet Immunology Workshop of ISBT was in concordance with the reference results. The b allele frequencies of 1060 platelet donors were 0.0052, 0.0590, 0.4684, 0.0019, 0.0118, 0.0165, 0.4670, 0.0085, respectively.

Summary/Conclusions: A multiplex PCR-SBT for genotyping HPA-1 to 6, 15 and 21 systems in only two amplification reactions was established. The distribution of these systems was analyzed in Chinese Han population.

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Abstract has been withdrawn

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A NEW DISCREPANCY OF HPA-3 GENOTYPING DUE TO A RARE HPA-27BW ANTIGEN IN A CONTEXT OF SEVERE NEONATAL THROMBOCYTOPENIA

G Bertrand[1], A Aarnink[2], C Nivet[1], A Jacques[2], M Cherel[1], V Renac[1] and A Kennel[2]

[1]*Platelet immunology Department, French Blood Services of Brittany EFS, Rennes* [2]*Histocompatibility Laboratory, University Hospital, Nancy, France*

Background: Fetal/neonatal alloimmune thrombocytopenia (FNAIT) results from maternal alloimmunization against fetal platelet antigens. Due to the scarcity of phenotyping reagents in platelet immunology, most laboratories perform genotyping but a number of uncharacterized mutations and single nucleotide polymorphisms located near HPAs have been reported to cause false genotyping results.

Aims: We report here the case of a 28 year-old woman from Angola who gave birth to a severely thrombocytopenic boy. Platelet immunology investigations were performed to identify the cause of neonatal thrombocytopenia.

Methods: Platelet genotyping was performed by PCR-SSP and sequencing, and antibody detection using the MAIPA method.

Results: An HPA-5b feto-maternal allo-immunization was identified. In addition, the mother and the newborn also carried a rare polymorphism (αIIb-c.2614C>A) corresponding to the HPA-27bw allele. The mutation is close to HPA-3 and within the sequence of the PCR-SSP primer used to amplify HPA-3a, which is why this allele was not detected in the newborn.

Summary/Conclusions: Rare platelet antigens should be investigated in absence of any non-immune etiology for fetal/neonatal thrombocytopenia coupled with the absence of evidence of feto-maternal incompatibility among the common antigens. This case also points up the importance of the localization of PCR primers used for HPA genotyping.

P-609

Abstract has been withdrawn

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INCREASED CD8 TREG AND DECREASED TH1 AND TH2 CELLS IN GPIBα DEFICIENT MICE: A POTENTIAL ROLE OF GPIBα IN IMMUNE HOMEOSTASIS?

J Sun[1,2,3,4], G Zhu[2,4], J Li[1,5,6,7], M Xu[1,2], P Chen[2,4,7], K Qian[3], J Yang[3], J Freedman[1,2,4,8] and H Ni[1,2,4,7,8,9]

[1]*Laboratory Medicine and Pathobiology, University of Toronto* [2]*Laboratory Medicine, Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Toronto, Canada* [3]*Blood Transfusion Research Institute, Shanghai Blood Center, Shanghai, China* [4]*Toronto Platelet Immunobiology Group, The Hospital for Sick Children and St. Michael's Hospital* [5]*Laboratory Medicine, Keenan Research Centre for, St. Michael's Hospital* [6]*Toronto Platelet Immunobiology Group, The Hospital for Sick Children and* [7]*Research and Innovation, Canadian Blood Services* [8]*Medicine* [9]*Physiology, University of Toronto, Toronto, Canada*

Background: Platelet GPIbα is the receptor for von Willebrand Factor and plays a critical role in thrombosis and hemostasis. GPIbα deficiency in humans is known as Bernard Soulier Syndrome (BSS), a bleeding disorder. Our previous studies demonstrated that the anti-platelet adaptive response in GPIbα$^{-/-}$ mice is significantly lower compared to β3 integrin deficient (β3$^{-/-}$) mice when immunized with the same-dose of GPIbα and β3 antigen, respectively (Thromb Haemost 2013), suggesting GPIbα deficiency may alter immune homeostasis leading to impairment of a general immune response. However, the roles of GPIbα in the immune system and consequently the immune response have never been explored.

Aims: We examine whether there is any difference in T cell subtypes in GPIbα$^{-/-}$ mice as compared with β3$^{-/-}$ mice and wild-type mice.

Methods: Subtypes of CD8 + T cells, CD8 + Tregs, CD4 + (Th1, Th2, Th17) and CD4 + Foxp3 + Tregs of peripheral blood lymphocytes from GPIbα$^{-/-}$, β3$^{-/-}$ and wild-type mice were phenotypically assessed from 5 to 10 weeks with fluorescence conjugated-antibodies and analyzed by flow cytometry.

Results: We did not observe a significant difference in the percentage of CD3 + CD8 + T cells and CD3 + CD8 + CD25 + Treg cells between β3$^{-/-}$ and wild-type mice in both 5 and 10 week old mice. Interestingly, GPIbα$^{-/-}$ mice had a higher percentage of CD3 + CD8 +, CD3 + CD8 + CD25 + and

CD3 + CD8 + CD103 + Tregs compared with β3$^{-/-}$ mice (% of CD3 + CD8 + : 24.44 ± 0.54 vs 21.78 ± 0.68, P = 0.001, % of CD3 + CD8 + CD25 + : 3.27 ± 0.29 vs 1.79 ± 0.39, P = 0.01,% of CD3 + CD8 + CD103 + : 9.44 ± 0.33 vs 7.74 ± 0.31, P = 0.005, Mean ± SEM). However, the percentage of CD3 + CD8 + CD28 + cells was lower than β3$^{-/-}$ (% of CD3 + CD8 + CD28 + : 3.33 ± 0.45 vs 6.18 ± 0.35, P < 0.0005) and CD3 + CD8 + Foxp3 + T cells exhibited no significant difference. Moreover, 10 week old GPIbα$^{-/-}$ mice still had a higher percentage of CD3 + CD8 + and CD3 + CD8 + CD103 + Treg cells compared to β3$^{-/-}$. Within CD3 + CD4 + T cells, both the total percentage of CD3 + CD4 + T cells and sub-types of CD4 + T cells including Th1 and Th2 were lower in GPIbα$^{-/-}$ compared to β3$^{-/-}$ mice (% of CD3 + CD4 + : 75.56 ± 0.54 vs 78.22 ± 0.68, P = 0.01, % of IL2 (Th1 response): 8.22 ± 0.68 vs 11.94 ± 0.98, P = 0.01; % of IL4 (Th2 response): 2.58 ± 0.41 vs 5.08 ± 0.31, P = 0.001). However, no significant differences between percentages of Th17 and CD4 + Foxp3 + Tregs were observed. Within CD8+ T cells, were significantly increased in GPIbα$^{-/-}$ compared with β3$^{-/-}$ mice.

Summary/Conclusions: These preliminary data demonstrate the percentage of CD8 + T cells and CD8 + Tregs (CD8 + CD25 + , CD8 + CD103 +) in GPIbα$^{-/-}$ mice are significantly higher than in β3$^{-/-}$ mice, while Th1 and Th2 polarized T-cells are decreased. Increased CD8 Tregs in GPIbα$^{-/-}$ mice may partially explain why it is more difficult to stimulate an immune response (e.g. anti-GPIbα antibody generation) in GPIbα$^{-/-}$ mice. Thus, these data uncover a potential novel role of GPIbα in shaping the immune repertoire which may significantly impact the immune system and the immune response. Further characterization and investigation of the immune response is in progress.

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EVALUATION OF GROWTH FACTORS AND CYTOKINES CONCENTRATIONS OF AUTOLOGOUS PLATELET-RICH PLASMA (PRP) AFTER LONG TERM STORAGE AT 4°C WITHOUT ANY PRESERVATION AGENT

B Yang[1,2,3], R Chen[1], K Wei[4], M Tsai[1], C Shiau[3] and H Shang[2]
[1]Department of Pathology, Blood Bank [2]Division of Clinical Pathology, Department of Pathology, Tri-Service General Hospital [3]Graduate Institute of Medical Sciences [4]Graduate Institute of Life Sciences, National Defense Medical Center, Taipei, Taiwan, China

Background: Platelet-rich plasma (PRP) is an autologous product derived from patient's own whole blood by utilizing the process of gradient density centrifugation. Multiple studies have demonstrated a role for PRP in accelerating and facilitating improved response to injury. The medical potential of PRP is largely due to the growth factors and cytokines derived from platelets. Recent reports disclosed the influence of the cycling freeze-thaw activation on growth factor and cytokine concentrations, but no study focus on variation of temperature effect during preparation of PRP.

Aims: The purpose of the study is to standardize the preparation of PRP with activated platelets in different temperature setting, which does not require the addition of any substrates and thus not alter the contents of the sample. We analyzed the effect of different temperature settings and long-term storage to the quantification of various growth factors and cytokines.

Methods: PRP samples were collected from 20 healthy donors and a half volume underwent incubation for platelets activation. EGF, IGF-1, PDGF-BB, TGFβ-1 and IL-1β were detected in 2 days after incubation in different temperature settings. There are two patterns of settings, including consistent pattern incubated in liquid nitrogen (LN), very-low temperature (-70°C) low-temperature (4°C and 15°C), mild-temperature (22°C and control), high temperature (37°C) for 60 min and alternative pattern with cooling-warming cycles (4 to 37°C) for 60 min (1cycles, 1.5cycles, 2 cycles and 6 cycles). The resulting growth factor and cytokine concentrations from PRP of different temperature settings were analyzed and compared using enzyme-linked immunosorbent assays (ELISA). The well-done preparation of PRP was stored at 4°C and analyzed the long term effect after 1 month and 6 months.

Results: The concentrations of EGF, PDGF-BB, and TGFβ-1 in PRP prepared from low-temperature, mild-temperature and high temperature settings were lower than which prepared from LN and −70°C settings. The concentration of IL-1β and IGF-1 had no different between five settings. Level of IL-1β, PDGF-BB, and TGFβ-1 in PRP prepared from liquid nitrogen were higher compared to very-low temperature settings. PRP from LN/0.5 h and -70°C/0.5 h group were kept 1 month at 4°C and the level of all the growth factor increased. Level of IL-1β and EGF in PRP increased and approximately two folds in EGF after 6 months storage at 4°C. However, level of IGF-1, PDGF-BB, and TGFβ-1 in PRP decreased and lower than fresh PRP.

Summary/Conclusions: This method is useful for in vitro laboratory experiments because it uses a physical, not chemical, mechanism of platelet activation. Despite wide variation of concentrations of platelets-derived growth factors and cytokines, alternative cooling-warming system is still the cost-effective and convenient method for PRP preparation. The growth factor levels on 1 month suggest that autologous PRP can be stored at 4°C without preservative agents, although in vivo studies are required in order to evaluate the clinical efficacy of the measured the growth factor levels.

P-612

PLATELET-DERIVED PF4 ACTS AS A WEAK APOPTOTIC AGENT FOR U266B1 AND K562 CELL LINES IN VITRO

A Goodarzi, F Yari, M Mohammadipour and M Deyhim
Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Islamic Republic of Iran

Background: Platelet factor 4 (PF4; CXCL4) is a homotetramer protein with 29 kDa molecular weight. This CXC chemokine stored in alpha granules and released following upon many agonists. PF4 has a high affinity with heparin and its main function against tumors is angiostasis which may lead to prevent tumor metastasis. This feature mainly mediated by CXCR3 on the endothelial cells. However, PF4 also participates in the pathophysiology of some diseases and can be evaluated as a valuable biomarker.

Aims: We evaluated the apoptotic effect of platelet-derived PF4 and recombinant PF4V1 on the U266B1 and K562 cell lines which express CXCR3 compared with Daudi as CXCR3-negative cell line.

Methods: PF4 was extracted from human platelet concentrates (PCs) by immunoaffinity chromatography and purified by concentration tubes. The quantity of obtained PF4 was measured by enzyme-linked immunosorbent assay (ELISA). Molecular weight and specificity was determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). Cell lines were treated for 72 and 96 h with 90 μg/ml of PF4 or 5 μg/ml of recombinant PF4V1. Apoptosis was assayed by using CD95, WST-1, active caspase-3, lactate dehydrogenase (LDH), and cell count. Paired t-test and Wilcoxon test were used for statistical analysis. P ≤ 0.05 was considered significant.

Results: Platelet-derived PF4 acts weakly to induce apoptosis in U266B1 and K562 cell lines. Our data showed that WST-1 and cell count had significant difference between control and experiment groups (P ≤ 0.05), while CD95, LDH, and active caspase-3 did not (P > 0.05). Likewise, recombinant PF4V1 could not show any considerable apoptotic effect on all markers (P > 0.05).

Summary/Conclusions: We observed that PF4 released from platelets had a weak potency to induce apoptosis in cancerous cell lines in vitro. Other factors may contribute to this process such as applied dose, purification method, cell line type, and its proteoglycan carrier. Moreover, our data clearly demonstrated that the native and recombinant forms of PF4 do not function similarly in the apoptosis pathway.

P-613

INFLUENCES OF RBC COUNT, HEMOGLOBIN CONTENT AND HAEMATOCRIT ON PLATELET COUNT, PROTHROMBIN TIME, ACTIVATED PARTIAL THROMBOPLASTIN TIME, THROMBIN TIME AND FIBRINOGEN IN A HIGH ALTITUDE POPULATION

R Zhang[1], X Yu[2], C Yang[1], F Liu[1], Z Wang[1] and C Li[1]
[1]Institute of Blood Transfusion, Chinese Academy of Medical Sciences, Chengdu
[2]Blood transfusion department, People's Hospital of Aba, Ma'erkang, China

Background: Although hypoxia has been reported to cause the significant change of red blood cells (RBCs) and increase the risk of thrombotic diseases in people who in residents at high altitude, the relationships between RBCs and factors which contributing to clot strength remain largely unclear.

Aims: To explore the relationships of RBC count, hemoglobin (HGB) content and haematocrit (HCT) on factors which contributing to clot strength in high altitude population.

Methods: A total of 433 volunteers were eligible for this study and were divided into three groups according to RBC count, HGB content and HCT respectively. PT, APTT, TT and Fbg were measured by clotting assays. RBC count, HGB content, HCT and platelet count were assessed by using an automated hematology analyser.

Results: PT and APTT showed significant positive correlation with RBC count, HCT and HGB content (r = 0.313, 0.257 and 0.230, resp. for PT; r = 0.240, 0.177 and

0.140, resp. for APTT; all p < 0.01) whereas a negative relationship was observed for PLT count (r = -0.100, -0.259 and -0.264, resp.; all P < 0.05). A small correlation was found between Fbg and HCT (r = 0.105; P = 0.028), TT and Fbg showed no correlation with RBC count, HGB content and HCT. Mean PT level was significantly higher in high RBC, HCT and HGB groups than in medium and normal groups (p < 0.05 for all comparison); mean APTT level was significantly higher in high RBC and HCT groups than in medium groups (p < 0.05 for all comparison), while mean PLT count was significantly lower in high HCT and HGB groups than in medium and normal groups (p < 0.05 for all comparison).

Summary/Conclusions: RBC count, HGB content and HCT was showed different effects on factors contributing to clot strength such as platelet count, Fbg, PT, APTT and TT. These new data on a high altitude population are quite helpful to the further studies of the formation mechanism of altitude thrombotic disease.

P-614

FLOW CYTOMETRY PLATELET CROSS-MATCHING FOR IMMUNOLOGICAL PLATELET REFRACTORINESS: THE ROLE OF MEAN CHANNEL SHIFT AS A PREDICTOR OF CORRECTED PLATELET COUNT INCREMENT

J Franz[1], I Fagundes[2], J Cardone[2], L Jobim[2], T Oliveira[2], D Speransa[1] and L Sekine[1]
[1]Hemotherapy [2]Immunology, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

Background: We have recently implemented flow cytometry platelet cross-matching at our center and analysed how some parameters would influence platelet count increment, especially mean channel shift, which is a variable conventionally evaluated dichotomously. Little is still known over platelet cross-match reference values and some of them are reproductions from solid organ transplantation experience.

Aims: To evaluate mean channel shift as a continuous predictor for platelet corrected count increment (PCI), while controlling for other relevant factors.

Methods: We have prospectively enrolled platelet transfusion refractory (PTR) patients into a platelet cross-match protocol guided by a flow cytometry screening. Data were collected regarding 24 h PCI that was based on corrected count increment (CCI) formula, ABO compatibility, the number of transfused platelets and flow cytometry derived mean channel shift (MCS). Cross-matches were performed by sensitizing platelets from donors with patient serum followed by IgG-FITC staining and acquired on FACS Canto II. Cross-matches were considered positive when MCS was equal or greater than 63 channels (1.5 SD from negative control).

Results: From 2016 March to 2018 January, a group of 11 patients were enrolled. These patients received a total of 176 crossmatched platelet transfusions (CPT), two-thirds of which (67%) were considered compatible (based on described criteria). The majority of transfusions were ABO-matched (65.3%). Median platelet count was 9 × 10ˆ3/mcL (6–13) previously to transfusion and 20 × 10ˆ3/mcL (12–31.5) afterwards. For compatible CPT, median post-transfusion platelet count (23 × 10ˆ3/mcL, 16–34) and PCI (7,554, 1,826–11,521) was higher than for incompatible CPT (15 × 10ˆ3/mcL, 9–26) and PCI (1,681, -0,560–6,870), P < 0.01. The correlation coefficient between PCI and MCS was -0.29 (P < 0.001), and between PCI and number of transfused platelets was 0.13 (P = 0.092). ABO incompatibility was not associated with PCI (P = 0.76) and MCS (P = 0.185). Although the dichotomic evaluation of Positive/Negative cross-match indeed proved itself an important predictor of PCI (mean difference of 4,576, 95%CI 1,656–7,495, P = 0.002), a linear association between MCS and PCI could also be identified, and a progressive decrease of PCI, of -0.541, was observed for each increment of 25 points of MCS. Median PCI per strata of MCS was: 0–50 (9,228, SE 1,438), 50–100 (5,374, SE 1,855), 100–150 (3,478, SE 1,373), 150–200 (3,443, SE 3,064) and >200 (2,651, SE 2,034), P = 0.001.

Summary/Conclusions: We have observed that for immunological PTR patients, ABO incompatibility and number of transfused patients may not influence final PCI as much as a compatible flow cytometry cross-match. Moreover, MCS presented a linear correlation with final PCI. While stratifying MSC values, we have observed that even MCS values that would be considered incompatible, from a dichotomous standpoint, eventually rendered adequate PCI values. This should not be overlooked, especially in critical situations. However, compatibility must still be sought to prevent further alloimmunization.

P-615

Abstract has been withdrawn

P-616

EVALUATION OF PLATELET CROSS-MATCH IN THE MANAGEMENT OF ONCOLOGY PATIENTS REFRACTORY TO PLATELET TRANSFUSIONS – A SINGLE CENTER STUDY

RN Makroo, D Fadadu, S Agrawal, M Chowdhry and P Karna
Department of Transfusion Medicine, Indraprastha Apollo hospital, New Delhi, India

Background: Platelet refractoriness can represent a significant clinical problem that complicates the provision of platelet transfusions and it is associated with adverse clinical outcomes and increases health care costs. Cross-match-compatible platelets are used for the management of thrombocytopenic patients who are refractory to transfusions of randomly selected platelets. Solid phase red cell adherence assay (SPRCA) technology allows platelet antibody screening and platelet cross match.

Aims: The aim of this study was to determine the effectiveness of cross-match-compatible platelets in a group of oncology patients' refractory to platelets.

Methods: Random ABO compatible 11 single donor platelets (SDP) and 454 random donor platelet (RDP) transfusions given to 60 refractory patients were studied. Patients were defined to be refractory if their 24-h corrected count increment (CCI) was <5 × 10^9/l following two consecutive platelet transfusions. Platelets were cross-matched by SPRCA and the CCI was determined to monitor the effectiveness of platelet transfusions.

Results: Four hundred and three (86.6%) were compatible by platelet cross-matching (8 SDP; 395 RDP) while 62 units (13.4%) were incompatible for the platelet cross match. When compared cross-match-compatible platelets with incompatible platelets, statistically significant improvements were found in the mean corrected count increment (P < 0.001 for each). Compatible platelet transfusions were associated with a good response in 76.8% of cases while incompatible platelets were associated with a good response in 41.1% of transfusion events (P < 0.001). The 24-h CCI (mean ± SD) was significantly higher for cross-match-compatible platelets (9,172 ± 181.4) than for incompatible ones (5,921.46 ± 223.5) (P < 0.0001).

Summary/Conclusions: Cross match compatible platelets lead to higher CCI for platelet refractory patients. Platelet cross-match using SPRCA technology is an effective and rapid approach for selecting compatible platelets in the treatment of thrombocytopenic cancer patients

P-617

HLA-ALLOIMMUNIZATION IN HEMATOLOGICAL PATIENTS

E Butina[1], F Sherstnev[2], E Vaskina[3], N Minaeva[3] and I Paramonov[4]
[1]Laboratory of Immunohematology [2]Transfusiology [3]Haematology [4]Director of the Institute, Federal State Institute of Science "Kirov research Institute of Hematology and Blood Transfusion of the Federal Medical and Biological Agency of Russia", Kirov, Russian Federation

Background: Platelet refractoriness arising from HLA-alloimmunization is a serious complication of transfusion therapy. Transfusion with HLA-matched platelets is required to reduce the risk of bleeding in refractory patients.

Aims: To study frequency of detection of anti-HLA alloantibodies in hematological patients.

Methods: The results of the determination of HLA antibodies in 1842 patients of the hematological clinic in 2013–2017 are analyzed. Screening and identification of antibodies were performed in a complement-mediated cytotoxicity assay and by flow cytometry (BD FACSCanto II, USA).

Results: HLA-antibodies were detected in 2.6% of hematological patients: 0.4% of men, 6.8% of women and 0.6% of children. Antibodies were established in 11.3% of patients with myelodysplastic syndrome, 9.9% - acute leukemia, 2.2% - aplastic anemia and 0.8% - other hematological diseases.

The most indicative criterion for assessing the degree of HLA-alloimmunization is Panel Reactive Antibody (PRA), calculated as the percentage of positive reactions between the patient's blood serum and lymphocytes from different donors. PRA of 10–24% was recorded in 27.1% of patients, PRA 25–49% - 18.8%, PRA 50–74% - 20.8%, PRA 75–99% - 33.3%. HLA-alloimmunization was detected in 55.1% of patients who are refractory to platelet transfusions.

Summary/Conclusions: Thus, despite the use of leukocyte-depleted blood components, the level of HLA-alloimmunization remains high in women, in patients with myelodysplastic syndrome and acute leukemia. HLA antibodies are one of the main reasons for the poor posttransfusion platelet increments.

P-618

PERSISTENCE OF PLATELET REACTIVE ANTIBODIES IN TRANSFUSED PATIENTS

L Pan[1], Z Liu[2] and J Xu[1]

[1]Blood Center of Zhejiang Province, Zhejiang provincial Key Laboratory of Blood Safety Research [2]Sir Run Run Shaw Hospital, Hangzhou, China

Background: Platelet-reactive antibodies, directed against the HLAs and HPA present on the platelet surface, are frequently associated with platelet alloimmunization and clinical refractoriness. A lot of clinical studies have described in detail the phenomenon of platelet antigen alloimmunization, while there are little reports focuses on the persistence of antibodies, especially in china.

Aims: The study was performed to investigate the persistence of platelet-reactive antibodies in transfused patients over a period of 5 years and evaluate this to their transfusion history and pregnancy history.

Methods: A retrospective examination was performed of all records of platelet-reactive antibodies in the blood bank computer database from 2013 to 2017. Records of patients who underwent at least one antibody investigation after an antibody had been detected were studied. Antibody was regarded as not persistent if after previous detection, the screening became negative for the antibody under study. Patients who switch to HLA-matched transfusions were excluded. Platelet-reactive antibodies were detected by solid-phase red-cell adherence (SPRCA) technique. The chi-square test was used to compare the incidence of antibody undetectability between groups.

Results: An analysis was performed of 59 records that fulfilled the criteria. Median antibody follow-up was 5 weeks (range, 1–288). The median age of the 59 patients was 58 years old. They included 29 males (49.2%) and 30 women (51.8%) who had been previously pregnant. In 59 patients, 29 patients (49.2%) became undetectable within 8 weeks, and 43(72.9%) antibodies became undetectable over the course of time. After initial negative screening investigations, antibodies in 3 patients were reformed. There were no differences in duration of antibodies positivity based on the patient previous transfusion numbers and gender(P > 0.05).

Summary/Conclusions: Clinically significant platelet reactive antibodies formation is probably more common than previously realized, because about 49 percent of platelet-reactive antibodies became undetectable within initial 8 weeks. there were no differences persistence rate of antibodies based on the patient previous transfusion numbers and gender.

P-619

INFLUENCE OF DONOR-SPECIFIC ANTI-HLA ANTIBODIES AND ABO COMPATIBILITY ON PLATELET CROSS-MATCHING OUTCOME: A SINGLE CENTER EXPERIENCE

A Arend[1], I Fagundes[1], J Cardone[1], L Jobim[1], D Speransa[2], J Franz[2] and L Sekine[2]

[1]Immunology [2]Hemotherapy, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

Background: Clinical platelet transfusion refractoriness (PTR) can be caused by immune and non-immune mechanisms. Immune PTR is mainly associated with Human Leukocyte Antigen (HLA) Class I alloimmunization. At our center, PTR management includes flow cytometry platelet cross-match (FCPXM) and Single Antigen Binding for HLA antibodies detection.

Aims: To evaluate the influence of donor-specific HLA class I (CI) antibody (DSA), parallel to the effects of ABO compatibility, on median channel shift (MCS) from FCPXM.

Methods: We have retrospectively evaluated 272 FCPXM involving HLA typed donors, concerning one HLA alloimmunized myelodysplastic syndrome patient (CI panel reactive antibody – PRA – 85%), between June and August 2017. Information on MCS, ABO compatibility and DSA were compiled from medical data. A positive FCPXM was defined by an MCS≥63, and the presence of DSA as having at least one HLA-A and/or HLA-B antibody with ≥1,000 mean fluorescence intensity (MFI), that was further stratified.

Results: DSA were observed in 220 (81%) cross-matches (164 of which had MFI levels higher than 10,000), resulting in 157 (58%) positive FCPXM. MCS values (median, P25–P75) were different among DSA strata: "no DSA" (14, -12–68.25) x "intermediate DSA" (66.5, 45–119.75)(P = 0.02); "no DSA" x "high DSA" (111.5, 61.25–182)(P < 0.001), "low DSA" (35.9, -8–75) x "high DSA"(P < 0.001). There was no difference between "no DSA" x "low DSA", and "intermediate DSA" x "high DSA". A Kendall-tau B correlation coefficient of 0.36 (P < 0.001) was observed between progressive concentrations of DSA and MCS. ABO group compatibility also seemed to influence resulting MCS (mean, standard error), even after controlling for the presence of DSA, as follows: ABO compatible (54.6, ±15.0) x Major incompatibility

(108.3, ±17.2)(P = 0.01), ABO compatible x Bidirectional incompatibility (129.6, ±12.4)(P > 0.001), Minor (68.0, ±5.4) x Major incompatibility (P = 0.023) and Minor x Bidirectional incompatibility (P > 0.001). No significant differences in MCS were found between ABO compatible and Minor incompatibility and between Major and Bidirectional incompatibility.

Summary/Conclusions: Three of the most prevalent HLA-A alleles in Brazilian southernmost region (A*01, A*03, A*24) were found in 142 (52%) of the enrolled donors. Patient PRA presented MFI >10,000 against these 3 antigens, which could explain 58% of positive FCPXM. Moreover, a high proportion of high DSA (60%) could be a result of the PRA 85% observed for this patient. Results for DSA strata allowed us to define 2 major DSA-oriented compatibility groups: no DSA/low DSA (median MCS below 63); and intermediate DSA/high DSA (median MCS above 63). We have concluded that DSA levels of up to 5,000 may not necessarily result in an incompatible FCPXM. On the other hand, MFI values exceeding 5,000 are systematically associated with a positive FCPXM. This finding reinforces the importance of DSA quantitative, rather than exclusively qualitative, evaluation when managing alloimmunized PTR patients. Also, ABO compatibility influenced results of MCS, even when DSA was controlled; supporting the importance of an ABO group guided platelet selection even for patients requiring FCPXM mediated support.

P-620

ESTABLISHMENT OF A LUMINEX BEAD TECHNOLOGY TO SIMULTANEOUS DETECTION OF ANTIBODIES AGAINST HLA AND HPA-2

S Tao[1,2], Y He[1,2], J He[1,2], F Zhu[1,2] and W Hu[1,2]

[1]Blood Center of Zhejiang Province [2]Zhejiang provincial Key Laboratory of Blood Safety Research, Hangzhou, China

Background: Platelet antibodies are closely related to platelet transfusion refractoriness (PTR). Of the PTR patients, 70–85% can detect antibodies against human leucocyte antigens (HLA) and 20–30% has antibodies against human platelet antigens (HPAs). Therefore, detection of antibodies against HLA and HPA is crucial for platelet transfusion therapy. However, a reliable method simultaneous detecting HLA and HPA antibodies has not yet been described in China.

Aims: To detect HPA-2 and HLA antibodies simultaneous by Luminex beads coupled with antibodies against platelet glycoproteins (GP)Ib/IX and HLA, and compared with monoclonal antibody immobilization of platelet antigens (MAIPA) assay.

Methods: Antibodies specific for GPIb/IX (clone: AK2) and HLA (Clone: W6/32) were separately coupled to Luminex xMAP beads LC10036-01 and LC10050-1, mouse anti-human IgG was coupled to Luminex xMAP beads LC10086-01 for positive control. The coupled beads were validated by anti-mouse/ rabbit IgG. Then, eight serum samples (L1–L8) containing HLA or HPA antibodies confirmed by monoclonal antibody-specific immobilization of platelet antigens (MAIPA) were tested in this study. Eight sera (N1–N8) without HPA or HLA antibodies were prepared from AB type blood donors for negative controls. Platelets were collected from four individuals (P1 to P4) with known HPA genotypes (P1:HPA-1aa, HPA-2ab, HPA-3ab, HPA-4aa, HPA-5aa, HPA-6aa, HPA-15ab; P2: HPA-1aa, HPA-2aa, HPA-3ab, HPA-4aa, HPA-5aa, HPA-6aa, HPA-15aa; P3: HPA-1aa, HPA-2ab, HPA-3aa, HPA-4aa, HPA-5aa, HPA-6aa, HPA-15bb; P4: HPA-1aa, HPA-2aa, HPA-3bb, HPA-4aa, HPA-5aa, HPA-6aa, HPA-15aa) and reacted with sera respectively, and then the reaction complexes were lysed and incubated with luminex beads mix, and then subjected to flow cytometric analysis on a Luminex100. Cut-off value was calculated, MFI≥ cut-off value was identified as positive.

Results: Significantly higher MFI values than cut-off values (9694 vs 81 for HLA, 4220 vs 219 for AK2, 2414 vs 20 for IgG) were observed in beads coupling confirmation experiment, suggesting that antibodies against GPIb/IX and HLA have been successfully coupled to Luminex beads. The results showed that the MFI values of L1, L2, L3, L4, L5, and L8 from LC10050 were significantly higher than cut-off value (1135~15261 vs 20~81), implying that these serum samples were anti-HLA positive. The MFI values of L2 and L6 from LC10036 were higher than cut-off value (775~935 vs 20~81) when reacted with P1 and P3, but lower than cut-off value when reacted with P2 and P4, illuminating that L2 and L6 were positive for HPA-2b antibody depending on the specificities of the HPA genotypes of platelets donors. L7, a sample positive for anti-HPA-5b, exhibited negative result in our Luminex beads technology, illuminating our technology could not be affected by other HPA antibodies. The other seven samples tested by Luminex bead technology were consistent with MAIPA results, illustrating that Luminex beads technology was capable of detecting HLA and HPA antibodies.

Summary/Conclusions: The Luminex beads coupled with GPIb/IX and HPA antibodies could be successfully used to detect HPA-2 and HLA antibodies simultaneous.

P-621

Abstract has been withdrawn

P-622

PLATELET IMMUNOLOGY SERVICE IN AN ACUTE REGIONAL HOSPITAL IN HONG KONG

K Yan, C Chan, Y Leung and C Lam

Division of Haematology, Queen Mary Hospital, Pokfulam, Hong Kong

Background: There is a high demand for platelet immunology service in Queen Mary Hospital in Hong Kong, which is an acute regional hospital with territory-wide tertiary and quaternary cares, including solid organ and haematopoietic stem cell transplantation (HSCT), haemato-oncology and a wide range of adult and paediatric surgical services. A total request for platelet immunology tests in 226 suspected autoimmune thrombocytopenia (AITP), 19 platelet transfusion refractoriness (PTR) and 8 neonatal alloimmune thrombocytopenia (NAIT) studies was recorded in the past 2 years.
Aims: Accredited platelet immunology service was established to support timely diagnosis and management of unexplained thrombocytopenia and platelet transfusion refractoriness.
Methods: Platelet antibodies were detected with monoclonal antibody-specific immobilization of platelet antigens (MAIPA), luminex, antigen-capture ELISA and platelet immunofluorescence test (PIFT). Regarding MAIPA, a panel of monoclonal antibodies was selected to target for CD41, CD61, CD49b/CD29, CD42a, CD42b, CD109, CD36 and HLA Class I antigens. Human Platelet Antigen (HPA) typing was performed by polymerase chain reaction-sequence specific primer (PCR-SSP) method, covering HPA-1, 2, 3, 4, 5, 6, 9 and 15 systems. CD36 phenotyping was done on platelets and monocytes by flow cytometry with CD36-FITC, CD64-PC5 and CD45-PC7 monoclonal antibodies. HPA typed platelet panel was established among Group "O" staff so that fresh platelets for labile HPA-3 and -15 antigens were readily available.
Results: From 1st January 2016 to 31st December 2017, 226 cases were received for platelet autoantibody study, mostly compatible with a clinical diagnosis of AITP. Others included unexplained scenarios of isolated thrombocytopenia after HSCT and peripheral consumptive thrombocytopenia, refractoriness to steroid and IVIG treatment, and thrombocytopenia associated with haematological malignancy and autoimmune diseases, etc. Among the 64 positive cases with platelet glycoprotein antibodies, 37 anti-GPIIb/IIIa (58%), 12 anti-GPIIb/IIIa+Ib/IX (19%), 9 anti-Ib/IX (14%), 4 anti-IIb/IIIa+Ia/IIa (6%) and 2 anti-IIb/IIIa+Ib/IX+Ia/IIa (3%) were detected. Out of the 19 PTR cases, 15 anti-HLA Class I (79%), 1 anti-HLA Class I+HPA-3a (5%) and 1 anti-HLA Class I+HPA-2b (5%) antibodies were detected. Regarding the 8 cases of suspected NAIT, 4 anti-HLA Class I (50%) and 1 "luminex only" anti-GPIIb/IIIa without defined HPA specificity (12.5%) were detected. The mother who carried the "luminex only" anti-GPIIb/IIIa was not thrombocytopenic and gave negative reactions in direct MAIPA and PIFT tests. While the thrombocytopenic baby gave positive reaction in direct PIFT test, the nature and specificity of the "luminex only" anti-GPIIb/IIIa antibody remained unresolved.
Summary/Conclusions: A substantial need of platelet immunology service was shown in the current study for an acute regional hospital in Hong Kong, with requests from all age groups across different clinical specialties, and diagnoses comprising 89% AITP, 8% PTR and 3% NAIT studies. Anti-GPIIb/IIIa followed by anti-GPIb/IX constituted the major platelet autoantibodies, being respectively found in 81% and 36% of autoantibody-positive cases. Anti-HLA Class I was frequently detected at 78% while anti-HPA or platelet glycoprotein antibody was only found in 11% of alloimmune thrombocytopenic cases. There is still a service gap in the identification of novel or rare HPA antigens and hereditary platelet disorders.

P-623

THE EVALUATION OF MAGNETIC ACTIVATING CELL SORTING (MACS) APPLICATION IN PLATELET MICROPARTICLES ISOLATION FROM PLATELET CONCENTRATE

L Tahmasbi[1], S Amini Kafiabad[2] and L kasraian[1]

[1]*Blood Transfusion Research center, High Institute for Research and Education on Transfusion Medicine- Microbiology department, Shiraz, Iran* [2]*Blood Transfusion Research center, High Institute for Research and Education on Transfusion Medicine, Tehran, Iran*

Background: There are different methods for isolation of cell-derived microparticles, that each one has different efficacy in purity and functionality of isolated microparticles population, such as centrifugation, flow cytometry and MACS. MACS technology is a suitable method for the isolation of viable and functionally active cells.
Aims: In current study we used the MACS technique for Platelet Microparticles (PMPs) because we need functionally active PMPs for further activity assay.
Methods: At first, microparticles were prepared by low and high speed centrifugation from platelet concentrate (PC) at the 5th day, Furthermore, PMPs isolated via µMACS Streptavidin Kit, PMPs immunophenotyping was done via flowcytometry method, then PMPs activity assay was performed by ZYMUPHEN MP-Activity. Data were analyzed by comparison test via Med Calc software. P-Value less than 0.05 were considered significant.
Results: The PMPs purity was increased after MACS application (CD41: 72.9% to 96.9%, CD61: 70.8% to 97.6%, CD62p: 58% to 83%), (P-value < 0.05) and the CD62P activity marker also was expressed on PMPs after using the MACS technique. Furthermore, the result of activity assay showed that isolated PMPs were functionally active (36.5% vs. negative control).
Summary/Conclusions: Conclusion: It seems that, MACS application for PMPs isolation is an effective method to improve the purity of PMPs without any effect on the PMPs activity.

P-624

USE OF PLATELET ADDITIVE SOLUTION (PAS), IS THIS BLESSING IN DISGUISE FOR TRANSFUSION MEDICINE

A Agrawal

Transfusion Medicine, Fortis Escorts Heart Institute, New Delhi, India

Background: India is among medium developing country with population over 1.25 billion with areas of difficult terrains, landslides and seasonal outbreaks of Dengue. Benefits of apheresis platelets(SDP) V/S random donor platelets (RDP) are well documented. But the challenge that comes is requirement of group specific donor. Arranging group specific donor is really a challenge especially in cases of international patients, outstation patients and patients that require numerous platelet transfusions in cases like dengue etc. and especially in corporate hospitals that have limited voluntary apheresis blood donor registry.
Advantages associated with use of PAS are: Greater removal of ABO-incompatible plasma, thus reducing the risk of hemolysis, product can be issued across all group patients, lesser allergic reaction to patients, lesser vasovagal reaction to donors, smooth inventory, wastage prevention.
Aims: Demonstrate clinical equivalence of PAS-SDP with group specific SDP if any.
Methods: This study was conducted in multispecialty tertiary health care, corporate hospital of Delhi/NCR where major patient client age is from International patients and Pan-India. Use of PAS(Platelet Additive solution) is approved by DCGI, India and Central Hospital Transfusion Committee of Group Hospital. Use of PAS was implemented on all apheresis prepared using storage solution for platelets using Apheresis platform.PAS is added later on after collection of hyperconcentrated PLT units.
Contaminating white blood cells were removed from all units by the leukoreduction system of the cell separator.
Study Duration: 6 Months.
All donors participating in this study met the Guidelines for the Selection of Blood Donors.
All platelets collected are stored at 22°C under constant agitation, undergo quality control check at Day 1 till Day 5 from platelet pouch even after product issue.
Study markers: Volume of the final product, platelet counts and mean platelet volume (MPV), pH, swirling movement by visual inspection, patient platelet count pretransfusion, patient platelet count on next day after transfusion (Day 1,3) if no fresh transfusion
Results: Totally, 130 apheresis units were prepared on PAS during the study. 126 units were issued to 77 patients. Four units were discarded being date expired.

99.2% of donors under the study were male and 47.7% in age group 18–30 years and 31.5% of blood Group O positive. Final platelet volume prepared was 300 ± 20 ml.MPV was within normal range 7.4–10.4 Fl. Swirling was fully maintained during the study (graded by visual inspection) in all units. Product pH was in the range of 7.1 ± 0.1,platelet count 1538 ± 17 × 103/µl. Patient platelet count was assessed before apheresis transfusion and then 24 h after transfusion. Mean percentage increment (MPI) was 232% and range 64.71%–650%.Mean calculated was 2.82 ± 1.42.No adverse transfusion reactions were noted in any case.

Summary/Conclusions: Use of PAS for apheresis platelets eliminates the need for group-specific platelets converting all SDPs to universal platelets, thereby helping in the better management of available groups without compromise in patient safety.PAS–SDP were comparable to normal SDP both in terms of Platelet count in the blood bag and platelet increment obtained in patients, thereby demonstrating clinical equivalence. No adverse reactions were reported with any of the PAS-SDP group indicating safety. papers on this subject, especially in the Indian subcontinent are few and larger studies are needed before PAS-SDPs become the norm.

Granulocyte Immunology

P-625

DONOR ANTI-HNA-3A, ANTI-HLA CLASS-I AND ANTI-HLA CLASS-II ANTIBODIES INDUCE NEUTROPHIL- AND MONOCYTE-MEDIATED HLMVEC DAMAGE IN A TWO-INSULT IN VITRO MODEL

A Sultana[1,2,3], M Dean[1,3,4], F Temple[1,2,3], M Burton[5], P Hassell[5], G Pahn[5], M Reade[2,6], R Flower[1,2,4] and J Tung[1,2,3,4]

[1]Research and Development, Australian Red Cross Blood Service, Kelvin Grove [2]Faculty of Medicine, The University of Queensland, Queensland [3]The Critical Care Research Group, The Prince Charles Hospital, Chermside [4]Faculty of Health, Queensland University of Technology, Brisbane [5]Platelet and Neutrophil Reference Laboratory, Australian Red Cross Blood Service, Kelvin Grove [6]Joint Health Command, Australian Defence Force, Canberra, Australia

Background: Despite the implementation of risk reduction strategies, transfusion-related acute lung injury (TRALI) continues to be a leading cause of transfusion-related mortality and morbidity. TRALI has been hypothesised to develop via a two-insult or threshold mechanism. The first insult is the patient's morbidity and the second insult is the transfusion, which cause cellular activation contributing to TRALI development. Antibodies targeting human neutrophil antigens (HNA) or human leucocyte antigens (HLA) in blood products can cause TRALI. Animal and laboratory models have sought to define the mechanisms by which TRALI develops. While neutrophils were initially considered as the primary cell responsible for causing TRALI, subsequent studies have identified other pathways dependent on the presence of monocytes and complement. The potential for multiple pathways to contribute to clinical TRALI and, the role of monocytes and complement remains unclear. A two-insult in vitro model of human lung microvascular endothelial cell (HLMVEC) damage was developed to further understand and characterise pathways involved in TRALI development.

Aims: To investigate neutrophil- and monocyte-mediated pathways of TRALI development in a HLMVEC damage model using serum from a donor implicated in a reported case of TRALI.

Methods: Granulocyte immunofluorescence and granulocyte agglutination testing confirmed the presence of anti-HNA-3a, anti-HLA class-I and anti-HLA class-II antibodies in serum from a donor implicated in a reported case of TRALI. HLMVECs were co-cultured with endothelial cell growth medium or lipopolysaccharide (LPS, E. coli O55: B5, 2 µg/ml) for 6 h (37°C, 5% CO_2) to model an underlying infection. Monocytes or neutrophils were isolated (Direct Monocyte and Direct Neutrophil Isolation Kits) from freshly collected whole blood and 0.2×10^6 monocytes or 1×10^6 neutrophils were added to HLMVECs for 30 min (37°C, 5% CO_2). Serum (10% final dilution) ± plasma as a complement source (3% final dilution) was then added for 30 min. Viable HLMVECs were determined via trypan blue staining by two independent observers. Statistical difference was determined at P < 0.05 by a one-way analysis of variance using a Tukey's post-test.

Results: In the absence of LPS stimulation, serum from a donor implicated in a reported case of TRALI did not induce neutrophil- or monocyte-mediated HLMVEC damage. The addition of a complement source to monocyte HLMVEC co-culture did not mediate or enhance damage. Donor serum did induce neutrophil-mediated HLMVEC damage when HLMVECs were first stimulated with LPS. Monocyte-mediated HLMVEC damage was only evident when HLMVECs were pre-stimulated with LPS and when both donor serum and complement source were added.

Summary/Conclusions: These results highlight the critical role of LPS in antibody-mediated HLMVEC damage, demonstrating the role of the patients' underlying pathology in predisposing TRALI development. Together these data provide preliminary evidence that antibody-mediated TRALI can develop via a neutrophil and, a monocyte and complement dependent pathway. As the donor serum contained anti-HNA-3a, anti-HLA class-I and anti-HLA class-II antibodies the pathway by which each of the antibodies induced HLMVEC damage remains to be elucidated. A more precise understanding of what cells, and to what degree, cause TRALI in humans could provide an avenue for potential prophylactic or therapeutic targets.

P-626

MOLECULAR AND FUNCTIONAL CHARACTERIZATION OF FCGRIIIB RECEPTOR-LIGAND INTERACTION: IMPLICATIONS FOR NEUTROPHIL MEDIATED IMMUNE MECHANISMS IN MALARIA

P Simtong[1,2], A Romphruk[3], A Traum[2], M Burg-Roderfeld[2,4], G Bein[2], K Jakubowski[2], A Dominik[5], M Theisen[6,7], I Kana[7], U Sachs[2] and S Santoso[2]

[1]The Centre for Research and Development of Medical Diagnostic Laboratories, Faculty of Associated Medical Sciences, Khon Kaen University, Khon Kaen, Thailand [2]Institute for Clinical Immunology and Transfusion Medicine, Justus Liebig University Giessen, Giessen, Germany [3]Blood Transfusion Center, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand [4]Faculty of Chemistry and Biology, Fresenius University of Applied Sciences, Idstein [5]THM University of Applied Sciences, KITE Centre of Excellence for Information Technology, Giessen, Germany [6]Statens Serum Institut, Copenhagen [7]Centre for Medical Parasitology at Department of International Health, Immunology, and Microbiology and Department of Infectious Diseases, University Copenhagen, Denmark

Background: Fcγ receptor IIIb (FcγRIIIb; CD16b) is a low-affinity glycoprotein that plays a significant role in phagocytosis and the clearance of immune complexes. FcγRIIIb is polymorphic expressing alloantigenic determinants, known as human neutrophil antigen (HNA)-1. Several studies reported the role of HNA on the pathomechanism of alloimmune mediated neutropenia, transfusion-related acute lung injury as well infection and immune complex diseases. Meanwhile, four HNA-1 (-1a, -1b, -1c and -1d) alloforms have been discovered. However, little is known about the role of the rare HNA-1c alloform. Recent evidence indicated that the inheritance of the rare HNA-1c alloform is protective for the malaria. However, the exact mechanism is not known.

Aims: In this study, we characterized the binding properties of different FcγRIIIb alloforms toward IgG and proved their relevance on the protection of malaria.

Methods: We used stable transfected cells and recombinant proteins expressing HNA-1aa, -1bb, and -1bc to characterize the binding properties of these FcγRIIIb alloforms toward IgG and proved their relevance on the efficacy of antibody-specific malaria clearance.

Results: Analysis of both, transfected HEK293 and recombinant proteins showed higher affinity toward IgG than HNA-1a and HNA-1b alloforms of FcγRIIIb. Accordingly, neutrophils derived from HNA-1c (+) individuals bound significantly stronger to IgG and antibodies against the Plasmodium falciparum Glutamate rich protein (GLURP) compared to HNA-1c (-) donors in the presence of P. falciparum merozoites.

Summary/Conclusions: These results indicate that amino acid substitution $Ala_{78}Asp$ responsible for the formation of HNA-1c results in high affinity FcγRIIIb. Consequently, binding of antibodies causes enhancement of neutrophil activation leading to effective clearance of malaria by intracellular ROS.

Fetal-maternal Immunology

P-627

ANTI-SW[A] IN A CASE OF FETO-MATERNAL INCOMPATIBILITY WITHOUT CLINICAL IMPAIRMENT IN THE FETUS/NEWBORN

N Nogués, E España, C González, I Moreno, N Boto, C Canals and E Muñiz-Diaz
Immunohematology, Banc de Sang i Teixits, Barcelona, Spain

Background: The Swann antigen (Sw[a], DI14) was identified in 1959 in the serum of a patient with autoimmune hemolytic anemia (AIHA) and assigned to the Diego system in 1998. Its incidence is less than 0.01% in all populations. It is usually identified in patients with AHAI or in multispecific sera. Due to its rarity, its clinical importance has not been established. We present a case of feto-maternal incompatibility with an antibody of anti-Sw[a] specificity identified in a pregnant woman that did not induce haemolytic disease of the newborn (HDN).
Aims: To characterize a clinical case involving a rare blood group specificity
Methods: Clinical Case. A 25-years-old woman native of Morocco, with no transfusion or pathological history of interest who gave birth to her third child presenting a positive direct antiglobulin test (DAT) at birth. The feto-maternal incompatibility study showed that both, the mother and the child shared a blood group A RhD positive, with no antibodies being detected in the maternal plasma at the beginning; however, the clearly positive result of the DAT was confirmed. In the two previous pregnancies there were no complications, although the second child also presented a positive DAT test whose cause was not established.
Results: A sample from the father was requested, having the same blood group A RhD positive. The cross-match test between the pregnant woman's plasma and her partner's red cells was strongly positive (4 +). The results indicated that the mother was carrying an antibody against a low-incidence antigen expressed in the father's red cells and most likely in the newborn. The antibody was of IgG class with a titer of 1024 against the father's red blood cells. The investigation of antibodies of low incidence in the maternal plasma excluded the presence of the most common antibodies and identified an antibody of anti-Sw[a] specificity. The father's phenotype was confirmed as Sw(a+). The study was complemented with the amplification and sequencing of a region corresponding to exon 16 of the SLC4A1 gene encoding Band 3. The 1936C>T change was identified in heterozygosity, which results in the appearance of tryptophan in residue 646 of the Band 3 protein. This allelic variant is associated with the Sw (a+) and SW1 + phenotype. sults in the appearance of tryptophan in residue 646 of the Band 3 protein. This allelic variant is associated with the Sw (a+) and SW1 + phenotype.
Summary/Conclusions: The reported case is informative in several aspects worth to remark: (1) It is a new case of the rare anti-Swa specificity; (2) its finding as the only specificity present in the serum sample; (3) the context of a feto-maternal incompatibility in which the antibody induced a positive DAT, but without clinical signs or symptoms in the newborn; (4) the molecular study confirming the serological findings and the Sw(a+) SW1+ phenotype of the father.

P-628

A NEGATIVE INDIRECT ANTIGLOBULIN TEST IN RHD NEGATIVE PREGNANT WOMAN WITH BMI 35 AFTER TWO INTRAMUSCULAR INJECTIONS OF IMMUNOGLOBULIN ANTI-D – CASE REPORT

I Maric and K Zeleznik
Immunohaematology, Blood Transfusion Centre of Slovenia, Ljubljana, Slovenia

Background: We present a case of a 27 years old D-negative pregnant woman, body mass index (BMI) 35, with vaginal bleeding in the 22nd week and premature rupture of amniotic sac membranes with prolapse of umbilical cord in the 26th week of pregnancy. She was injected with three doses of immunoglobulin (Ig) anti-D intramuscularly in gluteal area (the first one in the 22nd week, the second one in the 26th week and the third one four days after the second one), but her indirect antiglobulin test (IAT) tested with column agglutination technology was only borderline positive.
In Slovenia we have three different Ig anti-D products from two different manufacturers. According to the first manufacturer's instructions the route of administration can be either intramuscular or intravenous and BMI should be considered. With BMI

≥ 30 intravenous route is recommended because of an increased risk of lack of effect since peak concentrations of Ig anti-D may be lower. According to the second manufacturer's instruction the route of administration can be either intramuscular or subcutaneous if intramuscular application is contraindicated. The exact place of intramuscular injection is not defined with neither of manufacturers. Ig anti-D for intramuscular administration is slowly absorbed into the recipient's circulation and reaches a maximum after a delay of 2 to 3 days.
Aims: We tried to clarify the reason for IAT negativity after two intramuscular injections of Ig anti-D.
Methods: Serologic tests, D genotyping, flow cytometry (FC), Kleihauer-Betke test (KBT).
Results: With D genotyping we confirmed that the patient was really D-negative and excluded weak or partial D antigen, which might absorbed all of the injected Ig anti-D on her own RBC leading to almost negative IAT. The direct antiglobulin test (DAT) was also negative. We also excluded large fetomaternal haemorrhage (FMH) with KBT and with FC using anti-HbF monoclonal antibodies (mAbs). With FC using anti-D mAbs we excluded possible patient's RBC chimerism (the presence of a small proportion D-positive RBC apart from D-negative RBC), which couldn't be seen serologically, and also FMH with a D-positive fetus (the blood group of the fetus was unknown).
We assumed that with gluteal application Ig anti-D was injected in her fat tissue with very slow and minimal absorption into bloodstream. We recommended additional dose via intravenous route. Four hours after intravenous application of Ig anti-D a control IAT was performed and it was strongly positive confirming right application of drug and excluding other reasons for negative IAT before.
Summary/Conclusions: We excluded possible situations, which could neutralise the injected Ig anti-D: patient's D variant, RBC's chimerism and large FMH. With high BMI the thickness of subcutaneous tissue is greater so the needle that injects the drug needs to be longer to administrate drug into the muscle otherwise the drug stays in subcutaneous fat tissue with very slow absorption, which was probably the reason for postadministration low levels of Ig anti-D in our case. In our opinion higher BMI has to be taken into consideration when injecting Ig anti-D.

P-629

THE IDENTIFICATION OF ANTI-SEC (RH46) IN A PRENATAL PATIENT

S Pigneau, J Cote and C Pambrun
Canadian Blood Services, Ottawa, Canada

Background: A 29-year-old prenatal patient from New Guinea, gravida 2 para 1, presents at 34 weeks gestation with a panreactive allo-antibody (Ab). The patient is group O RHD+, DAT negative. Red cell genotyping did not identify any variant polymorphisms in the human erythrocyte antigens (Ag).
Aims: Determine the antibody specificity of a panreactive allo-antibody in a prenatal patient.
Methods: Standard serological indirect antiglobulin (IAT) and papain-IAT (PIAT) test methods were executed in this panreactive allo-antibody investigation. Testing was performed utilizing commercial reagent red blood cells (RBCs), in-house panel RBCs and frozen rare RBCs that were phenotype-similar and negative for high prevalence antigen (HPA). Advanced serological methods including fixation using untreated RBCs and elution studies (e.g. Gamma ELU-KIT II) were performed to determine if an Ab to a HPA was present. Serological phenotyping of the patient's RBCs was assessed using licensed antisera according to manufacturer's instructions. Erythrocyte antigens were interrogated by both a qualitative, PCR-based and hybridization-based genotyping test (BLOODchip IDCOREXT) utilizing Luminex xMAP technology and by sanger sequencing.
Results: Initial testing revealed 3 + by IAT and 4 + by PIAT with all RBCs tested except the autocontrol. A pattern of an auto/allo anti-e was suspected at immediate spin (IS), and/or auto/allo anti-Ce at 37°C. Phenotypically similar RBCs reacted 3 + and DEc/DEc RBCs reacted weak to 1 + by IAT suggesting an Ab to a HPA in the Rh blood group system. Rh[null] (RH29-) and D - - (RH17-) were non-reactive by IAT and PIAT indicating the presence of an Ab to a HPA in the Rh blood group system. Fixation/elution studies using DCe/DCe phenotypically similar untreated RBCs resulted in the removal of anti-e and anti-Ce and /or an Ab with specificity to a HPA. Fixation/elution studies using dcE/dcE resulted in the removal of an Ab to the HPA and the identification of anti-e. The elution was non-reactive by PEG-IAT with Rh[null] and D - - RBCs only indicating the presence of an Ab to a HPA. The patient's red cell phenotype and genotype confirmed as DCe/DCe. The patient's DNA was referred out for sanger sequencing of the RHCE gene. Molecular sequencing

determined that the prenatal patient was homozygous for RHCE*CeRN which is associated with a partial C and partial e predicted phenotype.

Summary/Conclusions: The serological investigation in conjunction with the molecular testing allowed for a final Ab identification of anti-Sec. Anti-Sec is the Ab produced to the HPA, RH46. Individuals who genotype as homozygous for the RHCE*CeRN express partial C and partial e Ag but also lack E and c antigens. For transfusion purposes, the only compatible RBCs are other RH:-46, Rh$_{null}$ and D–. The newborn was mildly affected, only requiring phototherapy but not transfusion support. Any future pregnancies may have clinical implications and therefore require monitoring for hemolytic disease of the fetus and newborn.

P-630

ANTI-U COMBINED WITH ANTI-D AND ANTI-C ALLOANTIBODIES IN A PREGNANT WOMAN: A CASE REPORT

M Hanna[1,2], E Kahwash[3], P Lesley[4], G Clarke[5], R Skeate[6] and L Shier[1,2]

[1]Department of Pathology and Laboratory Medicine, University of Ottawa [2]The Ottawa Hospital and Eastern Ontario Regional Laboratory Association, Ottawa [3]Canadian Blood Services, Halifax [4]Canadian Blood Services, Ottawa [5]Canadian Blood Services, Edmonton [6]Canadian Blood Services, Toronto, Canada

Background: Alloantibodies are produced in antigen negative individuals following exposure to foreign red blood cells (RBCs) during transfusion or pregnancy. The U antigen is part of the MNS system. It is present in almost all Caucasian and in 1–35% of the black population. U-negative individuals are always negative for S and s. Anti-U alloantibody, although extremely uncommon, can cross the placenta, coat U positive fetal RBCs and cause hemolytic disease of the fetus and newborn (HDFN). HDFN is most commonly caused by anti-D and to lesser extent, anti-E, anti-K and anti-C alloantibodies.

Aims: Case presentation: We report a case of pregnant woman with anti-D, anti-C and anti-U alloantibodies, who delivered a healthy baby with no hemolytic anemia. A 43 year old woman, gravida 4 para 3, presented at 37 + 6 weeks with pre-eclampsia. She was grouped as A negative with a positive antibody screen. Antibody investigation revealed anti-D (titre 4), anti-C (weak) and anti-U (titre 16). Extended red cell phenotyping showed K-, Jk(a+b-), Fy(a-b-), M-N+, S-s-. All previous pregnancies were uneventful with no neonatal complications.

No compatible units were locally available and Canadian Blood Services (CBS) were notified with a request for RBCs phenotypically matched for D, C, U, K, Jk, and Fy. No available frozen units matched the patient's phenotype. CBS identified a matched volunteer able to provide an urgent donation.

On the 10th day, the patient delivered a full term healthy male baby. The patient did not need any blood transfusion. At delivery, the bay had an APGAR score of 9 at 1 and 5 min. The baby cord blood group was grouped as A negative with no evidence of hemolysis (Hgb 156 g/l and total bilirubin < 35 μmol/l). The direct antiglobulin test (DAT) was positive (3 +). An acid eluate was non-reactive. Red cell phenotyping demonstrated a C-S-s+ phenotype. Despite the positive DAT, close follow-up of the neonate's bloodwork showed no evidence of hemolysis.

Discussion: This report illustrates a rare case of a pregnant woman with anti-D, anti-C and anti-U alloantibodies. This case emphasizes the importance of protocols dealing with rare or unusual circumstances.

Early notification of the hematopathologist on call to ensure accurate characterization of the immunizing antibodies is extremely important. In the presence of anti-D and anti-C antibodies, the possibility of anti-G should be kept in mind. The G antigen is part of the Rh system and appears as anti-C plus anti-D activity. The differentiation between these antibodies is not necessary for routine blood transfusion as patients will receive RhD and C antigen negative blood. However, it is important to distinguish these antibodies during pregnancy to determine the need for prophylactic RhIg.

It is also important to realise the challenge finding compatible red cell units for patients with alloantibodies to high-frequency antigens. Early notification of CBS is crucial to allow them to initiate a search for compatible units. Extended genotyping could be considered for patients with uncommon and/or multiple antibodies. Finally, vigilant perinatal follow up is necessary to monitor for the possible onset of HDFN.

P-631

A COMPARISON OF CALCULATIONS USED IN DIFFERENT COUNTRIES FOR ESTIMATION OF FETO–MATERNAL HAEMORRHAGE (FMH)

K Veale, J White, R Haggas and M Rowley

UK National External Quality Assessment Service, (UK NEQAS BTLP), Watford, United Kingdom

Background: Practices in estimation of feto-maternal haemorrhage (FMH), and anti-D immunoglobulin (Ig) dosing vary according to local policy, national guidelines, and anti-D Ig manufacturer. Variables in FMH include the technique used (acid elution (AE) or flow cytometry (FC)), and calculation variables include; maternal blood volume (MatBV), correction factor for size of fetal cells (CF), and the percentage of fetal cells which stain (FCS). An error may lead to sensitisation to the D antigen and potential haemolytic disease of the fetus and newborn. In the UK, British Society for Haematology (BSH) guidelines are followed, which for both AE and FC assumes a maternal red cell volume of 1800 mL, a CF of 1.22, and for AE only, a FCS of 0.92. UK NEQAS (BTLP) provide an EQA scheme for FMH estimation, with results being submitted as mL of packed cells (PC), using the BSH guideline calculations.

Aims: The aim was to gather information on how non-UK laboratories calculate estimated FMH, and how this impacts the EQA scheme and participants using alternative guidelines.

Methods: An online questionnaire designed to determine the calculations used for AE and FC testing was sent to 46 non-UK/Republic of Ireland participants in 14 countries, and also to 229 FC users in 39 countries by UK NEQAS Leucocyte-Immunophenotyping.

Results were filtered to remove duplicate and incomplete responses, and respondents who do not measure FMH.

Results: 31 full sets of results were analysed from 15 countries; 13 in 7 countries for AE, 23 in 14 countries for FC. 2/31 respondents do not currently participate in FMH EQA.

Six different guidelines were listed for FMH estimation; 12/31 stated no guideline for testing. Two reporting units were listed; whole blood (WB), and PC. Three CFs were stated; 1.0, 1.22, 1.3, and three FCSs; 1.0, 0.92, and 0.9. All respondents reported using a fixed MatBV for all patients; five different volumes were used; 1800 mL, 2400 mL, 2500 mL, 4735 mL, 5000 mL.

Summary/Conclusions: In some cases, respondents indicated that they reported results in WB or PC, but the overall calculations contradicted this; the significance of this is questionable provided dosing is performed using the correct reporting unit. A comparison of overall calculations showed that all result in similar bleed volumes, with BSH calculations giving the lowest. This indicates that overseas calculations would result in sufficient anti-D Ig being administered, compared to BSH guidance.

Two laboratories stated that different guidelines are used in clinical practice, but BSH guidelines are used for reporting EQA results. Reporting an FMH EQA result that has been calculated using a non-BSH formula will affect the accuracy score for the participant, and has the potential to skew the overall data used to calculate all scores. In response to this, FMH exercise instructions have been updated to specify that BSH calculations should be used to ensure comparable results and robust data.

This study has allowed us to understand and address the limitations of an international EQA scheme and to gain knowledge of overseas practice that can be used to inform UK guideline review.

P-632

COUPLE'S HPA-1 ALLELIC DISCORDANCE AND PREGNANCY LOSS

M Zadsar, M shaiegan, G Ahmad Zadeh Shad and S samiee

High Institute for education and research in transfusion medicine, Tehran, Iran

Background: Miss carriage and pregnancy losses are an important issue in married life. Many direct or indirect factors might play role to be encountered with e.g. hematological and immunological disorder. Likewise HPAs genotype also might attribute to the pregnancy outcome. To define the discordance of HPA-1 genotype in couple with the history of recurrent abortion, present research was designed.

Aims: Investigating the allelic frequencies and discordant of HPA-1 antigens between the couples by medical history of recurrent pregnancy loss and comparing by the Iranian blood donors.

Methods: Totally 75 couples with a history of recurrent abortion (without any apparent causes and before 20th week of gestational age) the HPA-1 was detected by the SSP-PCR method. Spss 16 (Chicago) was used to report the frequencies and T

test for comparison between two groups. Hardy Weinberg equation was applied to find the allelic frequency.

Results: Mean age of participants was 32.75.7 years (22–46), mean of abortion history and gestational age was 2.50.9 and 7.5 ± 0.7, respectively.

HPA-1a was found in all 150 person (HPA-1a; %100 and HPA-1b; %0). No discordant couple was found. Comparing to the HPA-1 frequency among Iranian Blood donors (HPA-1a; %98 and HPA-1b; %2) there were a subtle difference. P = 0.15

Summary/Conclusions: There were controversial concepts about the correlation between HPA-1 mutation and recurrent abortion. The present study could not support this association. However, as it was shown in previous studies, the prevalence of HPAs varied between different ethnic groups, so it could be suggested to investigate the role of HPAs other than HPA-1 in Iranian patients with the history of pregnancy loss.

P-633

SEVERE NEONATAL THROMBOCYTOPENIA DUE TO A FETO-MATERNAL ANTI-GROUP A ALLOIMMUNIZATION: A CASE REPORT

G Bertrand[1], A Leguen[2], L Delugin[3] and V Renac[1]

[1]Platelet immunology Department, French Blood Services of Brittany EFS [2]Clinic "La Sagesse" [3]Immuno-hematology Laboratory, French Blood Services of Brittany EFS, Rennes, France

Background: Fetal or neonatal alloimmune thrombocytopenia (FNAIT) results form a maternal alloimmunization against fetal platelet antigens.

Aims: We present the case of a 29 years old French woman who gave birth to her first baby at 38 weeks of gestation. Investigations were performed due to a suspicion of maternofetal infection at 24 h of life. No infection was detected. However, a moderate thrombocytopenia was observed the second day of life (132G/l), with a nadir platelet count the third day at 45G/l. Neonatal anemia did not appear before the 7th day after delivery (Hb 13.3).

Methods: HPA genotyping was performed by Sanger sequencing. Anti-platelet antibody detection was performed using the MAIPA method. Immunohematology investigations were carried out: antigen testing (ABO, Rh and Kell), and antibody detection with direct and indirect antiglobulin tests.

Results: Direct Coombs of newborn red blood cells (RBC) was IgG-positive (intensity: ++). RBC elution and antibody identification revealed the presence of maternal anti-A group antibodies: the mother was of blood group O, and the father and newborn of blood group A. Anti-A group antibody titer of the maternal serum was quantified at 1024 when tested against A1 donor's RBC. Investigations in platelet immunology did not reveal any platelet foeto-maternal incompatibility. No antibody was detected in the maternal serum when tested against donor platelets using the MAIPA. The cross-match of maternal serum against father's platelets was positive in MAIPA due to maternal anti blood group A antibodies. After adsorption of the maternal serum on father's RBC, the MAIPA cross-match of the maternal serum on father's platelets was negative, thus demonstrating that anti-group A antibody was responsible of the positivity.

Summary/Conclusions: In this case, neonatal thrombocytopenia was severe, but without any sign of bleeding: no post-natal therapy was needed and the newborn recovered spontaneously 7 days after birth. We demonstrated that thrombocytopenia was due to anti-group A maternal alloantibodies that crossed the placenta barrier and affected both RBC and platelet counts.

P-634

2–YEAR EXPERIENCE IN NON-INVASIVE PRENATAL DIAGNOSTICS OF FETAL RHD FOR TARGETED ANTI-D IMMUNOPROPHYLAXIS IN POLAND

A Orzińska[1], K Guz[1], J Duda[1], M Krzemienowska[1], P Bartoszewicz[1], S Purchla-Szepioła[1], M Jurkowska[2], M Pelc-Kłopotowska[1], A Kiszło[1], M Dębska[3], M Uhrynowska[1] and E Brojer[1]

[1]Department of Immunohematology, Institute of Hematology and Transfusion Medicine [2]GENOMED Health Care Centre [3]Department of Obstetrics and Gynecology, Medical Centre of Postgraduate Education, Warsaw, Poland

Background: Obligatory postnatal immunoprophylaxis of alloimmunisation by RhD antigen (RhIg) has been performed in Poland since early 1970ies. Antenatal administration has been recommended since 2016. As there is no national system of non-

invasive prenatal diagnostics of fetal RHD (RHD NIPD), RhIg is currently given to all RhD negative pregnant women. Literature reports state that about 40% of women receive RhIg unnecessarily since their baby is RhD negative. In addition, immunoprophylaxis is unwarranted for women with weak RhD type 1, 2 and 3. The decision of obstetricians to recommend RHD NIPT procedure is its free access at the Institute of Hematology and Transfusion Medicine (IHTM) in Warsaw.

Aims: To determine criteria for qualification to antenatal immunoprophylaxis based on preliminary results of RHD NIPT.

Methods: DNA isolated (easyMag, Biomerieux) from plasma of 144 pregnant women determined as RhD-negative with standard serology (in 8–33 week of gestation) was used for NIPT performed by real-time PCR on LC480II (Roche) with primers specific for exons 5 and 7 of RHD and CCR5. In two women whole blood DNA was isolated using Prepito DNA Blood D250 Kit (Perkin-Elmer Chemagen, Baesweiler, Germany) on chemagic Prepito (Chemagen, Germany) and tested for identification of RHD variant using RBC FluoGene RBC-Dweak/variant (Inno-Train, Kronberg/Taunus, Germany).

Results: In 93/144 cases the RHD NIPD results indicated that RhIg should be recommended (delta Ct $_{CCR5-RHD}$< 1) due to a RHD positive fetus. In 47/144 cases RhIg was not recommended as RHD gene was not detected in maternal cfDNA. In 4/ 144 cases similar Ct-values for RHD and CCR5 indicated a maternal D variant (delta Ct $_{CCR5-RHD}$ >2) and fetal RHD prediction was impossible. In 2/4 cases follow-up was performed and identified RHD*01W.2 (RhIG not recommended) and RHD*15 (RhIg recommended).

Summary/Conclusions: In about 34% of IHTM tested pregnancies the fetal genotype was RhD negative therefore RhIg immunoprophylaxis was unnecessary. Implementation of follow up procedure for weak RhD variant identification helps to eliminate RhIg immunoprophylaxis in cases of mothers with RHD*01W. 1, 2 and 3 alleles.

P-635

IS NON INVASIVE FETAL PLATELET GENOTYPING IN OTHER SYSTEMS THAN HPA-1 USEFUL TO MANAGE FNAIT?

Y Mammasse, C Chenet, C Martageix and R Petermann
Platelet Immunology, INTS, Paris, France

Background: Fetal and neonatal alloimmune thrombocytopenias (FNAIT) are caused by the development of alloantibodies against the main platelet membrane glycoproteins (GPIaIIa, GPIIbIIIa, GPIbIX) and CD109. In Caucasians, the estimated frequency is about 1 in 1000 live births. FNAIT may have devastating consequences such as an intracranial hemorrhage (ICH). In more than 70% FNAIT cases, the HPA-1 system is involved. Fetal platelet genotyping is usually formed using invasive procedures with a risk of bleeding and miscarriage. Therefore, different methods for non invasive prenatal testing (NIPT) are in development, but still under evaluation for routine use.

Aims: A former analysis in our reference laboratory highlighted that only 30% of referred FNAIT cases were related to fetomaternal HPA-1 incompatibility. Therefore, we have implemented NIPT for the 4 main platelet antigen systems HPA-1, -3, -5 and -15, which are implicated in more than 95% of FNAIT. The goal of this study was to determine whether the development of this strategy was adequate to precisely diagnose FNAIT in patient samples sent to our laboratory.

Methods: Fetal platelet genotyping was performed by using droplet digital PCR (ddPCR). In each case where NIPT results were confirmed on blood newborn sample or on amniotic liquid during the pregnancy, data were extracted and collected from mother and/or baby discharge hospital letters and we confronted information to fetal HPA genotyping results.

Results: 36 NIPT for 19 pregnant women were performed and results were confirmed by HPA genotyping on blood newborn sample or on amniotic liquid. We received 19 hospital discharge letters, which were not completely informative.

Results showed that 4/20 (20%) pregnant women were compatible with their fetus, 11/20 (55%) were incompatible in one HPA system including only 5 cases incompatible in HPA-1 (20%), 3/20 (15%) in two and 1/20 (5%) in three combined HPA systems. In 73.7%, we found a FNAIT history. All babies (n = 20 due to a couple of twins, 12 male and 8 female) were born alive except 2 due to medical abortion: i) one with ventricular dilatation at 22 WG with no platelet count results (HPA-1 incompatibility, antibody not tested) ii) one with ICH at 33 WG and a platelet count at 3 G/L (HPA-15 incompatibility, antibody not tested).

Summary/Conclusions: These results confirmed that doing non invasive fetal platelet genotyping in other systems than HPA-1 is essential since HPA-1 represents only 20% of NIPT, probably due to the lab expertise in the most difficult FNAIT cases. So, the development of our strategy focusing on simultaneously on HPA-1, -3, -5 and -15 was adequate with patients samples sent to our lab. However, our study also

shows the difficulties for a specialized laboratory to collect data from hospital discharge letters because of many missing data such as platelet count, baby's weight for example. Whatever, non-invasive fetal HPA genotyping using ddPCR allowed diagnosis of feto-maternal platelet incompatibility and can now be implemented in routine clinical testing.

P-636
FIRST TRIMESTER NONINVASIVE FETAL RHD GENOTYPING USING FROZEN DNA SAMPLES: VALIDATION AND OPTIMIZATION OF THE TEST TO IMPLEMENT A SCREENING PROGRAM

D Londero[1], T Stampalija[2], D Bolzicco[1], M Candolini[1], E Castro Silva[2], C Cortivo[2], C Dreossi[1], I Fantasia[2] and V De Angelis[1]

[1]*Department of Transfusion Medicine, Azienda Sanitaria Universitaria Integrata di Udine, Udine* [2]*Unit of Prenatal Diagnosis, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy*

Background: Recent introduction of noninvasive fetal RHD testing represents an important tool in the management of the Rh-D negative pregnant women and a first trimester screening allows early classification of pregnancies in terms of risk and targeted immunoprophylaxis.
Aims: The aim of this study was to introduce the first trimester fetal RHD screening at a regional level by validating and optimizing the use of a commercial kit.
Methods: The recruitment of 83 RhD negative pregnant women was performed at 11 to 13 gestational weeks. Fetal DNA was extracted robotically using QIAsymphony DSP circulating DNA kit from 2 ml of maternal plasma, and amplified by real-time PCR using the Free DNA Fetal kit RhD/Real-Time PCR, both on fresh or frozen DNA samples, to evaluate the stability of extracted fetal DNA. Assay accuracy and precision were evaluated in terms of sensitivity, specificity, repeatability and reproducibility by comparing the fetal RHD genotyping results versus cord blood RhD serological determinations and by performing tests in duplicate within the same run or different run.
Results: A total of 17/83 samples were used for process validation. All fetal RHD genotyping results were consistent with post-natal serological RhD tests on cord blood samples: 16 were RhD positive and 1 RhD negative (100% sensitivity and specificity). No differences were observed between fresh or frozen extracted fetal DNA giving 100% of concordance in precision parameters.
Summary/Conclusions: These preliminary findings confirm the feasibility of fetal RHD genotyping on first trimester samples and the benefits of process frozen DNA samples thus optimizing the laboratory routine organization. Larger scale study is in progress to routinely implement this test (GENIC, Friuli Venezia Giulia regional grant project), but these data encourage for the realization of a regional screening program at different gestational ages.

P-637
EVALUATION THE SRY TO CONFIRM THE PRESENCE OF FETAL DNA IN THE FETAL RHD GENOTYPING USING CFFDNA

MH Ahmadi and N Amirizadeh

Blood Group Genotyping Central Lab, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: With the discovery of cffDNA in maternal plasma in 1997 by Dennis Lo, the possibility of the fetal RHD genotyping was done using noninvasive methods. RH genotyping of the fetus in pregnant women that immunized with anti-D could be important. In these cases, if it turns out the baby is Rh positive, timely treatment and appropriate measures will be taken into the account and if the fetal Rh is negative, unnecessary invasive procedures such as serial amniocentesis and cordocentesis can be avoided. To confirm the presence of fetal DNA in maternal plasma, a specific marker should be used, which is specific for fetal and presents in maternal plasma. SRY gene is the most widely used marker in this issue, which exists only on the Y chromosome. Its presence in the DNA extracted from maternal plasma can prove the existence of fetal DNA in mother circulation used for male fetus genotyping tests.
Aims: The aim of this study is Evaluation the SRY to Confirm the Presence of Fetal DNA in the Fetal RHD Genotyping Using cffDNA.
Methods: In this experiment, 20 plasma samples were collected from pregnant women that were in a gestational period between 8 and 39 weeks and were aged from 19 to 28 years (mean 24.6 ± 3.5). DNA was extracted by SinaClon DNA

extraction kit and Real-time PCR reactions were done in triplicate by specific primers for SRY and ACTB genes. The results were compared to the neonate's sex determined at the birth time. The results were analyzed by SPSS version 22 using the Chi-square of independence test and Cohen's Kappa, and P < 0.05 was considered statistically significant.
Results: From the 20 maternal plasma samples considered for SRY genotyping, 10 (50%) revealed the presence of the SRY gene and 10 (50%) were negative for this gene. There was 100% concordance between fetal sex genotyping by real-time PCR and newborn's sex. As a result, the sensitivity, specificity and precision were calculated 100% for the SRY gene detection (p < 0.0005; K = 100%). The actin gene was detected in all samples.
Summary/Conclusions: SRY is a good marker to confirm the presence of fetal DNA in plasma. Use of this marker is only applicable in pregnant women who are carrying a male fetus but in cases which fetuses are female and fetal RHD genotyping results are negative, SRY cannot prove the presence of fetal DNA. In these cases, epigenetic markers should be used such as RASS-FA1.

P-638
PREANALYTICAL PHASE OF NON-INVASIVE FETAL GENOTYPING: DIFFERENT TYPES OF BLOOD COLLECTION TUBES AND CONDITIONS OF PLASMA SEPARATION

A Orzińska[1], K Guz[1], S Purchla-Szepioła[1], M Krzemienowska[1], P Bartoszewicz[1], M Dębska[2], I Kopeć[3] and E Brojer[1]

[1]*Department of Immunohematology, Institute of Hematology and Transfusion Medicine* [2]*Department of Obstetrics and Gynecology, Medical Centre of Postgraduate Education* [3]*Institute of Hematology and Transfusion Medicine, Warsaw, Poland*

Background: Non-invasive fetal antigen genotyping (NIPT) based on cell-free fetal DNA from maternal plasma is routinely used for predicting the antigen status of a child with the purpose of establishing precise management of the immunized pregnancy. The stability of fetal/maternal material is crucial for the accuracy of NIPT especially encoded by single nucleotide polymorphisms where the high background of maternal allele leads to unspecific results.
Aims: To compare NIPT with tubes routinely used at the Institute and those stabilizing maternal blood cells.
Methods: 2×10 ml of blood from 29 pregnant RhD-negative women was collected in parallel into EDTA vacutainer tubes with gel barrier (BD Vacutainer PPT, USA) and Cell-Free DNA Collection tubes (Roche). DNA isolated from fresh or frozen plasma using easyMag (Biomerieux) was examined by real-time PCR on LC480II (Roche) for the presence of fetal markers (exons 5 and 7 of RHD, SRY, ins/del polymorphisms) and CCR5 as a maternal marker. Results for fetal and maternal markers from the material collected into BD tubes and tested within 24 h were compared with results for the same material collected into Roche tubes and tested: A/ within 24 h (n = 18), B/ after storage from 2 to 4 days at ambient temperature (n = 24), C/ after plasma freezing (n = 27). Results from the material collected into Roche tubes and tested within 24 h were compared with results for the same material from Roche tube tested after: D/ 2 to 4 days (n = 13); and E/ plasma freezing (n = 18).
Results: In all compared groups the differences in fetal fraction were not statistically significant (mean Ct value for fetal marker in compared groups: 35.0 SD ± 0.9 versus A/35.2 SD ± 1.0, P = 0.3; 35.2 SD ± 0.7 versus B/35.4 SD ± 1.2, P = 0.6; 35.0 SD ± 0.8 versus C/35.4 SD ± 0.9, P = 0.1; 35.3 SD ± 1.0 versus D/35.9 SD ± 1.1, P = 0.08; 35.2 SD ± 1.0 versus E/35.0 SD ± 0.8, P = 0.5). The maternal fraction was significantly lower in blood collected into Roche and tested within 24 h than in blood from BD tubes (mean Ct for CCR5 in the groups: 35.1 SD ± 0.8 versus A/34.5 SD ± 0.9, P = 0.03). Also the maternal fraction was significantly lower if DNA was isolated from the fresh plasma and tested within 24 h than from frozen plasma (mean Ct for CCR5 in the compared groups: 35.1 SD ± 0.8 versus E/34.4 SD ± 0.9, P = 0.03). In the other groups there were no differences in maternal fraction (mean Ct for CCR5 in groups: 34.8 SD ± 1.3 versus B/35.0 SD ± 0.5, P = 0.5; 34.2 SD ± 0.9 versus C/34.5 SD ± 0.8, P = 1; 34.8 SD ± 0.5 versus D/34.9 SD ± 0.6, P = 0.4).
Summary/Conclusions: Collection of maternal blood into Roche tubes as well as further plasma preparation does not affect the fetal DNA fraction. In addition it stabilizes maternal DNA fraction provided it is stored at room/ambient temperature and processed within 96 h of venipuncture. If such conditions are fulfilled NIPT of fetal antigens in material collected to Roche tubes from the whole territory of Poland is sufficiently accurate.

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Abstract has been withdrawn

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TARGETED PROPHYLAXIS PROGRAM FOR D–NEGATIVE PREGNANT WOMEN BASED ON GENOTYPING FETAL RHD FROM MATERNAL BLOOD

I Maric, K Zeleznik, I Bricl and T Dovc Drnovsek

Immunohaematology, Blood Transfusion Centre of Slovenia, Ljubljana, Slovenia

Background: Slovenian Prenatal care law defines prenatal care and testing, including prophylaxis with immunoglobulin (Ig) anti-D of D-negative pregnant women. Every pregnant woman has to have done a blood group and indirect antiglobulin test (IAT) by the end of the 12th week of gestation. In every D-negative pregnant woman IAT has to be repeated in the 28th week of gestation before she receives Ig anti-D. If woman gives birth to a D-positive child she receives an additional dose of Ig anti-D within 72 h after giving birth. For adjusting the dose of Ig anti-D evaluation of fetomaternal haemorrhage (FMH) is necessary. Ig anti-D has to be given also to every D-negative pregnant woman in case of an event that could cause anti-D immunisation, such as vaginal bleeding, abdominal trauma, therapeutic termination of pregnancy, miscarriage, intrauterine procedure, ectopic pregnancy, intrauterine fetal death and external cephalic version.

Based on percentage of D-positive (81%) and D-negative (19%) women and ratio of homozygosity (DD) and heterozygosity (Dd) for D gen in Slovenian population we calculated that 41% of D-negative pregnant women give birth to a D-negative child hence administration of Ig anti-D is in these cases unnecessary. By discovering the presence of cell–free fetal DNA (cff-DNA) in maternal blood it is possible to genotype fetal D gen with non-invasive method and inject Ig anti-D only to D-negative pregnant women bearing D-positive fetus.

We are about to implement a new protocol of prophylaxis with Ig anti-D. In 26th week of gestation we will determine the presence of fetal D gen in maternal blood and prophylaxis with Ig anti-D will be based on the presence of fetal D gen in maternal blood.

Aims: Starting with 2018, only pregnant women bearing D-positive fetus according to cff-DNA D genotyping will receive Ig anti-D in 28th week of gestation.

Methods: Using real time PCR (in house method, reagents from Applied Biosystems) we will determine the presence of fetal D gen in maternal peripheral blood.

Results: There are around 20.000 births annually in Slovenia; around 4.200 of births are given by D-negative women. Based on Slovenian D gen population study that we performed in 2011 we concluded that around 1.720 (41%) of pregnant women give birth to D-negative child. On that conclusion we calculated expenses of old, not-targeted prophylaxis program and compare it with new, targeted prophylaxis program. Annual costs for the old program were on average 544.292,64 € and cost of new program is estimated on 547.938,24 €, with a net difference of 3.645,60 €.

Summary/Conclusions: The discovery of cff-DNA in maternal peripheral blood enabling noninvasive obtaining of fetal genetic material and progress in molecular technologies have made fetal D genotyping more accessible, thus making the implementation of targeted prophylaxis with Ig anti-D a reality. Estimated cost difference between old and new program is relatively small, especially comparing it to unnecessary administration of Ig anti-D to women that don't need it.

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PREVALENCE OF IRREGULAR ANTIBODIES IN KOREAN PREGNANT WOMEN AND THE OUTCOME OF THEIR NEONATES

H Lee[1], K Shin[2], H Kim[2], D Yoo[1] and S Song[3]

[1]Laboratory medicine, Pusan National University Yangsan Hospital, Yangsan
[2]Laboratory medicine, Pusan National University Hospital [3]Laboratory medicine, Inje University College of Medicine, Busan, Korea

Background: The frequencies of irregular antibodies in pregnant women, which cause hemolytic disease of the fetus and newborn (HDFN), vary between different study populations. Clinical manifestations of HDFN differ according to the specificities and degree of irregular antibodies. Therefore, awareness of the prevalence of maternal alloantibodies is important to manage the health of the fetus and neonate.

Aims: The aim of this study was to provide data on the prevalence and nature of maternal RBC alloimmunization and neonatal outcome. We compared the fetal and neonatal outcomes between pregnancies both with and without RBC antibodies.

Methods: The pregnant women who underwent irregular antibody screening for prenatal testing at an obstetrics clinic in single center were enrolled. The pregnant women who screened positive for irregular antibodies were selected as the test group and age-matched and obstetrics history-matched pregnant women selected as control group for evaluating pregnancy outcome according to irregular antibody. ABO/Rh (D) typing, irregular antibody screening, age, and obstetric history of the pregnant women, and the direct antiglobulin tests, bilirubin, ABO/Rh (D) typing, phototherapy history, and mortality and gestational age at birth of the pregnant women's babies were recorded.

Results: In total, 2,493 samples from 1,508 pregnant women were tested within the study period. The median age of the pregnant women was 33 (16–46). Of the total samples, 2.36% (59/2,493) showed positive results in the antibody screening test. After exclusion of duplicate samples from the same patients, the prevalence of irregular antibodies was 2.78% (42/1,508).Among these 42 women with irregular antibody, 9 women were not tested to identify the specificity of irregular antibody. Thus, 33 women was identified the specificity of the irregular antibody. Anti-D was the most frequently identified antibody, followed by anti-E and anti-Le[a] except unidentified or not tested cases. All Rh D-negative pregnant women had anti-D because of prophylactic immunization. The most common alloantibodies belonged to the Rhesus system (17/33, 51.5%). Between two groups, obstetric history including gravida and para, age and ABO/ blood type are not different statistically. Only the survival rate of the current pregnancy was statistically different (P = 0.047), transfusion history prior current pregnancy, four pregnant women were transfused packed RBC and does not different between test group and control group (P = 0.115). Eight pregnant women had anti-C or anti-D, one woman had a stillborn, and four living neonates developed hyperbilirubinemia. Of six pregnant women with anti-E alone or with other alloantibodies, three had spontaneous abortions or stillborns in the present pregnancy. Among six newborns with maternal anti-Le[a] and Jk[a], 4 neonates showed hyperbilirubinemia, but they had not spontaneous abortions or stillborns.

Summary/Conclusions: In conclusion, we found that the prevalence of irregular antibodies among Korean pregnant women was 2.78%. The most common significant antibodies belonged to the Rhesus blood group, namely anti-D, and anti-E combined with anti-c. The death rate of fetuses was higher in pregnant women with irregular antibodies than those without irregular antibodies. If the monitoring of pregnant women with irregular antibody of rhesus blood group and evaluation for HDFN in neonates with maternal irregular antibody of rhesus, Kidd, Lewis blood group performed, the perinatal mortality rate could be decreased.

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ANTIBODY SURVEY FOR PRENATAL CASES: HÉMA-QUÉBEC'S EXPERIENCE

M St-Louis[1], N Baillargeon[2], C Éthier[2] and J Pedneault[3]

[1]Affaires médicales et innovation, Héma-Québec, Québec [2]Laboratoire de référence et de cellules souches, Héma-Québec, Québec [3]Technologies de l'information, Héma-Québec, Montréal, Canada

Background: Héma-Québec is the sole blood bank provider for the Province of Québec servicing a population of 8.4 millions. Annually, the Immunohematology Reference Laboratory (IRL) receives 1500 requests from hospitals' blood banks to investigate antibody identification cases, pregnancy follow-ups, weaker antigen expression, transfusion reactions and various discrepancies. Among the services provided within the IRL, pregnancy follow-ups represents a third of the activities. In 2014, EdgeLab™ software (Haemonetics) was implemented to manage all clinical cases from receiving samples to reporting results to the requested hospital and to serve as an electronic database.

Aims: The present study was to survey the antibodies found specifically during pregnancy follow-ups to identify which ones were the most frequent. This also provided valuable information on titer and frequency of workups.

Methods: The data was extracted from the database using the pregnancy follow-up specific code from June 2, 2014 (implementation) until January 19, 2018. The resulting Excel file was manually analysed.

Results: During the 3.5 year-period, 795 pregnancy cases were received. Close to 50% were considered uneventful: 156 cases lack antibody (most referred for weaker D antigen expression), 69 cases had non-specific reactions (cold agglutinin, antibodies to red blood cells media, non-specific autoantibody without clinically significant underlying antibodies) and 169 cases showed blood group antigen specificity without clinical significance (auto-I, Bg, Ch1, 'HTLA', Le(a), P₁, Yt(b), Knops, D (RhIg)

and other autoantibody) (total of 394; 49.6%). The remaining 401 cases showed blood group antigen specificity with clinical significance. An exception was made for the numerous anti-M. For this study, they were all considered clinically significant even the IgM form. Among the 401 cases (1060 requests; average of 2.6 requests/case): 267 showed a unique antibody of which 104 were against an Rh specificity (39.0%), 2 antibodies were found in 86 cases (71 cases with at least one anti-Rh; 82.6%) and 48 cases had more than 2 antibodies (46 cases with at least one anti-Rh; 95.8%; overall 221/401 anti-Rh=55.1%). Anti-M was the most frequent (88 cases) followed by anti-E (47 cases) and anti-c (19 cases). Anti-c combined to anti-E were observed in 17 cases while anti-D + anti-C + anti-G ± other antibodies were identified in 12 cases. In terms of titers, most antibodies were too weak to titer. The highest was 1024 for 2 anti-K and 1 anti-D cases.

Summary/Conclusions: This study summarized the last 3.5 years in prenatal work-up in the IRL. It clearly showed that anti-Rh remain the major burdens in pregnancy management. Rare cases were also unraveled through this work. For example, three cases of anti-H in Bombay women, one case of anti-U and one anti-PP$_1$P^k. Day in and day out, the work is done. Antibodies are identified; however the whole picture is lost through the workload and the urgency behind some requests. This study showed the importance of pregnancy follow-ups in order to prevent hemolytic disease of the fetus and the newborn, and favor successful neonate outcome.

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USUAL AND UNUSUAL SPECIFICITIES OF RED BLOOD CELLS ANTIBODIES CAUSING FETAL ANEMIA: A TEN-YEAR RETROSPECTIVE STUDY BY THE FRENCH NATIONAL REFERENCE CENTER OF PERINATAL HEMOBIOLOGY

C Toly-Ndour[1], S Huguet-Jacquot[1], H Delaby[1], E Maisonneuve[2], J Jouannic[2], A Cortey[3] and A Mailloux[1]

[1]Unité Fonctionnelle d'expertise en Immuno-Hémobiologie Périnatale, Centre National de Référence en Hémobiologie Périnatale (CNRHP), Pôle de Biologie Médicale et Pathologie, Hôpital St Antoine [2]Service de médecine Foetale - Pôle Mère-enfant - Hôpital TROUSSEAU [3]Unité fonctionnelle de soins et d'expertise des incompatibilités foeto-maternelles et des ictères néo-natals - Centre National de Référence en Hémobiologie Périnatale (CNRHP) - Pôle Mère-Enfant, Hôpital Trousseau, Assistance Publique des Hôpitaux de Paris (AP-HP), Paris, France

Background: Fetal anemia could be induced by feto-maternal red blood cell incompatibility. If anti-D and anti-Kell antibodies are well known to cause severe fetal anemia, other specificities of red blood cells antibodies may be involved.

Aims: The aim of this work was to identify specificities of red blood cell antibodies that could be responsible for fetal anemia beside anti-D and anti-Kell, in a large number of pregnancies followed by the French National Reference Center for Perinatal Hemobiology (CNRHP).

Methods: We performed a retrospective extraction from our laboratory computing system (Synergy – Technidata) of the phenotypes and direct antiglobulin tests performed on fetal blood just before fetal transfusion from January 1st 2007 to December 31st 2016. We looked at the cause of the fetal anemia and, in case of anemia linked with feto-maternal incompatibility, we looked for the specificity of the antibodies involved. Maternal antibody titers, hemoglobin and bilirubin cord blood levels, as well as fetal reticulocyte counts were collected.

Results: Throughout this 10-year period, 279 fetuses received at least one transfusion. In 215 cases (77%), the fetal anemia was caused by feto-maternal red blood cell incompatibility. Anti-D was unsurprisingly involved in most cases of feto-maternal incompatibility (n = 174 (81%)), just followed by anti-Kell (n = 28 (13%)). Other antibodies involved (6%) were anti-c (N = 4), anti-E (N = 2), anti-Jra (N = 4 (with twins)), anti-M (N = 2) and anti-Kpa (N = 1).

Antibodies against c and E antigens are already known for their ability to cause severe Hemolytic Disease of the Fetus and Newborn (HDFN) with fetal anemia occurring mostly in the last trimester of the pregnancy.

Several cases of severe fetal anemia in the presence of high titer of anti-Jra or anti-M antibodies have already been described in the literature. For the respectively 4 and 2 fetuses concerned by anti-Jra and anti-M incompatibility in our study, maternal antibody titers were also high (> or equal to 32).

Cases of severe fetal anemia due to high titer of anti-Kpa antibodies (> 128) seem to be rare. To our knowledge, no other case has been described in the literature.

For anti-Jra, anti-M and anti-Kpa antibodies, the fetal anemia occurred after 26 weeks of gestation. In all cases, anemia was associated with a poor hemolytic process: negativity or weak positivity of the direct antiglobulin test and low total bilirubin levels. Low or moderate reticulocytes counts on cord blood suggest that these antibodies may act at least partly by suppression of the erythropoiesis, as described for anti-Kell antibodies.

Summary/Conclusions: The close monitoring of the fetus should not be reserved to pregnancies complicated with well-described antibodies (anti-D, anti-Kell, anti-c, anti-E). The presence of high titer anti-Kpa, anti-M or anti-Jra antibodies can also lead to severe HDFN. Since the anti-Jra is an antibody directed against a high prevalence antigen, the monitoring of anti-Jra immunized women requires a close cooperation with the national rare blood supply.

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Abstract has been withdrawn

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RED CELL ALLOIMMUNIZATION DURING PREGNANCY AT THE SOUTH BACKA DISTRICT OVER THE PAST TWO YEARS

N Bujandric and S Bogdanovic

Blood Transfusion Institute of Vojvodina, Novi Sad, Serbia

Background: Red blood cells (RBCs) antibody screen is performed during pregnancy to detect unexpected alloantibodies present in a maternal blood. A mother may have RBCs antibody because she has been exposed, through blood transfusion or through pregnancy, to RBCs other than her own. RBCs antibody can pass through the placenta to the fetal circulation and cause hemolytic disease of the newborn (HDN) defined as neonatal anemia and hyperbilirubinemia.

Aims: The aim of this study was to analyze frequency and type of clinically significant unexpected RBCs antibodies in the pregnant women population of the South Backa District of Vojvodina (Serbia) in period from 2016 to 2017.

Methods: Data obtained from the information system and protocols of the Blood Transfusion Institute of Vojvodina were used in a retrospective analysis of antibody screening result of the pregnant women with no transfusion history and with no RBCs alloimmunization in their previous pregnancies. Antibody was detected using indirect antiglobulin test (IAT), gel based technology. Tests were performed using a commercial screening reagent RBCs (ID-DiaCell I-II, Bio-Rad, DiaMed GmbH) on the automated immunohematology system IH-500 (Bio-Rad Laboratories, Switzerland). The antibody specificity was determined by gel technique with commercial 11-cell reagent RBCs panel (ID-DiaPanel, Bio-Rad, DiaMed GmbH. Switzerland).

Results: In the cohort of 5330 analyzed pregnant women, antibodies were found in 52 (0.98%): 49 had single antibodies, and 3 had multiple antibodies. The distribution of the antibody among sensitized pregnant women was: A) 10 (19.24%) antibody of undetermined specificity; B) 19 (36.54%) anti-D antibodies (16 single anti-D; 2 anti-D with anti-C; 1 anti-D with anti-Lua); C) the other clinically significant antibodies: 6 (11.54%) anti-E, 1 (1.92%) anti-e, 1 (1.92%) anti-c, 1 (1.92%) anti-K, 1 (1.92%) anti-Fya, 1 (1.92%) anti-Fyb, 1 (1.92%) anti-Jka; D) usually not clinically significant antibodies: 10 (19.24%) anti-M, 1 (1.92%) anti-Lea.

Summary/Conclusions: Despite RhD prophylaxis is performed in Serbia since 1970, antibodies detected in the majority of pregnant women (36.54%) in the South Backa District of Vojvodina had a specificity of anti-D. However anti-D antibodies in analysed period decrease in percentage comparing with 57.58% in period from last study 2003 to 2011.

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PREVALENCE OF UNEXPECTED RED CELL ANTIBODIES AMONG ANTENATAL WOMEN ATTENDING A TERTIARY CARE HOSPITAL IN COLOMBO, SRI LANKA

D N Gunasekara

Transfusion Department, National Blood Transfusion Services, Colombo, Sri Lanka

Background: Red cell alloimmunization, is a well-known cause of Haemolytic Disease of the Fetus and Newborn (HDFN) and it is a significant cause of fetal and neonatal morbidity and mortality in developing countries. Hence, timely detection of such alloantibodies in antenatal women is essential for early management of HDFN. Universal screening of all antenatal women is mandatory as per BCSH guidelines and is practiced in most developed countries. However in Sri Lanka, screening for alloantibodies during antenatal period is primarily being done for Rh D-negative women.

Aims: To make certain of the frequency of red cell alloimmunisation in antenatal women attending a tertiary care hospital.

Methods: A retrospective study was carried out on 4096 pregnant women attending antenatal clinics of a tertiary care hospital, Colombo, over a period of two years. The women were grouped for ABO & Rh D antigens and screened & identification done for alloantibodies by conventional tube method. The detailed obstetric histories of these women were reviewed.

Results: A total of 4096 pregnant females, 3,713 females were Rh D positive (90.6%) while 383 were Rh D negative (9.4%). With regards to the major blood group systems, O positive (40.8%) was the most common phenotype was followed by B positive (25.3%).

Out of those,58 females were found to have a positive antibody screening (62.37%) at either 12th or 28th weeks of gestation. A total of 72 antibodies were detected in 58 women during the said period, conclude an overall prevalence of alloimmunization of 1.42%. Positive antibody screening was seen in 42 (1.15%) of Rh D positive pregnant women and 16 (4.41%) of Rh D negative pregnant women. There was a statistically significant difference between alloimmunization rates in Rh D antigen negative and Rh D positive groups (4.41% versus 1.15%, P < 0.001).

Out of those alloimmunized women, 18 (29.34%) of them were found to possess single or multiple clinically significant alloantibodies (anti- D, c, E, Jk^b, S, M), and 41 (70.69%) had antibodies which are not known to cause HDFN (anti-Le^a, Le^b, P_1). Hence the risk of maternal alloimmunization with clinically significant antibodies implicated in causing HDFN was found to be 0.44%. Out of those clinically significant antibodies which are commonly and occasionally associated with HDFN, 61% (11) was Rh D negative and 39% (7) was Rh D positive.

Summary/Conclusions: The red cell alloimmunization frequency during pregnancy was 1.42% out of that 0.44% was antibodies with clinically significance, posing a risk for HDFN.

It is evident from this study that Rh D positive women are just likely as Rh D negative women to form clinically significant alloantibodies. Therefore, it is recommended that all pregnant women preferably be screened for unexpected antibodies irrespective of the Rh type during antenatal period in line with the guidelines. However as a developing country the financial burden of routine screening for irregular antibodies in all antenatal women, has to be weighed against the benefits.

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PREVALENCE AND ETIOLOGY OF HYPERBILIRUBINEMIA IN NEONATES WITH DAT TEST IN A SINGLE HOSPITAL IN KOREA

H Lee[1], H Kim[2], K Shin[2], S Jo[1], D Song[1], S Lee[1] and I Kim[1]

[1]Laboratory medicine, Pusan National University Yangsan Hospital, Yangsan
[2]Laboratory medicine, Pusan National University Hospital, Busan, Korea

Background: Hemolytic disease of newborn (HDN) is a disease in which the maternal Immunoglobulin G (Ig G) antibodies to the fetal red blood cell (RBC) antibodies cross the placenta and bind to the fetal RBC antigens leading to hemolysis. The clinical spectrum of the disease varies, including mild hemolytic anemia, hyperbilirubinemia, hepatomegaly, severe anemia with hydrops, and even death of the fetus. To diagnose the HDN and evaluate the cause of HDN, the direct antiglobulin test (DAT) of the RBC of newborn and indirect antiglobulin test of the serum of mother should be done.

Aims: The aim of this study was to provide data on the prevalence of neonatal hyperbilirubinemia and the etiology to analyze the data of neonates testing DAT

Methods: Infant patients who underwent direct antiglobulin test for perinatal testing at neonatal clinic in the Pusan National University Yansan Hospital from August 2008 to July 2017 were enrolled. DAT, total bilirubin, ABO/Rh (D) typing, phototherapy history, and the mortality and gestational age and bodyweight at birth of the infant were recorded. ABO/Rh (D) typing, irregular antibody screening and obstetric history of the infant's mothers were recorded. All statistical analyses were performed using computer software (SPSS 18.0, SPSS, Inc., Chicago, IL, USA), and results were considered statistically significant at P values < 0.05.

Results: In total, 303 neonates were tested within the study period. Of the total samples, 12.2% (37/303) showed positive results in the DAT test. Rate of getting phototherapy between DAT positive groups (75.7%) and DAT negative groups (71.1%) are not different statistically. However, newborns showing positive on DAT test were more longer phototherapy. Median initial serum total bilirubin levels (mg/dl) in DAT negative newborns and positive newborns are 16.2 (range, 0.2–36.6) and 16.1(range, 1.5–35.4) (P = 0.739). Median initial serum total bilirubin levels in Rh incompatibility, ABO incompatibility and others are 5.7 (range, 1.5–35.4), 17.4 (range, 0.9–36.6) and 16.2 (range, 0.2–33.0) respectively. Among total 303 neonates,

the age (days) at initial test were different from 1 day to 28 days. Initial serum total bilirubin levels between DAT positive groups and DAT negative of 2 days old neonates and 3 day old neonates were significantly different. Initial serum total bilirubin levels between Rh incompatibility, ABO incompatibility and others of 2 days old neonates were significantly different median level of 8.6 (range, 4.4–22.9), 14.6 (range, 3.1–17.9) and 6.8 (range, 1.7–14.5), respectively (P = 0.038).Total 217 neonates got phototherapy, serum total bilirubin level at peak during one admission were analyzed. The peak level were not significantly different, the day of peak were significantly different. Mean duration of phototherapy in Rhesus incompatibility were 6.16 days (SD, 3.76) and 3.92 days (SD, 3.0) in ABO incompatibility neonates (P = 0.033).Mothers with anti-E, c have a tendency to bore more babies than mothers with anti-D (P = 0.004), mothers who show O+ (P = 0.015). Neonates with maternal anti-E, c got more phototherapies. Gestational age were significantly different between neonates with maternal anti-D and ABO incompatibility (P = 0.004).

Summary/Conclusions: In our study, suspected Rh incompatibility neonates were more shortly reached to peak level of bilirubin than ABO incompatibility neonates. Positive rate of DAT in ABO incompatibility is 19.8% and 73.3% and Rh incompatibility. To detect HDN earlier, more sensitive eluate screening and careful maternal screening is required.

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SUCCESSFUL PREGNANCY COURSE IN FEMALE THALASSEMIC PATIENTS WITH ALLOIMMUNIZATION

A Azarkeivan[1], M Moghaddam[2] and F Ghotbizadeh[3]

[1]Thalassemia clinic [2]special Serology, Iranian Blood Transfusion Organization, Research Center [3]OB GYN, Tehran Medical University, Tehran, Iran

Background: Introduction: Alloimmunization can occur in transfused patients with hemoglobinopathies, and high prevalence of alloantibody production have been noted in β- thalassemia patients. Alloantibody against some RBC subgroups may occur in female thalassemic patients who if their husbands have these antigens; their fetus may inherit the antigens and may have risk of HDN in the fetus. Therefore, a complete history of prior alloimmunization should be elicited from all pregnant patients with thalassemia, and consideration should be given to doing alloantibody screening in early pregnancy to certificate existing titers. Also checking these RBC subgroups in her husband is very important. Here we describe case of thalassemia and Successful pregnancy course.

Aims: Here we describe case of thalassemia and Successful pregnancy course.

Methods: A 24 years old case of thalassemia intermedia who was on Hydroxy urea with no transfusion .She married and stopped her Hu by plan of pregnancy, 6 months later, she got pregnant and in her 10 weeks of pregnancy developed severe anemia(Hgb 7 g/dl) and received blood transfusion but two days after transfusion her Hgb dropped to 3 g/dl and didn't get better with other transfusion and was advised to terminate her pregnancy,

Results: She referred to us with Hgb 4 g/dl. On admission she had huge splenomegaly, low Hgb level. In antibody screening and antibody identification she had O + gp with Anti C and anti Fya; and low platelet count because of huge splenomegaly, Fortunately her husband in RBC Phenotyping was C neg and Fya neg,So, our fear was reduced about the risk of HDN in the fetus. The patient receive leukoreduced matched C neg and Fya neg blood without any immunosuppression or IVIgG. Her spleen size was reduced a little bit and now she is on 27 week of pregnancy with acceptable good fetal growth and her spleen was not any interfere on her course of pregnancy .We hope to terminate this pregnancy without need to splenectomy before delivery .

Summary/Conclusions: With improved life expectancy in the hemoglobinopathies, many women with thalassemia are now choosing to become pregnant. To increase the chances of a successful pregnancy, these patients should be under the care of a hematologist and an obstetrician from the beginning. Patients who are heavily alloimmunized and require RBC transfusion should receive extended phenotypically matched products. Also we should check paternal RBC phenotype to find the risk of HDN in fetus. So control of maternal Hgb and risk of HDN is two point of care in alloimmunized female thalassemic patients.

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IMMUNE ERYTHROCYTE ALLO–ANTIBODIES AMONG PREGNANT WOMEN ATTENDING ANTENATAL CLINIC IN A TERTIARY HEALTH FACILITY, BENIN CITY, NIGERIA

AS Adewoyin[1], O Adeyemi[2], B Ande[3] and O Awodu[4]

[1]Haematology and Blood Transfusion, Lagos State Health Service Commission, Lagos [2]Haematology and Blood Transfusion [3]Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin City [4]Haematology and Blood Transfusion, University of Benin Teaching Hospital, Benin City, Nigeria

Background: Maternal allo-immunisation is associated with adverse peri-natal outcomes such as haemolytic disease of the foetus and newborn. It is also a major source of morbidity among at-risk pregnant women who are exposed to multiple blood transfusions such as patients with sickle cell disease or major placenta previa. The magnitude/pattern of allo-immunisation and its pathologic consequences among Nigerian pregnant women in many parts of the country is poorly defined. This is largely related to absence of routine allo-antibody screening and poor quality data.

Aims: This study therefore aimed to determine the proportion and specificities of atypical maternal allo-antibodies among antenatal attendees at the University of Benin Teaching Hospital (UBTH), Benin City, South-South Nigeria. Possible attendant risk factors associated with allo-immunisation during pregnancy and childbirth in the study population was also assessed.

Methods: The study was a hospital based, cross-sectional survey conducted among pregnant women attending antenatal clinic at the UBTH between May and August 2015. One hundred and fifty participants were interviewed with a structured questionnaire to obtain data on parity, transfusion history and other clinical details. ABO/Rh D blood groups and haemoglobin phenotypes were retrieved from their hospital antenatal records. Allo-antibody screening and other serological tests were subsequently performed. Screening cells and panel of cells (albacyte reagent red cells) for detection and identification of unexpected allo-antibodies were procured from Lorne Laboratories UK, with Lot Numbers V159123 and V159601/V159602 respectively. Descriptive data were presented in means and proportions. Significant association between alloimmunisation and other variables were tested using chi square or fisher exact test. Ethical approval (Protocol number ADM/E22/A/VOL. VII/1094) was obtained from Institutional Review Board prior to the study.

Results: The mean maternal age of the participants was 31.55 years. The mean gestational age at the time of the study was 28.21 years. Most of the participants (60%) were in their third trimester, while 9.3% were in first trimester of pregnancy. Most of the participants (95.3%) tested positive for the Rh D antigen. The most prevalent haemoglobin phenotype was AA (77.7%), followed by AS (20.7%), SS (1.3%) and SC (0.7%). About ninety one percent of the participants (90.7%) were blood transfusion naïve. Seven of the participants (4.7%) had positive allo-antibody screens. Two (1.33%) were clinically significant maternal allo-antibodies (Anti-D and Anti-Lu[b]). No statistically significant association (p value > 0.05) was observed between alloimmunisation and variables such as gestational age, parity, haemoglobin phenotype, previous blood transfusions and Rh D negativity in this study.

Summary/Conclusions: Maternal alloimmunisation affects about 5% of pregnancies in Benin City, Nigeria. Atypical alloantibodies, Anti- D and Anti- Lu[b], were found in two participants (1.33% of total antibody screens). These are clinically significant allo-antibodies with potentials for adverse pregnancy and perinatal outcomes. Rh D isoimmunisation still occurs among pregnant women in Benin City, South-South Nigeria. No significant relationship was observed between unexpected maternal allo-antibodies and factors such as parity, haemoglobin phenotype and previous blood transfusion.

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COMBINED ANTIBODY TITRE INVESTIGATION IN PRENATAL PATIENTS

M Farrell[1], G Clarke[1,2], G Barr[2] and J Hannon[1,2]

[1]Department of Laboratory Medicine and Pathology, University of Alberta [2]Canadian Blood Services, Edmonton, Canada

Background: Management of potential hemolytic disease of the fetus and newborn (HDFN) relies on monitoring maternal antibody concentration by way of antibody titration. For individuals with multiple antibodies, separate titrations for each antibody are generally performed. Assessing antibody concentrations separately ignores in vivo conditions and may not be representative of the combined effect multiple antibodies can have on the fetus.

Aims: The aim of this study was to examine the difference between combined and separate titre levels when multiple antibodies are present. These results will help

determine if combined titrations reach a critical titre and signal the need for direct fetal monitoring earlier than the traditional single antibody titration method.

Methods: Twenty-nine samples containing various combinations of 2 different antibodies were examined. For each sample 3 titrations were performed: 2 titrations by the standard method where separate titre levels for each antibody were determined and a single combined titration method to detect the titre of both antibodies together. The separate method was achieved by tittering individual antibodies separately against reagent cells that expressed only one antigen of the combination of antibodies. The combined titre method was performed using reagent cells that expressed both antigens against which the antibodies were directed. Separate and combined titrations for every sample were tested in parallel using the indirect antiglobulin test by saline tube method. The only difference between separate and combined methods was whether the reagent cells expressed one or both antigens toward which the antibodies present were directed.

Results: Overall 17/29 samples (58.6%) showed an increased titre level with the combined titration method. Of the 12 samples that showed no increase, 10 contained a separate titre of < 1 for either one or both antibodies. Of the samples where both antibodies had a separate titre of ≥ 1, 13/15 (86.7%) showed an increased titre level with the combined titration method. An increase was also observed for 3/10 samples (30.0%) that had one separate antibody titre of < 1. Additionally, 1/3 samples (33.3%) that had a titre of <1 for both separate antibodies showed an increased level with a combined method. Titre increases ranged from one-fold (16 out of 17) to two-fold (1 out of 17) between methods. Furthermore, in comparison to the separate titration method, no decrease in the titre level was observed using the combined method.

Summary/Conclusions: This study demonstrates that, in cases where two antibodies are present, titrations performed by a combined method will produce titre levels equal to or higher than a standard separate antibody titration method. Based on these results, a combined titration will reach a critical titre level as early as, or earlier in gestation than antibodies monitored by a single titration method. Monitoring HDFN in patients with multiple antibodies using a combined titration method could potentially alert physicians to the need for additional testing and direct fetal monitoring earlier than the traditional single antibody titration approach.

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TITRATION OF RED CELL ANTIBODIES IN PREGNANCY – UK PERFORMANCE AND POLICY

J White, R Haggas, K Veale, C Whitham and M Rowley

UK NEQAS BTLP, Watford, United Kingdom

Background: UK NEQAS ABO titration (ABOT) exercises demonstrate wide variation in titration results within and between technologies. In the UK, titration (or quantitation) of non-ABO clinically significant red cell antibodies is used to inform clinical management in pregnancy. British Society for Haematology (BSH) guidelines for blood grouping and antibody testing in pregnancy (2016) provide algorithms for testing and referral. Pregnant women with Kell system antibodies (unless their partner is confirmed to be antigen negative) should be referred to a fetal medicine unit (FMU) when the antibody is first identified; titration should be undertaken at four-weekly intervals up to 20 weeks, two-weekly thereafter and referral made for non-invasive testing using cell free fetal DNA (cffDNA) at a gestation recommended by the reference laboratory.

Aims: To investigate UK practice in antenatal titration and referral, and requirement for EQA.

Methods: In 2017, UK NEQAS (BTLP) offered optional assessment of titration on an EQA sample containing anti-K (presented as an antenatal 'booking' sample). Laboratories used their in-house titration method and locally selected reagent red cells, and answered a questionnaire on practice.

Results: 45 UK and ROI laboratories returned IAT titration results; 35 (78%) using BioRad, 6 (13%) Ortho, 2 (4%) Immucor and 2 (4%) tube. 40/45 answered all accompanying questions. The range of results was 8 to 64; 43/45 (96%) within one dilution of the median (32). The endpoint was determined as the last weak reaction by 16/44 (36%), with 27/44 (62%) using 1 + , and one (2%) 2 + . The median result did not vary by endpoint or technology (BioRad/Ortho). 43/44 (98%) select reagent red cells with heterozygous expression of the relevant antigen where possible. 12/43 (28%) titrate in parallel the NIBSC standard anti-D and 35/44 (80%) the patient's previous sample (where available). Had this been a clinical sample 78% would request a paternal sample, 60% refer to a FMU at booking, 93% repeat titration within 4 weeks, and 16% refer for cffDNA testing.

Summary/Conclusions: Patterns of variation in IAT titration results by technology, as seen in ABOT data, were not observed, possibly due to this anti-K having a lower IgM component compared to ABO antibodies, and the variability of technologies in

detecting IgM by IAT. However, numbers in this exercise are low and further investigation would be required to confirm this hypothesis. The low referral rate of this hypothetical sample for molecular testing may reflect laboratories waiting for paternal K typing results or that cffDNA for K (KEL*01) is generally only offered after 20 weeks gestation, due to the increased risk of false negative results before this time.

Titration results are used to make decisions on testing strategies and referral to a FMU; however, the cut-off points used to make these decisions are not consistent. For antibodies other than anti-K, a titre of 32 is widely used as a trigger for further action, but this result does not necessarily represent the same concentration of antibody in all laboratories. An EQA pilot is being introduced in 2018 to monitor antenatal titration results and raise awareness of guidelines for testing and referral.

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Abstract has been withdrawn

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ANTI-D TITRATION BY TUBE METHOD: IMPACT OF DIFFERENT PARAMETERS ON TITER AND SCORE VALUES

A Adiogo, S Huguet-Jacquot, H Delaby, A Mailloux and C Toly-Ndour

Unité Fonctionnelle d'expertise en Immuno-Hémobiologie Périnatale, Centre National de Référence en Hémobiologie Périnatale (CNRHP), Pôle de Biologie Médicale et Pathologie, Hôpital St Antoine, Assistance Publique des Hôpitaux de Paris (AP-HP), Paris, France

Background: Antibody titration by tube method is still the main method used worldwide to quantify anti-red blood cells antibodies in situations of feto-maternal incompatibility. Based on titration results, thresholds to trigger a fetal specific follow-up with ultrasonography and Doppler are determined. Nevertheless titration by tube method is associated with substantial variabilities within and between laboratories.
Aims: The aim of our study was to determine the factors that could cause titer and score values variabilities within and between laboratories, in order to limit them We investigated the role of different parameters on anti-D titration results.
Methods: We performed anti-D tube titration and scoring with unilateral variation of one parameter on about 20 samples each time. We studied the following parameters: manual or automated dilution of samples, concentration of red cells (4 ± 2%), red blood cells phenotype (RH:1,2,3,4,5 / RH:1,2,-3,-4,5 / RH:1,-2,3,4,-5), use of single or pooled red blood cells, concentration of antiglobulin (pure, diluted 1/3), incubation time (30 ± 15 min), centrifugation speed (180, 500 and 780 g), reading delay after centrifugation (immediately, 5 or 10 min later) and reading by different operators using a 1 + end point procedure.
Statistical analysis was performed with Graphpad Prism (Wilcoxon test). Differences with p < 0,05 were interpreted as statistically significant. A difference of more than 1 dilution in the titer values was considered to be clinically significant.
Results: Titer and/or score values were significantly impacted by i) antiglobulin and red blood cells concentrations used, ii) red blood cells phenotype and iii) reader operator. The impact of these parameters is weak, as the differences are often under 1 dilution and non clinically significant. Use of pooled red blood cells, manual or automated dilutions, incubation time and reading delay after centrifugation didn't seem to have any influence on results.
Summary/Conclusions: Several parameters have a slight impact on anti-D titration results. However additioning these parameters may result in clinically significant variation. The use of a standardized detailed procedure and harmonization of the reading stape may reduce variabilities within and between laboratories.

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PRENATAL TITRES USING TUBE VS GEL TECHNIQUE

J Fung[1], L Bortignon[1], C Colavecchia[2], J Callum[2], Y Lin[2] and N Shehata[1]

[1]Transfusion Medicine Service, Mount Sinai Hospital [2]Transfusion Medicine, Sunnybrook Health Sciences Centre, Toronto, Canada

Background: Titration of an alloantibody to a red cell antigen is a semi-quantitative screening tool that can detect an increased production of maternal antibody during pregnancy. In the current standard of care, the titre contributes to the clinical decision

of whether and when to investigate further for fetal anemia. There are two common methodologies, the tube technique and microcolumn gel technique. Antibody titres differ according to the sensitivity of the technique utilized. The tube technique has been used as the standard technique and therefore critical titre values based on fetal/neonatal outcomes have been obtained. Several centers use the gel technique but titres corresponding to values by tube technique have not been definitively determined.
Aims: The aim of this study was to correlate the alloantibody titres against 3 red cell antigens; D, c, and K as determined by tube and gel technique in prenatal patients.
Methods: Titrations were performed using serial two-fold dilutions of plasma from prenatal samples. Each titre was performed in parallel by both the tube and the gel technique using the same prepared dilutions. The titre was expressed as the reciprocal of the highest dilution showing 1 + reaction for tube technique, and any reaction for the gel technique.
Results: Forty patients were studied and a total of 115 titrations were performed and ranged from undetectable to 1024 for each antibody (36 anti-D, 34 anti-c, and 45 anti-K). Overall, for 55 titrations (47.8%), the two methods generated results that were within one dilution of each other: 7 for anti-D, 4 for anti-c, and 44 for anti-K. 97.8% of anti-K titres were within one dilution (i.e. no change or an increase in dilution) of the titres detected by the gel technique. For 115 titrations, the gel method resulted in a titre that was 1.6 times higher with gel than with tube (2, 2.7 and 0.4 times higher for anti-D, c and K, respectively). The gel technique infrequently resulted in a titre that was lower than that detected by the tube technique.
Summary/Conclusions: Antibody titrations by the microcolumn gel technique showed higher titres than the conventional tube technique in 87 (75.7%) of all titrations. It may be possible to use a mean standardized value to correlate the two methodologies for prenatal alloantibody titrations. Prospective data are needed to validate our findings.

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Abstract has been withdrawn

Clinical Transfusion – Neonatal and Pediatric Transfusion

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IMPACT ASSESSMENT OF CHANGE TO COUNCIL OF EUROPE STANDARDS FOR POST-IRRADIATION RED CELL STORAGE PRACTICES IN A CANADIAN TERTIARY CARE PEDIATRIC HOSPITAL

D Kim[1], D Morrison[2,3] and N Au[2,3]

[1]University of British Columbia [2]Division of Hematopathology, BC Children's Hospital and BC Women's Hospital [3]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada

Background: Irradiation of red cells is known to cause membrane damage with resultant increase in supernatant potassium and hemoglobin levels. Current standards in Canada state that red cells may be stored for 28 days post-irradiation or until the unit's original expiry date, whichever comes first. However, in the near future Canada is expected to adopt a stricter approach based on the Council of Europe (COE) standards, dictating that irradiated cells must be transfused no later than 14 days after irradiation and no later than 28 days post-collection.
Aims: The aim of this study is to assess the potential impact of shorter post-irradiation red cell storage on red cell utilization in a tertiary care pediatric hospital with an on-site irradiator and utilizes a dedicated donor unit system for NICU patients.
Methods: Data on irradiated red cell transfusions was retrospectively obtained for a one year period from the transfusion laboratory computer system. Data elements included: donor unit number, collection date, irradiation date/time, transfusion date/time, and patient medical record number. These data were analyzed to determine: the age of red cells at irradiation, age of red cells at transfusion, interval between irradiation and transfusion, number of donor exposures for NICU patients, number of transfusions that would be considered unacceptable according to COE standards, and the change in donor exposures if COE standards were applied. Due to the

variability in red cell age at time of receipt from the blood supplier, a donor exposure range was calculated based on red cell units being either 2 days old or 7 days old at time of designation to a patient if additional units are required.

Results: 1751 transfusions were administered to 379 patients overall. 383 transfusions were administered to 117 NICU patients. 88.5% (1550/1751) of all transfusions and 87.7% (336/383) of NICU transfusions would be acceptable according to the COE standards. Overall, unacceptable transfusions include: a) red cells >28 days of age at time of irradiation (n = 163), b) pre-irradiated red cells transfused after 28 days of age (n = 20), and c) red cells transfused >14 days after irradiation (n = 18). For NICU patients, unacceptable transfusion would be due to irradiation of red cells after 28 days of age only (n = 47). 62.4% (73/117) NICU patients received more than one transfusion. Donor exposures ranged from 1 to 7. Increased donor exposures would occur in 20 to 25 patients (17.1% to 21.4% of all NICU patients) if COE guidelines were applied. There would be an increase of one donor exposure only in most patients (19–23 patients).

Summary/Conclusions: The majority of current irradiated red cell transfusions would be acceptable according to COE guidelines. Red cell utilization may increase, but this would likely be insubstantial. Approximately 20% of NICU patients may experience an increase in donor exposures, but in most cases there would be one additional donor exposure only. The benefit of administering less extracellular potassium and hemoglobin likely outweighs the risk of one additional donor exposure from a donor population that is carefully screened for known transmissible diseases.

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TAKE LESS, GIVE MORE: AN IMPROVEMENT INITIATIVE TO NEONATAL RED CELL TRANSFUSION

S Sng[1], M Heng[1], J Kong[2] and J Lam[3]
[1]Department of Pathology and Laboratory Medicine [2]Department of Neonatology [3]Paediatric Haematology/Oncology Service, KK Women's and Children's Hospital, Singapore, Singapore

Background: Transfusion of red cells is a crucial component of neonatal intensive care in very low birth weight (VLBW) neonates. Anaemia of prematurity develops over the first 10–12 weeks of life due to multiple factors including ineffective erythropoiesis and incomplete placental iron transfer. Iatrogenic blood loss from frequent blood sampling is a major contributory factor. Multiple blood transfusions are often required to maintain an optimal haemoglobin level tailored to each neonate's clinical condition.

Aims: To minimize blood sampling from VLBW neonates by reviewing the institution's neonatal transfusion guidelines, allowing transfusion of red cells to neonates less than 4 months without full compatibility testing of donor blood with their blood specimens.

Methods: A protocol termed as Neonatal Omission of Crossmatch (NeOXM) was introduced in November 2017 and prospectively reviewed from December 2017 to February 2018. The protocol was applicable to VLBW neonates weighing less than 1.5 kg and of chronological age less than 4 months. Testing was performed on specimens from both mother and neonate prior to any transfusions - maternal sample for ABO and Rh(D) grouping and antibody screen, neonatal sample for ABO and Rh(D) grouping and Direct Antiglobulin Test (DAT). If both the pretransfusion maternal antibody screen and neonatal DAT were negative, there was no need to provide a neonatal blood specimen for subsequent blood transfusion requests up to 4 months of age. Another requirement was availability of a historical neonatal ABO and Rh(D) group from a cord blood sample. Full compatibility testing would be required should there be any deviation from eligibility criteria. Leucocyte-reduced Group O red cells were selected for transfusion. Data reviewed included an evaluation of resources and testing time saved. The time taken from physician's request to blood administration was also monitored to study the effectiveness of direct blood product issue. Any adverse reactions after transfusions were also recorded.

Results: During the 3-month review, 38 neonates were enrolled in the NeOXM protocol. 2 out of 38 neonates were ineligible, due to unavailability of a maternal pretransfusion sample in 1 case and absence of a historical ABO and Rh(D) grouping record in the other. Out of the 36 eligible cases, only 1 neonate was subjected to blood sampling twice as the initial blood drawn did not meet all the pretransfusion testing guidelines.

A total of 58 units of blood were transfused to 19 neonates but not subjected to compatibility testing. 23 blood –taking processes were avoided due to NeOXM protocol. The cost of a ABO and Rh(D) grouping and compatibility testing for each unit is $34 and $38 respectively. The total cost savings for patients are $2986. Without the need to test for compatibility, processing time of blood unit for patient was

shortened from 30 min to 3 min for each transfusion. No adverse reactions were observed from any uncrossmatched transfusion.

Summary/Conclusions: The NeOXM protocol has resulted in cost savings for patients and also enabled a faster time to blood administration from blood order.

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LIVE VACCINES AFTER RED BLOOD CELL TRANSFUSION: TIME TO REVISIT?

A Zabeida[1], C Renaud[1], M H Lebel[1], M Cloutier[2] and N Robitaille[1]
[1]Pediatrics, CHU Sainte-Justine, Montreal [2]Héma-Québec, Québec, Canada

Background: Current American and Canadian guidelines recommend to delay measles, mumps, rubella (MMR) and varicella immunization by 5–6 months following transfusion of unwashed red blood cells (RBC) due to potential interference by serum antibodies. Thus, patients chronically transfused with RBC commonly suffer from a delay or absence of MMR/varicella vaccination. There is a paucity of data concerning the true effect of transfusions on live attenuated vaccine immunization. The recommendations may thus be unfounded, and prevent valuable vaccination opportunities for children with frequent blood transfusions.

Aims: The primary aim of this project was to determine MMR vaccine immunogenicity in patients chronically transfused with RBC. A secondary aim was to quantify the amount of MMR-specific antibodies in packed RBC.

Methods: MMR-specific IgG antibodies were quantified in 25 pediatric patients who received both doses of the MMR vaccine less than 6 months post-transfusion while they were on a chronic RBC transfusion program for sickle cell disease, β-thalassemia major, Diamond-Blackfan anemia or pyruvate kinase deficiency. MMR-specific antibodies were also quantified in 30 samples of packed RBC supernatants, and the results were divided among blood donors born before versus after 1976 (likely to have MMR antibodies from natural infection versus vaccination).

Results: Immunity to each of the MMR vaccine components was found to be 68 - 76%. There was no formal control group; long-term immunity rates in the literature are ≥ 90% for all MMR components. Those who received RBC transfusions less than 6 months prior to serology sampling did not have higher antibody titers than those transfused ≥ 6 months ago. In the supernatants of packed RBC for blood donation, 20% of donors were found to have immune-level IgG antibodies to either measles, mumps or rubella for those born after 1976 (likely MMR vaccination), versus 100% of donors born before 1976 (likely natural immunity).

Summary/Conclusions: This is the first study of the effect of RBC transfusions on MMR vaccine immunogenicity. Although lower than the rates reported in the literature, the results suggest a high rate of immunogenicity to each component of the MMR vaccine in patients immunized less than 6 months post-transfusion. The amount of immune-level antibodies against MMR was found to be significantly lower in blood donors born after 1976 who were more likely to have been vaccinated with MMR rather than have had natural infection with either of these viruses. This argues in favor of natural infection providing quantifiably higher levels of antibodies compared to vaccination, and it can be inferred that antibody levels to vaccine components will become lower in future blood donations, as more and more blood donors will have been vaccinated. Weighing the risks and benefits of disease prevention in a highly vulnerable population, a re-evaluation of immunization delays post RBC transfusions is called for.

P-659
POSITIVE COOMB'S TEST AMONG PALESTINIAN NEWBORNS. CAUSES AND CLINICAL CONSEQUENCES

MY Asees[1] and A Rezeq[2]
[1]Medical Technologist, PMC [2]QA, CBB, Ramallah, Palestinian Territory

Background: Hemolytic disease of the fetus and newborn (HDFN) is caused by the destruction of fetal/neonate red blood cells due to red cell antibodies produced by the mother. As a result, fetal hydrops during pregnancy or neonatal anaemia and jaundice occur after birth. However, the introduction of routine postnatal prophylactic anti-D immunoglobulin for Rh D negative women has obviously reduced this form of HDFN. Direct Antiglobulin Test (DAT) is the cornerstone for the detection of antibodies bound to red cells and is a valuable test aiding in the diagnosis of HDFN.

Aims: In this study, we aimed to determine the causes and consequences of positive DAT in newborns in Central Blood Bank in Palestine over a period of 12 months.

Methods: A retrospective cohort study was conducted at the Central Blood Bank in Palestine during the year 2017. A total of 957 newborns were analyzed and their data included DAT, blood group, antibody status of mother and child (Indirect Coomb's Test).

Results: Over the study period, a total of 957 newborns were analyzed. The number of newborn with positive DAT was 87 cases (9.09%). In 97.3% of cases, the underlying cause of the HDNB was the ABO blood group mismatch between mother and infant, in 1.33% of cases the mother had non-A/B red cell allo-antibodies, and in (1.33%) both of above factors were present. Among the 87 positive DAT in newborns, (63.2%) were grouped as A+, (25.3%) newborns were B+, (4.6%) newborns were A- and (3.4%) newborns were O + . Regarding mothers blood groups whom their newborns were positive for the DAT, (78.2%) mothers were grouped as O+, followed by O- (10.3%) and B- (1.1%), respectively. Among these 87 mothers, (2.3%) had a positive indirect coomb's test (n = 2/87), while most mothers had a negative indirect coomb's test. About 53 newborns (60.9%) had neonatal jaundice that required treatment, of which 30 of them have required single phototherapy treatment (n = 30/53, 56.6%), 21 have required double-then-single phototherapy (n = 21/53, 39.6%) and 2 newborns have required an intensive followed by double then single phototherapy treatment (n = 2/53, 3.8%). Regarding the other 34 neonates, eight of them did not require any phototherapy treatment (9.2%), while data regarding the phototherapy treatment for the other 26 neonates were not found (29.9%). None of the newborns have required exchange transfusion

Summary/Conclusions: The most common cause for a positive DAT in neonates in Palestine in the year 2017 was ABO blood group incompatibility between mother and child, despite that other causes (e.g., alloimmunization, drugs) should also be explored.

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THE EFFECTS OF LOWER PLATELET TRANSFUSION THRESHOLDS (L-PLAT) ON THE INCIDENCE OF BLEEDING IN CHILDREN WITH CHEMOTHERAPY INDUCED THROMBOCYTOPENIA

SZ Lim[1], M Lim[1], R Bhattacharyya[1] and J Lam[2]

[1]Pediatric Medicine, KK woman and children's hospital [2]Pediatric Medicine, KK Woman and Children's Hospital, Singapore, Singapore

Background: The benefit of prophylactic platelet transfusion in reducing bleeding complications in chemotherapy induced thrombocytopaenia is not based on robust evidence. Recently published international guidelines recommend much lower thresholds compared to conventional transfusion practice. A quality improvement project was conducted reviewing existing platelet transfusion practice in the paediatric oncology department of KK Hospital. Changes in platelet transfusion practice were made, and the effects were studied.

Aims: The primary aim of the study was to examine if there was any increased incidence of clinical bleeding after the revision of prophylactic platelet transfusion thresholds. The secondary aim was to examine if revision of prophylactic platelet transfusion thresholds led to a reduction in the platelet transfusions administered.

Methods: The retrospective study was conducted in May to July 2014, prior to the revision of the platelet transfusion guideline. Thirty two patients received one hundred and ninety six platelet transfusions in our inpatient oncology ward. The respective platelet count, indication of transfusion and bleeding severity for each of these transfusions were studied. A more restrictive platelet transfusion guideline was subsequently implemented in April 2017, with revision of the prophylactic platelet transfusion thresholds (from $20 \times 10^9/l$ to $10 \times 10^9/l$ in stable and afebrile patients, and from $30 \times 10^9/l$ to $20 \times 10^9/l$ in patients with fever or sepsis). The prospective study was conducted from April to June 2017 to review the effects of the more restrictive transfusion strategy, which included patients in the oncology ward, the oncology day therapy unit and the oncology outpatient clinic. This study included patients who (1) received platelet transfusions, (2) met criteria for platelet transfusion under the previous guideline but not under the revised guidelines and were therefore not given transfusions, or (3) had clinical bleeding. A total of twenty seven patients receiving eighty four platelet transfusions were reviewed. The World Health Organization (WHO) scale for bleeding (Miller, Cancer, 1981) was used to assess the severity of bleeding. Chi square test of independence was used to explore the relationship between the type of transfusion protocol and the incidence or severity of bleeding.

Results: There was no statistically significant increase in the rate of bleeding in the restrictive transfusion strategy group (16.5%), as compared to the more liberal transfusion strategy (17.4%) (p = 0.848). A breakdown of the clinically significant bleeds by WHO grades showed that in the restrictive transfusion strategy group, there were no WHO Grade 4 bleeds, no increase in the number of patients with Grade 3 bleeds

(2 patients), and a reduced incidence of Grade 1 and 2 bleeds (from 42 to 22) as compared to the liberal strategy group. In addition, data collected over three months showed that seventeen platelet transfusions were avoided in accordance with decreased thresholds of the revised guidelines, resulting in a 22% reduction of the number of prophylactic platelet transfusions. The resultant estimated amount of annualised cost saving is approximately $35400 (USD).

Summary/Conclusions: We conclude that the lower prophylactic platelet transfusion thresholds adopted in our new guideline are safe, with no increased incidence or severity of bleeding. In addition, reduction in the number of platelet transfusions translates into reduced cost, less demand on precious platelet units and improves patient safety by avoiding transfusion related risks.

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Abstract has been withdrawn

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CORRELATION BETWEEN CONVENTIONAL COAGULATION TESTS AND ROTEM IN CHILDREN

R Joshi and S Ganu

Women's and Children's Hospital, Adelaide, Australia

Background: Historically conventional coagulation tests like PT, INR, APTT, Platelet count and Fibrinogen level has been used in the management of coagulopathy. Viscoelastic coagulation tests such as ROTEM have gained renewed interest in the safe management of coagulopathy in adult and paediatric patients. However, the correlation between the conventional coagulation tests and ROTEM has not been investigated in paediatric population before to conclude whether they are reciprocal to or replacement of each other.

Aims: To study the correlation of standard coagulation tests with ROTEM in infants undergoing craniofacial surgery

Methods: Local human ethics committee approval was obtained for the prospective study. The study was conducted over 2 years time in Women's and Children's Hospital. The data was collected from children aged 6 months to 1 year undergoing craniofacial surgeries in Women's and Children's Hospital. All those ROTEM test results where the ROTEM was done along with conventional coagulation tests at the same time were collected for analysis.

Results: 76 children (49 boys and 36 girls) were included in the study who underwent craniofacial surgeries from 2015–2017 in Women's and Children's Hospital, Adelaide. The age range was from 6 months to 12 years. Spearman's Coefficient of correlation test was performed to see the correlation between conventional coagulation tests and ROTEM results. PT and INR showed a statistically significant correlation with EXTEM-CT, EXTEM-CFT, EXTEM-alpha and EXTEM-MCF. Fibrinogen level showed a statistically significant correlation with FIBTEM-A5, FIBTEM-A10 and FIBTEM-MCF.

Summary/Conclusions: Amount of fibrinogen needed to correct coagulopathy can be determined by monitoring the clot strength in FIBTEM (A5, A10 and MCF) where the decision can be taken very quickly by point of care ROTEM test. Correlation between INR and EXTEM-CT can be useful in clinical setting like warfarin reversal. However, further study with higher number of patients is needed to draw a definitive clinical conclusion.

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POSTNATAL INTERVENTION FOR THE TREATMENT OF FNAIT: A SYSTEMATIC REVIEW

J Baker[1], N Shehata[2], M Murphy[3], A Greinacher[4], T Bakchoul[5], E Massey[6], L Lieberman[7], D Landry[8], S Tanael[9], D Arnold[10], S Baidya[11], G Bertrand[12], J Bussel[13], M Kjaer[14], C Kaplan[15], J Kjeldsen-Kragh[16], D Oepkes[17], H Savoia[18], G Ryan[19] and H Hume[20]

[1]St. Michael's Hospital, The Hospital for Sick Children [2]Departments of Medicine and Obstetric Medicine, Mount Sinai Hospital and Canadian Blood Services, Toronto, Canada [3]NHS Blood & Transplant, Oxford University Hospitals and University of Oxford, Oxford, United Kingdom [4]Institute of Immunology and Transfusion Medicine, University Hospital Greifswald, Greifswald [5]University Hospital Greifswald and University of Tuebingen, Tuebingen, Germany [6]Diagnostic and Therapeutic Services, NHS Blood and Transplant, Bristol, United Kingdom [7]University Health Network, University of Toronto, Toronto [8]Canadian Blood Services, Ottawa [9]Canadian Blood Services, Toronto [10]Division of Hematology and Thromboembolism, McMaster University, Hamilton, Canada [11]Australian Red Cross Blood Service, Brisbane, Australia [12]Platelet Immunology Department, French Blood Services of Brittany (EFS), Rennes, France [13]Weill Cornell Medicine, New York, New York, United States of America [14]University Hospital of North Norway and Finnmark Hospital Trust, Hammerfest, Norway [15]Retired and formerly, Institut National de la Transfusion Sanguine, Paris, France [16]Department of Clinical Immunology and Transfusion Medicine, Regional and University Laboratories, Lund, Sweden [17]Department of Obstetrics, Leiden University Medical Center, Leiden, Netherlands [18]Royal Children's Hospital, Melbourne, Australia [19]Fetal Medicine Unit, Mount Sinai Hospital, Toronto [20]Division of Haematology/Oncology, CHU Sainte-Justine, University of Montreal, Montreal, Canada

Background: Fetal and neonatal alloimmune thrombocytopenia (FNAIT) may result in life-threatening bleeding.
Aims: This systematic review of postnatal management of FNAIT examines transfusion of human platelet antigen (HPA)-selected or unselected platelets, alone or in combination with IVIg, on platelet increments, hemorrhage and mortality.
Methods: MEDLINE, EMBASE and Cochrane database searches were conducted as well as bibliographic review from 1946 until January 12, 2016. We selected original research published in English with five or more newborns diagnosed with FNAIT, and at least one of the interventions and one of the outcomes of interests in the study. Two individuals extracted data independently. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to assess overall study quality categorized by outcome. The results could not be combined as a meta-analysis due to the heterogeneity of the treatments and outcomes, and limited quality.
Results: Thirteen studies fulfilled the inclusion criteria. There were three prospective studies and no randomized controlled studies. The studies were of low quality according to GRADE. We were unable to determine whether the HPA-selected transfusion affected ICH or mortality as the timing of the ICH that was the predominant cause of death could not be ascertained. HPA-1a was the predominant cause of FNAIT in 12 studies, ranging from 75% to 100% of neonates. Of 389 neonates treated, 89% received platelet transfusions: all had an increase in their platelet count with platelet transfusion, with either selected or unselected platelets and with or without IVIg. The duration of thrombocytopenia was described only in one study to be in the range of 0–1 days in 17 patients treated with HPA selected platelets, 1–8 days in six patients treated with HPA unselected platelets and 0–1 in three neonates treated with HPA selected and unselected. Most neonates with platelet counts <30 × 10^9/l were transfused; however, none of the studies determined an optimal platelet transfusion threshold. HPA-selected platelet transfusions tended to result in higher platelet increments and longer responses than HPA non-selected platelets. Available studies have not clearly demonstrated benefit of adding IVIg to platelet transfusion alone.
Summary/Conclusions: The literature is sparse, limited to descriptive studies that rarely addressed specific outcomes other than post-transfusion platelet count. Platelet transfusions were commonly used to increase platelet counts in patients with FNAIT and severe thrombocytopenia and/or bleeding. HPA-selected platelets are preferred if immediately available but if unavailable, unselected platelets may be used until HPA selected platelets are available as they do raise the platelet count. Evidence for adding IVIg to platelet transfusion is lacking.

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INTRAUTERINE TRANSFUSION IN PATIENT WITH PHENOTYPE (–D–) AND TRANSFUSION IN NEWBORN

S Villa[1], S Ghirardello[2], R Temporiti[1], E Raspollini[1] and M Pizzi[1]

[1]Centro Trasfusionale [2]Neonatal Intensive Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Background: Our policy for intrauterine fetal (IUFT) and neonatal transfusion involves the use of concentrated blood cells (EC), preferably group 0 Rh negative (cde/cde), fresh (<5 days), from periodic donor, compatible with mother's and/or newborn's plasma, hematocrit 70 + 5%, for IUFT and 55 + 5% for the newborn.
Aims: Efficacy and safety of EC transfusion not fully compliant with our policy in the management of a particular case of pregnant women with a phenotype (-D) with anti-Hro antibodies.
Methods: 1) For IUFT on the mother samples are performed: AB0 group determination and complete Rh phenotype, indirect and direct antiglobulin tests (IAT and DAT) and cross match with automatic method on BioVue® Innova (Ortho Clinical Diagnostics) and extended typing in molecular biology. 2) For the neonatal transfusion are performed: group determination AB0 (direct only) and Rh phenotype, IAT, DAT and cross match with automatic method (Innova).
Results: 1) mother's group is A Rh (D) positive, phenotype –D–, with alloantibodies anti-Hro. Our Rare Bank Units service, found the only donor available in the region with phenotype (–D–). The unit, just donated, has been divided into two aliquots of about 100 mL: the first, concentrated to a hematocrit of 70 + 5%, irradiated, compatible with the mother's plasma, was transfused in utero the day after the donation; the second, worked as the first, was transfused in utero after 13 days from the donation (fetal Hb increased from 8 to 13.4 g/dl).
2) 21 days after the last IUFT an elective caesarean section was performed at the 35th week of gestation, delayed clamping of 2 min, newborn's weighs 2,040 g, Hb 11 g/dl, reticulocyte 0.13% (tot 40,000/ml), bilirubin 2,23 mg/dl. She is assisted with respiratory support with 21% NCPAP for 48 h, then spontaneous breathing; at 12 h of life is subjected to phototherapy for 12 h. Bilirubin remains stable throughout the hospitalization, no further need for phototherapy. In 5th day 1 g/Kg of Immunoglobulin is infused, in 7th day a therapy with erythropoietin, iron and folic acid is started. The Hb remains stable during hospitalization, no need for transfusions. At the dimission (22 days of life): Hb 8.1 g/dl, reticulocyte 6,6% (tot 182,000/ml). Group and phenotype performed at birth unreliable for previous IUFT, presence of anti-Hro antibodies, negative DAT.
3) Next hospitalization to 35 days of life for anemia, Hb 7.6 g/dl, bilirubin 2.6 m/dl. 15 mL/Kg of EC group 0 Rh(-D-) was transfused. We used an aliquot taken from a deglycerolized EC because donors compatible are not available. Following failure to increase Hb (7.9 g/dl and bilirubin 3 mg/dl) at 38 days of life, a further 15 mL/Kg of the same unit of deglycerolized EC is transfused with an increase of Hb to 10.7 g/dl, bilirubin 3.6 mg/dl. DAT remains negative from birth. The child is discharged on the following day.
Summary/Conclusions: For both procedures (IUFT and neonatal transfusion), we did not comply with the recommendations of the blood transfusion standards and our policy, due to the rarity of the needed EC. Good clinical results and absence of adverse reactions have been observed.

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MAXIMISING STOCK HOLDING COMPATIBILITY OF COMPONENTS FOR BMT PATIENTS

D Johnson[1], L Chapple[1] and F Chowdhury[1,2]

[1]Blood Transfusion, Imperial College Healthcare NHS Trust [2]Clinical, NHS Blood and Transplant, London, United Kingdom

Background: Bone Marrow Transplant recipients are usually transfusion dependent for many months. Providing blood products for recipients with complex major and minor compatibilities can be problematic. As a NHS Trust, supporting a Paediatric BMT Centre specializing in haemoglobinopathy disorders, it is essential that blood component ordering is appropriate to maximise cross patient ABO and RhD compatibility in line with national guidelines. However, it is equally important to meet individual patient requirements, without delays and minimising component wastage. To facilitate best cross patient compatibility, we reviewed upcoming BMT protocols with the aim of implementing the inclusion of ALL compatible ABO and RhD groups of Red Cell, FFP, CYRO and Platelet components into the protocols prior to transplantation.

Aims: To maximise cross compatibility of blood components for BMT patients to minimize delays and product wastage whilst meeting individual patient requirements.

Methods: 1) To review patient BMT protocols for 1st, 2nd, 3rd and 4th line compatible component groups prior to transplantation.

2) To engage with clinical teams and service leads, to highlight the potential benefits to patient care as well as patient blood management (PBM).

3) To provide training across the transplant team on major and minor group blood product compatibility.

Results: Comparing stock holding for BMT patients, 12 weeks after implementing the changes showed a reduction of 10 RBC units and 1 Platelet unit in stock. We have also been able to reduce our stock holding of group O and B plasma products by approximately 10 units in total. Changing our policy also resulted in fewer patients with possible compatibilities missing from the BMT protocols. Of the 7 patients reviewed before the change 3 had missing RBC groups, and all 7 were missing platelet and plasma groups. Following the change only 1/6 patients were missing RBC groups, 4 platelet groups and 3 plasma groups. Also 1 patient (with no major or minor incompatibilities) was missing no compatible product groups. While these numbers are not large the savings equate to over £5200 and the most significant improvement is the potential decrease in delays to provide compatible products resulting from a reduced need to await delivery of stock from NHSBT.

Summary/Conclusions: Since the changes were implemented there have been cost savings of over £5200 with 26.1% reductions in missing RBC compatibility groups, 33.3% reductions in missing platelet compatibility groups and 50% reduction in missing groups for Plasma products. The change in practice has led to potential reductions in delays to over 25% of BMT patients' transfusions.

UNIVERSAL BILIRUBIN SCREENING: A NEW HOPE TO LIMIT EXCHANGE TRANSFUSION IN SEVERE HYPERBILIRUBINEMIA

V Bakhru, R Dara, J Bakhru and S Choudhary

Pediatrics and neonatology, Prakash hospital, Jaipur, India

Background: 60–80% of normal newborns present with jaundice during the first two weeks of life making neonatal jaundice, the most common diagnosis in the post-natal period. Generally, bilirubin levels rise soon after birth but risk factors can accelerate the bilirubin levels, leading to severe hyperbilirubinemia, defined as bilirubin level of greater than 20 mg/dl necessitating need for exchange transfusion. At this severity, bilirubin crosses the blood brain barrier which results in potential neurological squeal - kernicterus which is associated with high mortality, acute encephalopathy, cerebral palsy and hearing loss. Neonatal jaundice is recognized as a major problem in Asian countries and its data on incidence is not available as vast majority of births still occur at home. To prevent severe hyperbilirubinemia, primary aim is adequate feeding while secondary prevention includes vigilant monitoring of neonatal jaundice.

It was recommended by the American Academy of Pediatrics (AAP) 2004 guidelines that all newborns should have a bilirubin measurement done before discharge from the hospital. At our center we started universal bilirubin screening program in 2015.

Aims: The aim of the study was to assess the impact of universal bilirubin screening on incidence of severe hyperbilirubinemia and use of phototherapy and need for exchange transfusion.

Methods: This was retrospective cohort study directed at neonates with ≥35 weeks' gestation. Protocol followed was measuring Total serum bilirubin (TSB) at 24–60 h and at 3 to 5 day follow-up visits. Clinical risk factors were identified systematically. Data collected were patient demographics, bilirubin levels, phototherapy use, exchange transfusions, length of stay (LOS), jaundice-related emergency department visits and jaundice-related readmissions.

Results: A total of 1345 neonates were enrolled during the study period (January 2015 to December 2017). Maternal age was 23 ± 4.4 years and birth weight was 2.7 ± 0.6 kg (both mean ± SD). Twenty two neonates were excluded from the study as they were shifted to neonatal intensive care unit (8 infants) or consent was refused (14 infants). 1210 (90%) neonates completed the follow-up and were included for final analysis. Visible jaundice was observed in more than 80% of study neonates during the first week of life. Phototherapy was required for 121 (10%) of the infants, of whom 87 (7.2%) were treated during the birth hospitalization and 34 (2.8%) were treated after discharge. Fifteen neonates (2.1%) had TSB levels ≥20 mg/dl during birth hospitalization and were treated by phototherapy. None of the neonates required exchange transfusion. Median length of stay was 76 ± 5 h. Two neonates were admitted as jaundice related emergency requiring exchange transfusion, which were initially lost to follow up.

Summary/Conclusions: Vigilant monitoring of neonatal jaundice via universal bilirubin screening is a useful tool for preventing the complications of severe hyperbilirubinemia. Universal implementation of this screening can be considered as an effective protocol in the developing countries, though there is increased cost was involved in pre-discharge screening and post-discharge follow-up visits. However, this increase in cost was balanced by reduced costs from fewer emergency visits, hospital readmissions and need for exchange transfusions.

CURRENT STATUS OF BLOOD TRANSFUSION PRACTICE AMONG CHILDERN IN SICHUAN, CHINA

R Zhang[1], Z Wu[2], Z Wang[1], F Liu[1], C Li[1], C Yang[1] and S Rao[2]

[1]Institute of Blood Transfusion, Chinese Academy of Medical Sciences and Peking Union Medical College, [2]Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital, Chengdu, China

Background: Children as a special patient group, their clinical transfusion should receive more attention. However, in China, till now, there was no transfusion guidelines for neonates and older children, and few transfusion-related issues and practices in the pediatric patient population were reported.

Aims: A concise review of blood transfusion practice among pediatric patient population was carried out to get full knowledge of current status of blood transfusion practice among children in Sichuan, China.

Methods: A survey dealing with some issues regarding children blood transfusion was performed, using a questionnaire sent to 139 hospitals in Sichuan, China.

Results: 92.1% (128/139) hospitals returned the questionnaire. No hospital had transfusion guidelines in pediatric populations and most of the children transfusions rely largely on "expert opinion" rather than experimental data. Less than 50% hospitals had small package blood products which used for children and no hospital had granulocyte concentrates for neonatal patient transfusion; the percentage of hospitals which offered detection of neonatal hemolytic disease and identification of difficult blood types were 57.0% (73/128) and 23.4% (30/128); only 14.06% (18/128) hospitals had carried out plasmapheresis for children.

Summary/Conclusions: In China, many aspects of the children blood transfusion process should be improved, high-quality studies on children transfusion practice needed to be taken and a transfusion guidelines for neonates and older children was needed to guide pediatricians in the transfusion of children.

CLINICAL EFFICIENCY OF TRANSFUSION OF VIRUSINACTIVATED AEREA PLASTIC THROMBOCYTES IN CHILDREN WITH ONCOGEMATOLOGICAL DISEASES

T Issayev[1], D Kuanyshbay[1], F Aliyeva[2] and M Kaspakova[2]

[1]Public health, Astana Medical University [2]National Scientific Centre, Astana, Kazakhstan

Background: To study the clinical efficacy of transfusion of virus-inactivated apheresis platelets.

Aims: To study the clinical efficacy of transfusion of virus-inactivated apheresis platelets.

Methods: We studied the corrected platelet gain after transfusion of virus-activated apheresis platelets in children with oncohematological diseases (n = 30).

Transfusion efficiency indicator: corrected platelet gain, which was estimated at 18.0 ± 6.30 h after transfusion, using absolute platelet counts, body surface area, and the number of transfused platelets. Typological random sample: 30 children with hematological diseases at the age from 5 months to 18 years. Research period: January 1 to January 31, 2018. Clinical base: National Science Center for Maternity and Childhood, Astana. Study design: retrospective analysis.

Results: Gender-age structure: boys -73.3%, n = 22, girls - 26.7%, n = 8; children from 0 to 11 months. - 3.3%, n = 1; from 1 to 3 years -16.7%, n = 5; from 4 to 6 years - 30.0%, n = 9; from 7 to 12 years - 33.3%, n = 10; from 13 to 15 years - 10.0%, n = 3; from 16 to 18 years - 6.7%, n = 2. Nosological structure: solid tumors - 36.7%, n = 11, acute lymphoblastic leukemia - 23.3, n = 7; acute myeloblastic leukemia - 20.0%, n = 6; Acquired aplastic anemia - 13.3%, n = 4; myelodysplastic syndrome - 6.7%, n = 2.

In the course of the analysis, the average corrected platelet gain is 15.49 * 109 / L, the median is 13.73 * 109 / L.

Clinical efficacy was noted in 93.3%, n = 28 children of transfusions of virus-activated apheresis platelets, in 6.7%, n = 2, there was no effect.

In one case, in a child with a myelodysplastic syndrome, a low level of adjusted platelet gain is 1.35 * 109 / L. a massive splenomegaly was observed. In the case of a child with osteogenic sarcoma - SPT-2.68 * 109 / l. there were no clinical factors contributing to posttransfusion thrombocytopenia, the fact of the development of refractoriness to transfusion of virus-activated apheresis platelets is possible.

Summary/Conclusions: 1. For the purpose of early detection of refractoriness to platelet transfusions, monitoring of the corrected platelet gain should be considered as routine practice.

2. In order to prevent refractoriness, produced by alloimmunization, it is advisable to solve the problem of HLA-typing and determining the cross-antigen compatibility of the donor and recipient.

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WHEN DO MIXED FIELD REACTIONS APPEAR IN MAJOR AND BI-DIRECTIONAL ABO INCOMPATIBLE STEM CELL TRANSPLANTS?

F Chowdhury[1], H Dawson[2] and B Robertson[2]
[1]Haematology [2]Blood Transfusion, Imperial College Healthcare NHS Trust, London, United Kingdom

Background: A mixed field (MF) reaction refers to the presence of two distinct populations of red cells; agglutinated cells with un-agglutinated cells. MF reactions are most commonly seen after recent ABO incompatible transfusions or in patients undergoing stem cell transplantation from a non-group identical donor. There is no published data on how soon MF reactions are seen in ABO incompatible transplant patients.

Aims: To analyse transfusion data from Stem Cell Transplants to see when mixed field (MF) reactions are first seen in major and bi-directional ABO incompatible transplants.

Methods: We reviewed all the paediatric stem cell transplant protocols to ascertain those that had been undertaken between 01/01/2015 –31/12/2017. We then identified all the major ABO mismatched transplants from this list and reviewed blood transfusion records to identify the RBC group of blood given to the patient in the pre-engraftment phase of the transplant. All ABO testing was performed on EDTA anti-coagulated blood samples using gel column agglutination (Biorad). Repeat testing was performed on a second sample. Patient RBCs were evaluated for reactivity with anti-A, anti-B and anti-A, B. From our transfusion IT records we ascertained when each patient first presented with a mixed field pattern i.e. the beginning of the recipient's change of blood group.

Results: Out of 86 stem cell transplants undertaken during the 3 year period, 11 were major ABO incompatible transplants (with data obtained on 9/11), 7/86 were bi-directional ABO mismatched and 16/86 were minor mismatched transplants. Of the major ABO incompatible transplants the earliest mixed field was seen 35 days post-transplant, the longest took 125 days, with the average MF being visible from day 62 post transplant. Out of 7 bi-directional transplant recipients, we had data for 5, the earliest MF was seen 34 days post-transplant and the longest took 78 days, with average at 56 days

Summary/Conclusions: The majority of our major ABO incompatible transplant recipients developed a mixed field pattern at approximately 2 months from date of transplant. Further study would be needed to see if those patients with earlier presentation of MF required less transfusion support +/- better outcomes.

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Abstract has been withdrawn

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BLOOD TRANSFUSION IN DEEPENOCYTE CHILDREN AT GOOD BERGER HOSPITAL–TSHIKAJI, KANANGA/DRCONGO

J Ilunga Mulaja[1], D Bashimi[2] and L Basungula[3]
[1]Public health, Equilibre International [2]Internal Medicine [3]Laboratory, Good Shepherd Hospital of Tshikaji, Kananga, Congo

Background: During this treatment, transfusions are also performed in case of anemia less than 7 g/100 ml. This retrospective work we present takes into account all transfusions made in sickle cell children from 2010 to 2016. Here anemia is the only reason for transfusion.

Aims: 0f this work is to address all the problems inherent to these transfusions without any great rigor.

Methods: a) Hardware: The work involved 91 sickle cell children regularly followed from 2010 to 2016

b) Methods: The study of hemoglobin was carried out by electrophoresis on cellulose acetate at alkaline and acidic pH, followed by quantification of the fractions; these hemoglobin studies were performed at more than two months of transfusion and at the parents'.

Results: 1. The type of Hb in patientsThe group studied is composed of 47 boys and 44 girls distributed in the different electrophoretic phenotypes

2. Frequently encountered complications

The osteoarticular pains are the most frequently found in our patients 42,86%. Then we have anemia 23.07% which are found only in homozygous sickle cell patients. In contrast, 31.87% of sickle cell patients have never had serious complications.

Discussions: The majority of children (63.74%) had their first sickle cell crisis between 6 and 11 years old. The first sign of discovery of the most common illness is osteoarticular pain 44.74%. Anemia, a relatively unknown sign of parents, is a reason for consultation only in 6.58% of cases; all transfusions were made according to the Hb level (less than 7 g / 100 ml); 27.4% of sickle cell patients were transfused in total, of whom 96% were SSFA2 and one SC.

Summary/Conclusions: This retrospective work shows the lack of rigor with which sickle cell children were transfused to consultation sickle cell disease hospital good shepherd in the period from 2010 to 2016. It was mainly used whole blood, that with all risks of allo -immunization that could occur. Transfusions were isoforms, but no search for irregular agglutinins was performed prior to transfusion. No HIV and / or HBV serology was also performed in sickle cell patients.

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ADVERSE TRANSFUSION EVENTS OF HEMOCOMPONENTS BY WHOLE BLOOD AND BY APHERESIS IN PEDIATRIC PATIENTS

L Sommese[1], M De Pascale[1], S Signoriello[2], M Vasco[1], C Iannone[1], S Perrotta[3] and C Napoli[1,4,5]
[1]U.O.C. Division of Clinical Immunology, Immunohematology, Transfusion Medicine and Transplant Immunology, Regional Reference Laboratory of Transplant Immunology, AOU, Department of Internal and Specialty Medicine [2]Department of Mental Health and Preventive Medicine [3]Department of Woman, Child and General and Specialist Surgery [4]Department of Medical, Surgical, Neurological, Metabolic and Geriatric Sciences, Università degli Studi della Campania "Luigi Vanvitelli" [5]IRCCS SDN, Naples, Italy

Background: In children, the incidence of adverse transfusion reactions is higher than in adult patients. In this respect, blood collection and blood preparation have to be continuously improved to reduce the risk of transfusion related to adverse events especially in these patients.

Aims: The aim of this study was to assess the occurrence of adverse transfusion reactions of hemocomponents by whole blood and by apheresis in pediatric patients.

Methods: Between 2011 and 2015, n = 214 pediatric patients were transfused with hemocomponents obtained by whole blood and by apheresis collected from U.O.C. Division of Clinical Immunology, Immunohaematology and Transfusion Medicine of Università della Campania "Luigi Vanvitelli". Adverse event was described as minor allergic reaction, febrile episodes, vomiting, or presence of dyspnea and bronchospasm. Comparison between transfused components and presence/absence of adverse event were assessed using Pearson's chi-square test.

Results: Data from pediatric patients (n = 144 onco-haematologic and n = 70 thalassemic patients) were analyzed. Male gender was 56% (60% and 46% respectively in onco-haematologic and thalassemic patients), mean age was 12.0 ± 9.9 years (8.5 ± 5.3 and 19.4 ± 12.8, respectively in onco-haematologic and thalassemic patients). Median time of observation was 0.50 years (interquartile range (IQR) 0.11–0.83) in onco-haematologic patients, and 4.9 years (IQR 3.2–4.9) in thalassemic

patients. In that period, 12,531 units of hemocomponents were transfused (2,662 in onco-haematologic and 9,869 in thalassemic patients). No difference in proportions of adverse events between whole blood and apheresis was observed (0.3% in whole blood and 0.3% in apheresis, p-value chi-squared test=0.98). Same results were found considering separately onco-haematologic (0.6% in whole blood and 0.3% in apheresis, p-value chi-squared test=0.49) and thalassemic patients (0.2% in whole blood and 0.3% in aphaeresis, p-value chi-squared test=0.57).

Summary/Conclusions: No difference in post-transfusion adverse events related to whole blood and apheresis both in onco-haematologic and thalassemic pediatric patients was observed. All blood components have shown the same transfusion safety in pediatric patients.

Therapeutic apheresis

P-674

RAT KILLER (YELLOW PHOSPHORUS) POISONING – A PROMISING INDICATION FOR THERAPEUTIC PLASMA EXCHANGE

D Sachan[1], I Kaliamoorthy[2], A Rajakumar[2], C Kumar[2], D Jothimani[2], S Reddy[2], K VH[2], M Vij[3] and M Rela[2]

[1]Transfusion Medicine [2]Institute of Liver diseases & transplantation [3]Pathology, Gleneagles Global Health City, Chennai, India

Background: Accidental or suicidal consumption of rat killer poison, which contain yellow phosphorus (YP) component, could lead to death. YP could cause acute liver failure (ALF), cardiac arrhythmias, bone marrow depression and renal failure. Liver transplantation (LT) is the only successful treatment option in ALF once patient develops acute liver failure following consumption of YP, as of now. Therapeutic plasma exchange (TPE) provides a potential therapeutic option to support liver function and provide scope for regeneration in ALF. However, there is no literature regarding the role of TPE in YP poisoning.

Aims: To identify if the TPE reduces mortality and increase transplant free survival in patients with YP poisoning

Methods: This is a prospective study and was approved by institutional ethical committee. All adults who have consumed YP received standard medical therapy and TPE was indicated if INR >3, ALT or AST elevation>1000, Encephalopathy, or any significant changes in liver biopsy. The TPE was performed using Optia Spectra centrifugal apheresis (Terumo BCT) for 5 consecutive days. 1.0 plasma volume exchange was performed with Fresh frozen plasma and 5% albumin as replacement fluid. All patients were monitored for any transfusion or procedure related adverse events and were given calcium prophylaxis. The patients were monitored for liver function test, renal function test, Arterial Ammonia, ABG, INR, and liver biopsy. Patients were also monitored for changes in Pre and post TPE (after 2 h) cytokine levels

Results: During the study period (Dec 2015 – January 2018), 30 patients M:F 1:1, mean Age 28 (range 15–53) were admitted with YP poisoning induced ALF. Average time from YP intake to Admission was ranging from (1–10 days) average 3.7 days. Baseline Investigations showed elevated INR 4.0 (0.9 – 8.69), and raised liver enzymes AST 1567 (14 - 6139), ALT 669 (17–2056). A total of 139 procedures were performed with average 5 Procedure (2 to 8 procedures) were performed in consecutive days with average 4840 (2769 - 8371) ml blood volume processed with average 2419 ml (1424–3822) plasma exchange. There were 4 minor allergic reactions and no major adverse reactions during TPE procedures. Cytokine Analysis showed significant increase in anti- inflammatory cytokines IL 4 and IL 10 after plasmapheresis while the proinflammatory cytokine IL 6 (P < 0.02) and fibrogenic cytokine TGF β (P < 0.02) showed a significant decrease.

The patients showed significant improvement in serum ALT and AST levels and coagulation status. 20 patients improved without need for Liver transplant and were discharged at average 9 days (5–30 days). 2 patients required urgent liver transplant 15 and 9 days respectively after poison intake. These 2 post LT patients had developed graft dysfunction in the postoperative period and improved after post LT TPE (1 and 5 cycles). The post TPE liver biopsies showed histological improvement in form of reduction in hepatocyte necrosis compared to pre TPE. 2 patients expired due to multi organ failure.

Summary/Conclusions: This is the first study highlighting the role of TPE as an effective treatment intervention for patients with Yellow phosphorus poisoning along with standard medical therapy. Our initial experience provides a strong recommendation for TPE in reducing mortality and improved survival in native livers in patients with YP poisoning.

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PLASMA EXCHANGE IN PATIENTS WITH ARRHYTHMIAS DUE TO MYOCARDITIS

V Kulikova[1], A Nedostup[1], O Blagova[1], V Zaidenov[2], A Kupriyanova[3], I Nechaev[1] and A Ragimov[1]

[1]I.M. Sechenov First Moscow State Medical University [2]Institute of Transplantology and Artificial Organs [3]Research Clinical Institute of pediatrics, Moscow, Russian Federation

Background: Elimination of anti-heart antibodies which detected in patients with arrhythmias due to immune-mediated myocarditis improves cardiac function and antiarrhythmic drugs' effect.

Aims: to investigate the clinical efficiency of plasma exchange (PE) in patients with arrhythmias due to immune-mediated myocarditis in comparison with control group without PE.

Methods: There were 20 patients with arrhythmias resistant to antiarrhythmic drugs (AADs) (mean age 61.5 ± 10.1 years, premature atrial contractions (PACs, n = 3), premature ventricular contractions (PVCs, n = 8) more than 3000 per day, and atrial fibrillation (AF, n = 9)) in the treatment group and 26 patients (mean age 42.4 ± 11.9 years, PACs (n = 4), PVCs (n = 12), AF (n = 10)) who were followed without PE. All the patients had two or more fold increase of at least two anti-heart antibodies (AHA) level (to cardiac nuclear antigens, endothelial, cardiomyocytes, conduction and smooth muscle cells antigens). Patients of the treatment group were underwent a single volume therapeutic PE. Study groups patients underwent endomyocardial biopsy (EMB, n = 5), cardiac CT (n = 13), MRI (n = 12), myocardial perfusion scan (n = 25), and coronary angiography (n = 10) to diagnose myocarditis. All the patients were treated either with immunosuppression drugs or without them. Both groups of patients underwent clinical evaluation including AHA level detection and Holter monitoring at baseline and at FU visits in about 6 and 12 month

Results: AHA to cardiomyocytes level significantly decreased (P < 0.05) in control group with arrhythmias. Thirteen treatment group patients with arrhythmias (65%) in and 15 (58%) patients in control group were classified as responders as they achieved a decrease of PAVs and PVCs or AF frequency > 75% relative to baseline. AADs were eliminated in 4 treatment group patients and in 5 control group patients. Treatment group responders were characterized by higher level of AHA to cardiac nuclear antigens at baseline (P < 0.05). Nine (45%) treatment group patients with arrhythmias and nineteen (73%) control group patients got methylprednisolone respectively, P > 0.05. The mean dose was 8[4;16] and 16[10;24] mg per day (P > 0.05)

Summary/Conclusions: PE improves AAD's effect in patients with immune mediated arrhythmias. There were 65% treatment group responders in patients with arrhythmias. Initial high AHA level to cardiac nuclear antigens (more than 1:40–1:80) was good outcome predictor in patients with arrhythmias. PE helps avoid using immunosuppressive medications or reduce high doses of it.

P-676

FIRST EXPERIENCE WITH A NEWLY DEVELOPED SINGLE-USE IGE IMMUNOADSORBER COLUMN IN PATIENTS WITH ATOPIC DERMATITIS

N Lindlbauer[1], D Meyersburg[2], G Mayer[1], M Laimer[2], J Bauer[2], E Rohde[1,3] and C Grabmer[1]

[1]Department of Transfusion Medicine [2]Department of Dermatology, Paracelsus Medical University Hospital [3]Spinal Cord Injury & Tissue Regeneration Center (SCI-TReCS), Salzburg, Austria

Background: Atopic dermatitis (AD), also known as atopic eczema, is a chronic, inflammatory condition of the skin that affects 20–30% of children and 5–10% of adults in industrialized countries. Some patients with severe AD tend to have high total serum IgE levels. Treatment with the anti-IgE antibody omalizumab however was abandoned because it was ineffective in reducing highly elevated IgE serum levels and no significant clinical improvement of AD has been seen in meta-analysis. Recently published data showed promising results for the treatment of AD patients with IgE Immunoadsorption (IA), still carrying in mind that also further complex immune dysregulation other than IgE might be the crucial mechanism in AD.

Aims: The aim of the current study is to determine safety and efficacy of IgE IA with the newly developed single-use IgE immunoadsorber column IgEnio® (FreseniusMedical Care, Bad Homburg, Germany).

Methods: This open-label pilot study enrolled four patients with severe AD (SCORAD ≥ 50) and elevated IgE levels (> 750 kU/l). All patients received three cycles of IA (IgEnio, FreseniusMedical Care, Bad Homburg, Germany). The first cycle consisted of three consecutive treatments followed by two cycles with two

consecutive treatments. All cycles were performed on a monthly regimen. The two-fold plasma volume of the patient was separated by centrifugation with an apheresis device (Spectra Optia, Terumo BCT, Lakewood, CO, USA). Anticoagulation during treatment was maintained by continuous citrate dosage at a volume/citrate ratio of 1:18 and sodium heparin 70–80 IU/kg body weight. Efficacy of IA was determined by immunoglobulin levels (IgE, IgG, IgM, IgA) before, during and up to 4 weeks after termination of treatment. Clinical improvement was dispassionately evaluated with the SCORAD index by two experienced dermatologists up to 4 weeks after the last treatment cycle.

Results: IA was well tolerated in all patients and during a total of 28 procedures only mild adverse events were recorded. During each cycle IA resulted in a significant decrease of IgE levels, although rebound of IgE levels in a saw tooth manner after each IA cycle was seen in all studied patients. In total, IA selectively depleted 79,03% of IgE until the end of each treatment cycle. The average reduction of SCORAD index from all patients until the end of the study period was 37,12%.

Summary/Conclusions: This study provides first evidence that IgE IA with the newly developed column IgEnio® is a safe and well-tolerated therapy for patients with severe AD. Despite the fact that IgE levels rose to initial values after each cycle, we could observe a significant average reduction of SCORAD index until the end of the study period. Long time follow-up of patients will assess the long-term impact of this novel therapeutic strategy.

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DESENSITIZING EXPERIENCE OF DONOR–SPECIFIC ANTIBODIES IN HEART AND LUNG TRANSPLANTATION AND TRANSFUSION SUPPORT

H Lee[1], K Shin[2], D Song[1], S Lee[1], I Kim[1] and H Kim[3]

[1]Laboratory medicine, Pusan National University Yangsan Hospital, Yangsan [2]Laboratory medicine, Pusan National University Hospital [3]Laboratory medicine, Pusan National University Hospital, Busan, Korea

Background: Antibody-mediated rejection (AMR) can occur in patient with donor specific antibodies (DSA). Patients waiting for heart or lung transplantation, often have lots of preformed HLA antibodies. This results in the presence of DSA, when the patients arranged to designated organ candidates. The possibility of receiving organ transplantation again is very low, desensitization of DSA is important. We aimed to analyze the DSA characteristics, protocol of desensitization of DSA on recipients of heart and lung and amount of blood transfusion peri-transplantation period.

Aims: We aimed to analyze the DSA characteristics, protocol of desensitization of DSA on recipients of heart and lung and amount of blood transfusion peri-transplantation period.

Methods: From May 2013 through June 2017, 21 patients underwent the heart transplantation and 32 patients got the lung transplantation. DSAs were classified as preformed if found prior to transplantation, whereas if found only after transplantation, they were classified as de novo. Patients group were categorized according to presence of DSA. Patients who had any type of DSA were classified as DSA+ group, patients without DSA as DSA- group. Among DSA+ group, reclassified into perform PCPF and no PCPF according to treatment of plasmapheresis. Perioperative hemoglobin and platelet were recorded. Transfusion between 7 days before operation and 7 days after operation were analyzed.

Results: Among 53 patients, total 14 patients had DSAs among them eight patients had the preformed DSA, four patients had de novo DSA and two patients had both type of DSAs. Overall, 14 patients (26.4%) were had DSAs. 10 patients (18.9%) had the preformed DSAs. According to type and strength of DSAs, 4 patients with preformed DSAs underwent additional treatment of PCPF to maintain the immunosuppressant therapy. Two patients had strong preformed DSAs, according to guidelines for antibody incompatible transplantation, are hard to get transplantation, we tried to desensitization. After desensitization with PCPF and immunosuppressant, the patients did not show an AMR episode and also an infection. Other two patients underwent PCPF despite of DSA with low MFI value, the physician decide the need of PCPF. During the operation of transplantation, 8.47 ± 3.42 units of pRBCs are transfused to heart recipients and 12.78 ± 9.98 units to lung recipients (P = 0.030). Also, 2.19 ± 2.04 units of FFP were transfused in heart recipients and 10.00 ± 7.91 units in lung transplantation (P = 0.000). Amounts of platelet transfusion were not significantly different, 12.33 ± 7.34 and 23.06 ± 19.05 in heart and lung, respectively (P = 0.006). Mean PT (INR) right before transplantation were significantly different between heart recipients (1.52 ± 0.50) and lung recipients (1.23 ± 0.37) (P = 0.032). Mean aPTT were significantly different between heart recipients

(59.03 ± 31.66) and lung recipients (43.01 ± 18.8) (P = 0.029). Mean Hb (g/dl) and PLT (K) between heart recipients and lung recipients were not significantly different.

Summary/Conclusions: In case of multiple strong DSAs are desensitized by cocktail protocol of immunosuppressant and plasmapheresis, especially PCPF to maintain the effect of immunosuppressant. PCPF adjuvant to administration of immunosuppressant is effective to prevent AMR and infection. Perioperative Hb and PLT were not different between heart and lung transplantation, more blood transfusion for lung transplantation were done. Intensive transfusion support is need in lung transplantation.

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INDICATIONS, EFFICACY AND SAFETY OF THERAPEUTIC APHERESIS IN NEPHROLOGY PATIENTS: SINGLE CENTRE EXPERIENCE FROM INDIA

D Setya[1], A Tiwari[1], D Arora[1], G Aggarwal[1], S Mehta[1], S Bansal[2], A Ratan[1] and G Bhardwaj[1]

[1]Immunohematology and Transfusion Medicine [2]Kidney diseases and Renal Transplant, Medanta - The Medicity, Gurgaon, Gurgaon, India

Background: Therapeutic Apheresis (TA) serves as a rescue therapy in many patients with kidney diseases and these indications have expanded dramatically in the past few years. Rapid removal of undesirable antibodies and immune complexes remains the prime rationale for adopting plasmapheresis as a therapy. However, there is limited data available regarding the indications, efficacy and safety of TA in nephrology patients.

Aims: To assess the efficacy and safety of TA in different nephrological indications.

Methods: This was a retrospective analysis of TA performed in adult and pediatric nephrology patients at a tertiary healthcare centre from January 2010 to December 2017. TA included all conventional plasma exchange, cascade plasmapheresis and immunoadsorption procedures. Demographics, clinical condition, ASFA category, procedure parameters like blood and plasma volume processed, anticoagulant used, volume and type of replacement fluid administered, adverse reaction events and clinical response were noted.

Results: A total of 190 patients (63 females and 127 males) underwent 842 sessions of TA for different indications. 184 and 658 procedures were performed for 24 pediatric and 166 adult patients respectively. Mean age of presentation in pediatric age group was 9.21 years while in adults it was 43.08 years. 639 procedures (75.89%) were conventional plasma exchanges, 182 were cascade plasmapheresis (21.61%) and 21 were immunoadsorption (2.49%). Mean blood urea and serum creatinine prior to initiation of plasmapheresis of all indications except desensitization was 158.78 mg/dl and 4.95 mg/dl while at the time of termination it was 73.05 mg/dl and 3.34 mg/dl respectively. Replacement fluid was plasma in 303 procedures (35.98%), 5% albumin in 412(48.93%) and a combination of plasma and 5% albumin in 127 procedures (15.08%). Acid Citrate Dextrose remained the preferred anticoagulant. As per departmental standard operating procedure, patients with body weight <20 kg i.e. 25 procedures (2.96%) required priming of the kit with albumin or red cells. Patient outcome in terms of survival was 76.84%; 79.16% in pediatric and 74.69% in adult age group. Thirty-nine procedures (4.63%); 12 in pediatric and 27 in adults were associated with adverse events in the form of shivering(12), urticaria (3) and catheter related complications(6).

Summary/Conclusions: Findings of this study highlight the efficacy and safety of TA in pediatric and adult nephrology patients.

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THE MAGIC OF THERAPEUTIC PLASMA EXCHANGE WORKS IN HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS !!!

S Nayak and M Bajpai

Transfusion Medicine, Institute of Liver and Biliary Sciences, New Delhi, New Delhi, India

Background: Hemophagocytic lymphohistiocytosis (HLH) is a disorder of fulminant immune response. Therapeutic plasma exchange (TPE) has been documented to produce optimal response in such patients. However, this disease has yet to find a place under the various categories of indications for TPE in the ASFA classification.

Aims: We summarize six cases of HLH in children who were successfully treated with therapeutic plasma exchange.

Methods: Data on pediatric patients diagnosed with HLH treated with TPE in our institute during the study period of July 2016 to December 2017 was compiled. The diagnosis and treatment of HLH was based on the HLH 2004 protocol. The data collected included the demographics, age, weight, clinical history (complains at admission, signs, symptoms, factors necessitating TPE, clinical status post-TPE sessions), drugs administered, laboratory parameters (blood counts, ferritin, triglycerides, fibrinogen, bone marrow aspiration reports) and the course during the hospital stay. TPE procedures were done on Spectra Optia (Terumo BCT) using ACD-A as anticoagulant and fresh frozen plasma as the replacement fluid. Patient vitals were continuously monitored throughout the procedure. Plasma volume exchanged was 1.5 to 2 volumes at a rate of 10 to 40 ml/min of plasma extraction through a dialysis catheter of appropriate caliber placed in the internal jugular or the femoral veins. TPE were done till symptomatic (resolution of fever and hepatosplenomegaly) and/or laboratory parameters (increased blood counts, decreased ferritin levels) improved.

Results: A total of 27 procedures of TPE were done on the 6 patients aged 2–17 years, who had secondary HLH (Primary etiologies being Dengue, Hepatitis A, EVB i.e. Epstein Barr virus). Each of the patients had high grade fever transiently responding to antipyretic, moderate to severe hepato-splenomegaly, cytopenia (hemoglobin 5–7.3 g/dl, platelet 14000–150000/μl, TLC 1500 -11000/μl) on presentation. Average of ferritin was 47237 ng/ml (327 to 109000 ng/ml), triglyceride was 474 (299–898) mg/dl and fibrinogen 198 (88–384 mg/dl). Bone marrow aspiration done on four of the six patients showed 3–5% hemophagocytes. Three of the six patients received 1–2 TPE, 2 patients required 5–6 TPE and one patient received 12 sessions of TPE. Five of the six patients improved with TPE, IVIg 0.5–1 g/kg and methyl prednisolone 10–30 mg/kg. Timely diagnosis and initiation of TPE sessions along with other medications was effective. However, one of the patients who had HLH secondary to EBV, received 12 sessions of TPE and chemotherapy for the viral infection, succumbed in spite of all efforts.

Summary/Conclusions: The response of secondary HLH to TPE with IVIg and steroids was found to be satisfactory in our patients.

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ROLE OF THERAPEUTIC PLASMAPHERESIS IN DESENSITIZATION OF HIGH RISK HLA SENSITIZED KIDNEY TRANSPLANT CASES: AN EXPERIENCE OF 12 CASES FROM A SINGLE CENTER IN INDIA

PK Pandey[1], N Agarwal[1], A PANDEY[1], A Devra[2], V Sinha[3] and A Bhatt[3]
[1]Transfusion Medicine and Transplant immunology [2]Kidney Transplant [3]Nephrology and Kidney Transplant, Jaypee Hospital, Noida, India

Background: Antibody mediated rejection (AMR) remains the major cause of graft failure after kidney transplantation. The presence of donor specific anti-human leukocyte antigen (HLA) increases the risk of AMR after kidney transplant. Patient develops anti HLA antibody as a result of previous exposure such as a prior transplant, blood transfusion or pregnancy. However, a desensitization protocol enables renal transplantation in such high risk patients where patient doesn't have other donor.

Aims: the aim of present study was to find the effect of plasmapheresis in HLA sensitized kidney transplant cases

Methods: This was a single center retrospective observation of 12 cases of kidney transplants done in HLA sensitized patients between June 2016 and Dec 2017. All patients were desensitized with pre-transplant plasmapheresis and low dose IVIG/rituximab. The TPE was done using COM. TEC (Fresenius Kabi, Germany). 1.5 volume of TPE was done using 5% albumin as replacement fluid. Luminex cross match with donor lysates (DSA) using Luminex (Immucor, USA) was done before, during and after the plasmapheresis to monitor effectiveness of TPE. AHG lymphocytotoxicity crossmatch assay (AHGCDC-XM) and flowcytometry cross match (FCXM) (BD FACS Canto) were done before the start of TPE and just before the transplant. All the procedures were done using departmental SOP and manufacturer's instructions. AHGCDC-XM was interpreted and reported as per the ASHI guidelines and for FCXM T-cell median channel shift (MFI) >52, B-cell MFI >146 were considered positive. DSA class I and class II MFI >500 were considered positive. The target Luminex DSA mean fluorescence index (MFI) was <500, along with negative CDC-Crossmatch and negative FCXM for both T- and B-cells. Effectiveness of TPE was measured using DSA.

Results: There were a total of 12 cases that required desensitization. Mean age of recipients and donors was 44 years (18–60) and 34 years (18–60), respectively. In recipients, M/F ratio was one. There were a total of 3 retransplant (second) cases. Pre TPE mean serum creatinine was 4.68 mg/dl (1.4–11.62). All patients had history of previous blood transfusion while all female recipients were multiparous. There were two cases that had ABO incompatibility along with HLA sensitization. DSA

class I was positive in two patients (mean MFI=4943) while class II was positive in five (mean MFI=7490). Remaining five were positive for both class I (mean MFI=3633) and class II (mean MFI=1259). AHGCDC-XM and FCXM were positive in all cases. Mean number of pretransplant TPE procedures required were 5 (2–11) while post-transplant 1.1 (2–4) procedures required. All patients were on regular follow-up till compilation of data. Protocol Biopsies revealed no evidence of tissue injury or C4d deposits. The mean serum creatinine concentration at last follow-up was 1.045 (0.9–1.25) mg/dl

Summary/Conclusions: Plasmapheresis is an effective modality for reducing antibody loads to prevent AMR. Though, the role of TPE has been very well acknowledged in ASFA guidelines (category 1, recommendation 1B) but still such high risk transplants are being done in very few centers of India.

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PROGNOSTIC FACTORS OF RESPONSE TO PLASMA EXCHANGE IN THROMBOTIC MICROANGIOPATHY. 15 YEARS EXPERIENCE IN A MEDICAL CENTER IN MEXICO

J Trejo Gomora[1] and E Añorve Hernandez[1,2]
[1]Hematology, Issste Hrlalm [2]México City, Mexico City, Mexico

Background: Thrombotic microangiopathy (TMA) is a set of processes that leads to an alteration of the vascular endothelium and presents characteristic findings in the peripheral blood smear of a microangiopathic hemolytic anemia (schistocytes), characteristic laboratory data (elevation of reticulocytes and lactate dehydrogenase (LDH)), creatinine and thrombocytopenia of variable intensity. Over the last few years, different physiopathological mechanisms have been described that determine the appearance of a TMA in each of the different situations, which should allow a different therapeutic approach. Some fundamental tests for the diagnosis of TMA (ADAMTS13, ADAMTS 13 inhibitor and ADAMTS13 activity) are inaccessible at the time of initial assessment in Mexico.

Aims: To know the prognostic impact of some serum markers in the initial response to plasma exchange (PE) in TMA

Methods: Observational study, retrospective retrolective longitudinal, by means of multivariate analysis by linear regression, we obtained impact variables to know the response of the disease to PE. Patients with a diagnosis of TMA entry were included, who received initial treatment with intravenous steroid and PE with fresh frozen plasma compatible with 1.5 volumes. We excluded patients with saline solution replacement with albumin, replacement volumes different to 1.5 times and those who presented a transfusion reaction, as well as using another immunosuppressive therapy different intravenous steroid.

Results: From 2002 to 2016, 19 patients were included (14 women), the mean age was 45 years (17–61 years) .Once patients blood group 0 + , seven A + and one B + . Ten patients responded (response: platelets above 150,000 / μL, without transfusion and absence of clinical data from TMA) to PE (mean PE number to obtain response: 3.5 PE). The group of non-responders, the mean of biomarkers at the time of diagnosis of TMA and prior to the start of PE: Hb 7.4 g / dL, platelets 27,000 / mL, 12% schistocytes, LDH 1927U / L, creatinine 3.1 mg / dL versus Hb 7.5 g / dL, platelets 16,000 / mL, 9% schistocytes, LDH 1717U / L, creatinine 1.7 mg / dL for the group of patients that did respond to PE. Only achieving statistical significance in the levels of creatinine and platelets ($P < 0.05$)

Summary/Conclusions:: In centers where we do not have ADAMTS13 serum levels, at the time of diagnosis, platelet and creatinine levels can serve as initial prognostic markers of response in TMA to PE.

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NATIONAL APHERESIS REGISTRY RESULTS FOR THE FISCAL YEAR 2017 BY THE KOREAN SOCIETY FOR APHERESIS

H Kim[1], Y Hong[1], J Hyun[2], T Kim[1], J Park[1], K Park[1] and K Han[1]
[1]Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul [2]Department of Laboratory Medicine, Hallym University College of Medicine, Hwaseong, Korea

Background: Nationwide apheresis registry can give us information on the current status and trend regarding apheresis procedures. Data can be compared with other countries to find and understand differences in perspectives, indications, technology, and clinical practice. The Korean Society for Apheresis (KSFA) has launched an online web based registry system for apheresis procedures since 2006.

Aims: We report the registry data from the fiscal year 2017.

Methods: Information on apheresis procedures and instruments used were reported on the online registry system by voluntarily participating hospitals in Korea. Information from blood centers were also collected by email.

Results: A total of 758,006 apheresis procedures were performed at blood centers (plasmapheresis, 72.2%; platelet+ plasma, 25.8%; plateletpheresis, 2.0%). The number of instruments used at blood centers was 824 (Autopheresis-C, 31.6%; PCS2, 31.1%; MCS+, 13.6%; Amicus, 13.2%; Trima, 10.6%). Among 2,920,416 platelet units supplied (apheresis platelets counted as 6 random donor platelets), 47.9% were apheresis platelets. Thirty-five hospitals reported 12,795 cases of apheresis procedures. COBE Spectra (35.8%) and Amicus (17.9%) were the most widely used instruments. Therapeutic plasmapheresis was the most frequent procedure (57.7%) followed by autologous peripheral blood stem cell (PBSC) collection (19.6%), allogeneic PBSC collection (11.3%), donor leukapheresis (4.7%), and therapeutic leukapheresis (3.5%). Centrifugation was the dominant technique (92.4%) for therapeutic plasmapheresis, followed by primary membrane filtration (5.7%), double-filtration (1.4%), and postcentrifugal plasma filtration (0.4%).

Summary/Conclusions: Our apheresis registry has been well run for 11 years. Major revision and update on the registry planned this year will help us achieve better understanding on the apheresis status of our region.

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Abstract has been withdrawn

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TREATMENT OF ACUTE ANTIBODY–MEDIATED REJECTION: IMMUNOADSORPTION

R Ciotola, M Mottola, M Mottola, C Bruno, C Arcopinto, N Adinolfi, O De Cenzo and B Zuccarelli

Immunohematology Service, A.O.R.N.dei COLLI, Napoli, Italy

Background: The cardiac transplantation is currently considered the treatment "gold standard" for the therapy of terminal heart failure. Despite the introduction of powerful immunosuppressive drugs, the acute rejection of the transplanted organ represents the most serious complication of cardiac transplantation. Cardiac allograft rejection can be hyperacute, acute cellular (ACR), acute antibody-mediated (AMR) or chronic (CAV, Chronic Allograft Vasculopathy), as well as by classification of the ISHLT (International Society for Heart and Lung Transplantation). The pathophysiology of AMR suggest a prime role for antibodies, B cells, and plasma cells, and the complement system. The same factors are likely to be involved in the appearance of CAMR. This event has been associated with donor-specific or non-specific anti-HLA antibodies that can be present either at transplantation or appear subsequently, even after many years.

Aims: Benefits of treatment with immunoadsorption techniques in the cardiac allograft rejection.

Methods: We have treated two patients who underwent orthotopic heart transplant about ten years ago, which over the years had developed CAV and for the occurrence of signs of congestive heart failure, the first patient with E.F. (Ejection Fraction) 25% and the second patient with E.F. 15%, were hospitalized in November 2017 at the Department of Cardiac Surgery. The patients underwent the endomyocardial biopsy (EMB) and the determination of HLA antibodies (PRA) and for both has been diagnosed of AMR Therefore, our Service was contacted to introduce the therapeutic treatment with Immunoadsorption (IA)in addition to immunosuppressive therapy. The treatment was performed with the cell separator (Com.Tec) the plasma of apheresis is guided into adsorbers (GLOBAFFIN) with device ADAsorb:1/die for 4 days followed, in the following week on alternate days by monitoring antibody, for a total of 7 treatments.

Results: At the end of the treatments, the dosage of anti-HLA antibodies in the first patient were significantly reduced with simultaneous improvement of the clinical and echocardiographic (E.F. 50%) conditions, in the second patient, despite remains unchanged the antibody titer, there is a clinical improvement accompanied by increased cardiac function (E.F. 25%).

Summary/Conclusions: In the two cases treated, the procedure with IA has proved an effective strategy for the treatment of AMR: in the first case, with an evidence of laboratory investigations (reset of HLA antibodies), while in the second case, with a significant clinical improvement such as to imply that the effectiveness of this treatment depends on the removal both of HLA antibodies circulating and of inflammatory mediators involved nell'AMR.

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USING PLASMA TREATED WITH RIBIFLAVIN AND UV LIGHT IN THE THERAPY OF PATIENTS WITH THROMBOTIC THROMBOCYTOPENIC PURPURA

M Antelo[1], P Sanchez-Antón[1], S Zalba[1], A Aranguren[1], P Rodriguez-Wilhelmi[1], M Ayape[2], J Garcia-Erce[2], I Ezpeleta[1] and M Cardoso[3]

[1]*Haematology and Hemotherapy* [2]*Banco de Sangre y Tejidos de Navarra, Complejo Hospitalario de Navarra, Pamplona, Spain* [3]*Blood Centre Segment, Terumobct, Zaventem, Belgium*

Background: According to well-established guidelines, acquired idiopathic thrombotic thrombocytopenic purpura (TTP) should be treated with therapeutic plasma exchange (TPE) as early as possible so that circulating ultra-large von Willebrand factor molecules and auto-antibodies against ADAMTS 13 protease can be removed from circulation while newly infused fresh-frozen plasma can restore ADAMTS levels. Fresh frozen plasma (FFP) treated with a pathogen reduction technology (PRT) that uses riboflavin and UV light (FFP/RB) has been commercialized in Europe since 2008 (used since 2010 in our Blood Centre). The quality of FFP/RB complies with the specifications of the CoE guidelines according to the literature. Moreover, hemovigilance data attests for the safety of the blood product.

Aims: To report about the treatment of four patients diagnosed with primary idiopathic TTP with therapeutic plasma exchange until remission, using FFP/RB.

Methods: Four patients (2 females; 2 males) diagnosed with primary idiopathic TTP were treated with therapeutic plasma exchange of 1.5 volumes per day using FFP/RB in combination with corticosteroids (prednisone 1 mg/Kg/day) until remission. TPE was performed with the Spectra Optia system from Terumo BCT. The four patients showed at treatment start no detectable ADAMTS 13 activity, three of them with detectable levels of anti-ADAMTS 13 and one of them with neurological symptoms.

Results: Serum lactate dehydrogenase (LDH) levels were increased in the four patients (average 593 U/l, range 448–717). Creatinine levels remained stable (1.17 mg/dl at the beginning of treatment of and 0.97 mg/dl at remission). Average platelet count at the beginning of treatment was 21×10^9/l (range 4–41). Remission was attained after an average of 7 PE sessions (range 6–9), platelet counts reaching average of 244×10^9/l (range 181–337) and LDH levels of 204 U/l (range 183–238). No severe adverse events were observed despite the high volume transfusion of plasma; two mild cutaneous reactions were observed with good response to anti-histaminic treatment. Historical data from our department about previous treatment of TTP patients (n = 6) with TPE using standard FFP (quarantine plasma) showed an average number of sessions till remission of 8.

Summary/Conclusions: Plasma treated with riboflavin and UV light was adequate and safe for the treatment of TTP in our four patients in a standard regimen of 1.5 Vol. of plasma per day with the accompanying corticosteroid therapy.

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Abstract has been withdrawn

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ERYTHROCYTAPHERESIS, USEFUL ADJUNCT THERAPY IN PATIENTS WITH SEVERE MALARIA. HOSPITAL–BASED BLOOD BANK EXPERIENCE

N Garcia Muñoz, S Ortega Sanchez, R Ramoneda Novas, S Garcia Nuñez, M Miguel Moral, S Casals Villan, Y Garcia-Moreno Mora and M Gonzalez Medina
Apheresis and transfusion, Blood and tissue bank, Barcelona, Spain

Background: Severe Plasmodium falciparum malaria is a significant health problem worldwide especially in developing countries.

Aims: To report the use of automated erythrocytapheresis as an adjunct to artesunate in the management of severe Plasmodium falciparum malaria with hyperparasitaemia in three patients

Methods: Between 2012 and 2017 we have treated three patients affected of severe Plasmodium falciparum malaria by a combination of anti malarials and non-pharmacological measures. The devices used were COBE Spectra system in cases one and two and Optia Spectra in the third one

Results: Patient one: A 50-year-old Spanish man with end-stage idiopathic dilated cardiomyopathy received a heart allograft. On day 15 post HT he presented fever,

chills and hypotension requiring noradrenaline. Bilirubin was elevated to and hemoglobin dropped from 8.7 g/dl to 6.9 g/dl Peripheral blood smear showed intracellular parasites compatible with P.falciparum (parasitaemia rate of 15%). Quinine and doxycycline was administrated. Hyperparasitaemia and immunosuppression due to HT were severe so we considered adjunctive therapy in order to rapid removal of altered red cells from circulation. Rate of parasitemia decreased to 8%, at this point artesunate was given. After one more day of pharmacological treatment the rate became negative.

Patient two: a 33-year-old Spanish man who traveled to Ghana and did not take prophylaxis. One week later of his arrival he started with fever but he did not consult any medical institution since one more week. Such severe the clinical condition was that patient had to be transferred to our hospital. Hypotension, renal failure and disseminated intravascular coagulopathy requiring noradrenaline were developed .Peripheral blood smear showed intracellular parasites compatible with P.falciparum (parasitaemia rate of 18%). We added quinine to previous doxycycline. We performed automated erythropheresis treatment as supportive care and also the patient received artesunate.

Patient three: a 79-year-old French woman who traveled to Papua New Guinea and also did not take prophylaxis. She presented with fever and seizure during the flight back to his country. The pilot decided to land at Barcelona airport due to the severity symptoms. At the arrival to our hospital the patient developed progressively delirium and coma as manifestation of cerebral malaria. The peripheral blood smear showed intracellular parasites compatible with P.falciparum with hyperparasitaemia (>30%). The emergency service decided treatment with artesunate and control of parasitaemia in the next 8 h. In that case the adjunctive treatment with automated erythrocytapheresis was not considered in a first place. Notice that we do not still have a proper protocol in those situations. The control rate parasitaemia did not decrease more than 25% so the automated erythrocytapheresis was performed. Unfortunately the patient died 36 h later

Summary/Conclusions: Non-pharmacological measures to reduce the parasite burden in severe malaria must be considered in exceptional cases as adjunctive strategy to solve the emergency. Automated erythrocytapheresis is a safe procedure and should be performed in severe situations if it is easily available. However antimalarials should not be delayed.

Eventually we emphasize the need to establish consensuated procedures:

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THERAPEUTIC ERYTHROCYTAPHERESIS: 15 YEARS' EXPERIENCE IN A BLOOD BANK SETTING

E Rombout-Sestrienkova[1], E Reuser-Kaasenbrood[2] and M van Kraaij[1]

[1]Transfusion Medicine, Sanquin Blood Bank, Amsterdam [2]Donor affairs, Sanquin Blood Bank, Maastricht, Netherlands

Background: Since 2002, Sanquin Blood Bank applies therapeutic erythrocytapheresis (TE), mostly for treatment of hereditary hemochromatosis. Since then, the number of patients, procedures and indications has excessively grown. Conform our guidelines we accept all patients for reduction of red blood cell (RBC) treatment with the exception of patients with recent myocardial infarction, serious arrhythmias, recent neurovascular events or a history of epilepsy with grand mal during the last 3 months.

Aims: The aim of the study was an observational review of consecutive patients treated with TE at Sanquin Blood Bank during 2002–2017 .

Methods: We performed a retrospective analysis of all TE procedures with emphasis on patient characteristics and adverse events occurring during these procedures.

Results: Between 2002–2017, in total 295 patients have been treated; 196 (66.4%) males and 99 (33.6%) females with a total of 2149 TE procedures. The majority of patients (n = 221; 75% of total patients) were treated for hereditary hemochromatosis with a total of 1721 (80.1%) procedures. The second largest group were patients with polycythemia vera with a total of 20 (6.8%) patients and 67 (3.1%) procedures. In 14 (4,7%) patients treatment was applied because of hyperferritinemia with unknown diagnosis with a total of 33 (1.5%) procedures. A further 11 (37%) patients with secondary hemochromatosis post-transplantation, caused by multiple transfusions in history, were also successfully treated. In this group a total of 128 (5.9%) procedures were performed. The same number of patients were treated because of secondary polyglobulia caused by heart or lung disease, with in total 124 (5.8%) procedures. A total of 13 (4.4%) patients with chronic non-alcoholic steatohepatitis or alcoholic hepatitis were treated with 29 (1.3%) procedures. Two (0.7%) patients diagnosed with porphyria cutanea tarda needed 6 (0.3%) treatments and two (0.7%) patients with aceruloplasminemia were treated with 35 (1,6%) procedures. One (0.3%) patient with the diagnosis hereditary erythrocytosis was treated with 6 (0,3%) treatments.

There were no serious adverse events reported. Mild or very mild complications occurred during 113 (5.3%) of all procedures, with 73 patients (24.7%) experiencing at least one complication during the course of treatment. From these patients with adverse events, 33 were females and 40 males. Half (50.4%) of all reactions (in 30 patients) were citrate reactions: muscle cramps, paresthesia's and nausea, that responded to simple measures such as reducing whole-blood flow rate and/or oral administration of calcium tablets, milk or both. Dizziness during or shortly after procedure was noticed 39 times in 32 patients. A near vasovagal collapse occurred during 12 procedures in 10 patients. In 2 patients pain in the arm was experienced shortly after the procedure. Furthermore arrhythmia with normal blood pressure, an experience of itch at the place of venesection, and occurrence of hypoglycemia were reported in 3 individual patients.

Summary/Conclusions: From 2002–2017 a variety of patients (n = 295) with either iron overload or high red blood cell mass were treated with TE in a blood bank setting. In 5,3% of 2149 procedures mild or very mild complications occurred, but no serious adverse events were reported. This confirms that TE can be safely applied in a blood bank setting.

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EFFECTIVENESS OF THERAPEUTIC PLASMA EXCHANGE (TPE) IN A CRITICALLY ILL CHILD WITH SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

PK Pandey[1], N agarwal[1], E kaul[2] and S goel[3]

[1]Transfusion Medicine and Transplant immunology [2]Hematology and bone marrow transplant [3]critical care medicine, Jaypee Hospital, noida, India

Background: HLH is a syndrome of pathologic hyperactive inflammation due to unchecked immune activation. HLH is a life-threatening clinical syndrome that occurs in all age groups, primarily recognized in pediatric age group patients. In developing countries, it remains relatively under-diagnosed. Diagnosis of HLH is based on the HLH 2004 diagnostic criteria proposed by HLH society. This criterion requires fulfilment of five of eight clinical tools. Though, TPE has not been approved as a definitive treatment modality in management of secondary HLH but few case reports have shown its beneficial effects in calming the cytokine storm.

Aims: To observe the effect of TPE in HLH.

Methods: This observation was done in a tertiary healthcare center in the national capital region of India. Complete blood count like Hemoglobin (Hb), platelet count (PC), total and differential leukocyte count were done using XN 1000 (SYSMEX, USA). Biochemical parameters like serum Ferritin, fibrinogen, triglycerides, lactate dehydrogenase (LDH), liver function tests (LFT), kidney function tests (KFT) were done with Vitros 5600(OCD). Coagulation parameters PT and APTT were measured on Destiny plus (Tcoag, Stago).Bone marrow biopsy was done to detect hemophagocytosis and rule out lymphoid malignancy and aplasia. Diagnosis was made based on HLH 2004 criteria.

Results: Patient (14 years /M) was absolutely well one week ago. He presented to our hospital with the chief complaints of persistent fever, bodyache, throat pain and decreased oral intake for one week. Vital were persistently low (Systolic/diastolic 90/ 40 mm Hg) even after infusing 1500 ml of normal saline (0.9%). Patient was then shifted to medical ICU for further treatment and broad spectrum antibiotic and ionotropic support (noradrenaline) started. Hematology consultation was taken in view of pancytopenia and deranged coagulation (TLC- 1X109/l, PC-22X109/l, Hb-8.2 g/dl, PT-18.2 sec, APTT-36 sec). other parameters relevant to HLH were investigated which showed convincing results in favour of HLH (LDH- 2860 IU/l, Fibrinogen-50 mg/dl, Ferritin- 3600 ng/ml, fasting triglyceride- 384 mg/dl). His LFT, KFT and coagulation profile were grossly deranged. Bone marrow biopsy was done which demonstrated features characteristic of HLH. Due to progressive deterioration of clinical conditions he was intubated and started on IV methylprednisolone pulse and TPE. After three sessions of TPE his clinical condition improved remarkably and he was switched to IV Dexamethasone as maintenance treatment. TPE was done using COM.TEC (Fresenius Kabi, Germany). One standard TPE procedure was 1.5 plasma volume exchange using fresh frozen plasma as replacement fluid. Slowly his organ function improved and he was extubated. During hospital stay patient required transfusion of 2 units of packed red cells, 12 units of FFP, 4 units of single donor platelet concentrates and 24 units of cryoprecipitates. He was discharged after 16 days of hospital admission. At the time of discharge, hematological, biochemical and coagulation parameters were within normal range.

Summary/Conclusions: In developing countries like India, where infections are still a prime concern to the physicians, making an accurate diagnosis of HLH is a great concern. High suspicion, timely diagnosis and early start of TPE can be life saving in such patients.

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THALASSEMIA INTERMEDIA WITH SEVERE POST-SPLENECTOMY PULMONARY ARTERIAL HYPERTENSION RESPONSIVE TO WHOLE BLOOD EXCHANGE

SK Ballas[1] and S Schuster[2]

[1]Thomas Jefferson University [2]Penn Medicine Hematology Oncology, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America

Background: Pulmonary hypertension (PH) is a controversial complication of β-thalassemia. The controversary centers on the diagnosis of the accurate type of PH and its management. Here, we describe a patient with pulmonary arterial hypertension (PAH) diagnosed with right heart catheterization and successfully treated with whole blood exchange (WBE).

Aims: Demonstrate the safety and efficacy of WBE transfusion for the treatment of severe PAH in a patient with β-thalassemia intermedia.

Methods: A 41-year-old man of Greek ancestry presented with progressive dyspnea and acute cor pulmonale secondary to PH. Past medical history was remarkable for history of β-thalassemia intermedia, extramedullary hematopoiesis, iron overload, splenectomy and chelation therapy with deferoxamine. Findings on physical exam included respiratory distress with respiratory rate of 33/min, pulse 113/min, pulse oximetry 92% on two liters oxygen, blood pressure 137/73 and temperature 38°C. Lung exam was clear to auscultation and heart exam revealed split S2. Hematological, biochemical and imaging studies were done by routine methods. The α-globin/non α-globin synthetic ratio was determined by column chromatography on carboxymethyl cellulose in 8 M urea of radioactive globin prepared from peripheral blood incubated with ^{14}C-leucine. β-thalassemia mutations were determined by polymerase chain reaction (PCR) and reverse dot blot hybridization. The deformability index of RBC was determined by osmotic gradient ektactometry and whole blood viscosity was determined by viscometry. Right heart catheterization and whole blood exchange were done by established methods.

Results: Hemoglobin (Hb) level was 6.5 g/l, mean corpuscular volume (MCV) 68 fl, white blood cell (WBC) 11, 700/μl, platelet 418,000/μl and arterial blood gas with pH 7.45, pCO2 26, pO2 57. Hb electrophoresis showed Hb AF, Hb F 26.5% and Hb A2 9.5%. Molecular diagnostics showed that he had deletion of one α gene, the α-globin/non α-globin synthetic ratio was 2.67. β-thalassemia mutations showed that the mutation on one β-chain was -87 C → G and the mutation on the second β-chain was IVS 1-110 G → A. Thus, his Hb genotype is -α/αα, β+/β+ and the specific mutations were: β$^{-87\ C\ \rightarrow\ G}$/β$^{IVS\ 1-110\ G\ \rightarrow\ A}$. The deformability index of his RBC was 40% of normal control and his whole blood viscosity was increased by 38% of normal. Cardiac catheterization revealed severe PAH with mean pulmonary artery pressure (MPAP) of 60 mmHg with normal pulmonary capillary wedge pressure of 10 mmHg. Because of the possibility that the decreased deformability of his RBCs and his increased whole blood viscosity worsened his PAH, WBE was performed. This resulted in dramatic and prompt clinical improvement. Whole blood exchange was repeated every 4–6 weeks and within 3–4 months there was no evidence of pulmonary hypertension by echocardiography. Unfortunately, the development of multiple RBC alloantibodies associated with difficulties in finding compatible RBCs, the chronic WBE transfusion was interrupted and performed less frequently depending on the availability of compatible RBCs. He was also maintained on therapy with calcium channel blockers. With time, there was gradual worsening of his PAH leading to his death about 8 years later at the age of 52 years due to cardiopulmonary complications.

Summary/Conclusions: Whole blood exchange is a safe method to treat severe post-splenectomy PAH complicating β-thalassemia intermedia and possibly other types of β-thalassemia.

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RATIONALIZATION AND OPTIMIZATION OF THE THERAPEUTIC PLASMA EXCHANGE APPLICATION

Z Kirov

Department of Clinical Transfusion, Blood Transfusion Institute Nis, Nis, Serbia

Background: Therapeutic plasma exchange (TPE) is a nonselective, nonspecific method used for the separation of circulating agents, an automated apheresis procedure with extracorporeal circulation aimed at reducing the concentration or elimination of pathogen from the blood plasma, to reimburse the removed volume with suitable liquid. TPE is used in a number indications, which are currently classified in to four separate categories. The category I includes diseases in which the TPE is standard – the primary treatment option. For disorders of category II, TPE is an additional, supportive therapy, usually in combination with other treatment modalities. In the category III are pathological conditions, in which the exact role of

apheresis is not still safely defined – validity of TPE application, as well as the achieved effects are individual. The category IV includes diseases in which performing of TPE has not been proven effective.

Aims: Continuous introduction of new and more effective immunomodulatory and other medications, the indications for performing TPE and achieved effects require continuous critical re-evaluation. For this reason, the aim of this work was analysis of the feasibility of this type of treatment, with the categorization of indications, are essential for understanding the place and role of TPE in the treatment of these patients group.

Methods: Retrospective analysis of indications for the total of 1284 TPE during the period from 2012 to 2017, as well as categorization according to criteria AABB at the Blood Transfusion Institute Nis, Serbia, has been done. TPEs are performed using the blood cell separator Haemonetics MCS+, according to the applicable standards and recommendations about the number and frequency of procedures, optimized time of application and the amount of extracted plasma.

Results: All of 1284 TPE procedures are analysed and categorized, and the following results were obtained, category I was represented in 43,1%, 28,9% category II, category II –III in 21,3% and category III in 6,7%, while category IV was not presented. The most common indication was myasthenia gravis (MG) 71 patiens,291 TPE, followed by Guillain – Barre syndrome with 42 patients,169 TPE, multiple sclerosis 31 patients, 114 TPE, hiperbilirubinemia 27 patients, 101 TPE, CIDP 14 patients, 52 TPE, and thrombotic thrombocytopenic purpura (TTP) was represented in 7 patients, 31 TPE, and other in I, II, III category.

Summary/Conclusions: The results suggest that the indications for TPE predominantly belong to category I and II, while disorders in the category IV were not presented. This can be interpreted as rationalization and optimization of the TPE application, as a special form/modality of the treatment. The positive therapeutic effect of TPE in the treatment of patients depended upon the nature of the basic disease, its stage, general condition, volume of plasma removed and additional therapy.

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THERAPEUTIC PLASMA EXCHANGE IN NEUROMYELITIS OPTICA SPECTRUM DISORDER– A CASE REPORT

G Kaur[1] and A Kaur[2]

[1]Immunohematology and blood transfusion, Dayanand Medical College and Hospital, Ludhiana, Punjab, India [2]Immunohematology and blood transfusion, Dayanand Medical College and Hospital, Ludhiana, India

Background: Neuromyelitis Optica Spectrum Disorder (NMO-SD) is a recently proposed unifying term for NMO which is also called Devic's disease, and related syndrome. It is characterized by longitudinally extensive transverse myelitis, that is associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4–IgG), which can leave one quite debilitated at presentation with unilateral or bilateral optic neuritis. If not treated appropriately, most of the NMO-SD patients lose functional vision in at least one eye or unable to walk. High dose of steroids is usually given as first line of treatment in acute attacks. But non responders to steroids are treated with plasma exchange, as a rescue therapy.

Aims: To study the therapeutic effect of plasma exchange in patients having acute attack of NMO-SD.

Methods: A 55 years old female, housewife by profession presented with right sided weakness for 20 days which started as numbness in right upper and lower limb which progressed to weakness. The same course was followed over 5–7 days on the left side of body but only left lower limb was involved. There was associated band like sensation in waist rising upwards till nipples. On admission of patient in hospital, the muscle power was 1/5 and 4/5 in right and left upper limb respectively, 1/5 and 3/5 in right and left lower limb respectively. Lhermitte's sign was positive. MRI spine showed long segment myelitis. There was no abnormality detected in CSF analysis. Anti-aquaporin antibodies detection came out to be positive. Working diagnosis of NMO-SD was made and solumedrol pulse therapy was initiated. But weakness further increased over next 2 days and plasma exchange was planned.

Before commencement of procedure, the following investigations were analyzed; Hemoglobin- 15.7gm/dl, hematocrit- 48.5, platelets- 222 × 10^3/μl, INR- 1.02, fibrinogen- 233 mg/dl, aspartate aminotransferase- 32U/l, alanine aminotransferase-79U/l, total serum proteins-6.7 g/dl, albumin- 3.7 g/dl, globulin- 3gm/dl and serum electrolytes which were within normal range.

Plasma exchange was performed on Hemonetics MCS+ as a single arm procedure. 5 procedures were performed every alternate day with exchange of 1 plasma volume. Replacement fluid used were normal saline and fresh frozen plasma in ratio of approximately 40/60 percent. After last procedure additional transfusion of fresh frozen plasma was done as fibrinogen levels were declining initially after

procedures. Patient was monitored throughout for pulse, blood pressure, respiratory rate, SpO$_2$ and temperature. All sessions went uneventful except third when patient experienced shivering but was managed appropriately.

Results: Patient showed minimal improvement after first 2 procedures but after third, power was seen to be improved in right lower limb and left upper limb. She was able to lift her arm and flex her elbows and knees after 5th cycle. Power was 3/5 and 4/5 in upper and lower limbs respectively. Neck muscles and truncal weakness also improved. Patient was discharged after 3 days of last plasma exchange. On follow up after 15 days, she showed increased range of motion in both the limbs and improved sensations in affected regions.

Summary/Conclusions: Plasma exchange was performed in timely manner in adjunction with steroid therapy can cause marked improvement in acute episodes of NMO-SD and help in successful outcome.

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Abstract has been withdrawn

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INTRACRANIAL HEMORRHAGE IN LEUKEMIA PATIENTS: PRELIMINARY RESULTS OF AN ONGOING NESTED CASE CONTROL STUDY

LL Cornelissen[1,2], A Kreuger[1,3], R Middelburg[1,3], E Beckers[4], P von dem Borne[5], J Kuball[6], K de Vooght[7], J Zwaginga[1,2], J Kerkhoffs[1,8] and J van der Bom[1,3]

[1]Center for Clinical Transfusion Research, Sanquin Research [2]Department of Immunohematology and Blood Transfusion [3]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden [4]Department of Hematology, Maastricht University Medical Center, Maastricht [5]Department of Hematology, Leiden University Medical Center, Leiden [6]Department of Hematology [7]Department of Clinical Chemistry and Hematology, University Medical Center Utrecht, Utrecht [8]Department of Hematology, Haga Hospital, Den Haag, Netherlands

Background: Intracranial hemorrhage is one of the most serious bleeding complications in thrombocytopenic hemato-oncology patients. To prevent such bleeding complications patients frequently receive prophylactic platelet transfusions based on the platelet count. However, the evidence for low platelet count as an independent risk factor is inconclusive. Other clinical risk factors are thought to also modify the bleeding risk.

Aims: To describe the association of platelet counts, transfusions and clinical risk factors like age, sex, infection and medication in the previous seven days with the risk of intracranial hemorrhage in patients with acute leukemia.

Methods: Nested case control study in a cohort of leukemia patients in four hospitals. Cases with intracranial hemorrhage were identified with a regression model previously designed to identify patients with major hemorrhages. Controls were matched on diagnosis, therapy and time. Cases were excluded in case of inability to identify suitable controls, uncertain date of intracranial hemorrhage or irretrievability of clinical data. Clinical risk factors were recorded from medical records for seven days preceding the bleeding for cases, or for the corresponding index period for controls. Univariate conditional logistic regression was performed to explore the association of bleeding with platelet count and potential risk factors.

Results: We identified 39 cases in four hospitals of which 25 were excluded for one of the exclusion criteria. Fourteen cases and 44 controls were included in the case control analysis. Most patients had acute myeloid leukemia (63.8%). 79.3% of the cases received remission induction for a new or relapsed leukemia, 3.5% received consolidation therapy, 3.5% allogeneic stem cell transplantation and 13.8% were admitted for disease or treatment related complications. Having a morning platelet count <10 × 10^9 was not associated with increased bleeding risk (OR 0.88, CI 0.10 to 8.13). Age was associated with an increased bleeding risk (OR 1.1/year, CI 1.01 to 1.18). Sex showed no relevant association (women: OR 1.21, CI 0.39 to 3.78). Compared to none, receiving one or two platelet transfusions in one week was associated with intracranial hemorrhage (OR 4.3, CI 0.70 to 26.28). For three or more platelet transfusions this risk increased (OR 6.4, CI 1.07 to 37.65. p-value for trend=0.044).

Furthermore, presence of an infection proven by any positive culture or positive polymerase chain reaction (OR 2.58, CI 0.65 to 10.30) and usage of antihypertensive medication (OR 12.2, CI 1.36 to 110.36) were associated with an increased risk of intracranial hemorrhage.

Summary/Conclusions: Age, usage of antihypertensive medication and the presence of a culture or polymerase chain reaction proven infection were associated with an increased risk of intracranial hemorrhage. Also, the need for platelet transfusion was associated with an increased risk of intracranial hemorrhage. Although this does not imply causality, these conclusions could be relevant in platelet transfusion decision making.

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IRONING OUT ANAEMIA IN PREGNANT WOMEN

C J Flores[1], P Crispin[2], F Sethna[2], B Stephens[2], M Burgess[2], K Osborn[3], E Knights[3], J Grech[3], P Paramanathan[4], S Kay[4], F Hong[1], T Roberts[5], T Spigiel[5], S Minck[6], B Saxon[3,5] and O Maternity Blood Management Improvement Team[2,3,4,7]

[1]Clinical Services and Research, Australian Red Cross Blood Service, Melbourne [2]Canberra Hospital and Health Service, Canberra [3]Women's and Children's Health Network, Adelaide [4]Darling Downs Hospital and Health Service, Toowoomba [5]Clinical Services and Research, Australian Red Cross Blood Service, Adelaide [6]Clinical Services and Research, Australian Red Cross Blood Service, Brisbane [7]Australian Red Cross Blood Service, Adelaide, Australia

Background: Iron deficiency (ID) is common in pregnancy and increased iron demands often lead to iron deficiency anaemia (IDA). This can impact on both the baby (e.g. increased risk of low birth weight and prematurity), and the mother (e.g. antenatal depression and increased risk of postpartum haemorrhage). Antenatal ID can go unnoticed if haemoglobin (Hb) alone is measured, resulting in a missed opportunity to optimise a woman's iron status and haemoglobin before delivery. The Blood Service partnered with three hospitals to align current practice with national Patient Blood Management (PBM) guidelines, Module 5 Obstetric and Maternity (2015).

Aims: To implement systems to improve antenatal detection and management of ID (ferritin ≤ 30 μg/l) and IDA

Methods: The partnerships, spanning March 2015 to March 2018, used clinical practice improvement (CPI) methodology. Initial data identified variation in IDA management across all sites. Tools developed included Maternity IDA assessment and management flowcharts, which included routine 1st and 2nd trimester ferritin screening. Iron therapy was recommended for women with ID or IDA. To address patient education, a maternity patient handout on recommended oral iron preparations was introduced. Education was provided to all staff involved with implementing the initiatives. Patient Hb, ferritin and phone based patient satisfaction surveys were measured. Staff feedback was actively pursued and collected.

Results: Prior to the CPI, antenatal ID/IDA assessment and management was varied at the three hospitals. Previous obstetric guidelines and local protocols only recommended Hb screening. According to maternity staff, the flowcharts helped them to become confident in blood test interpretation and management of ID and IDA and, provided a 'long needed guidance and consistent approach'.

Hb and ferritin requests increased in each trimester at all hospitals. Overall, 67% (66%–68%) of women screened with ferritin tests were iron deficient. Hospital data across all sites showed that anaemic maternity patients at delivery (Hb ≤110 g/l) had higher chances of being transfused compared to non-anaemic patients. Following the introduction of CPI tools, the rate of anaemia intrapartum fell from 12.2% to 3.6% at the first hospital and from 16.1% to 11.5% at the second hospital.

Prior to the partnership there was minimal patient education about iron and poor compliance with oral iron therapy across all hospitals. Feedback from women who received the iron prescription maternity handout indicated that it was useful [92% (82%–100%)]. Reported compliance with oral iron therapy was up to 95%. Consistent positive feedback was received from women across all hospitals.

Summary/Conclusions: Better systems to identify and manage ID/IDA in pregnant women can have significant benefits for both mother and baby. The Blood Service and hospital partnerships provided practice improvements in maternity blood management which were aligned with PBM guidelines and are now embedded in practice. Routine ferritin screening reliably detects ID in pregnancy, which allows early provision of iron therapy and results in improved Hb before delivery. From the successful results, a Maternity blood management practice improvement toolkit is being developed that may be translated readily into other institutions.

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PREVALENCE AND PATHOGENICITY OF MATERNAL RED BLOOD CELL ALLOANTIBODIES

L Lieberman[1,2], J Buckstein[2], J Callum[2], R Cohen[2], C Cserti-Gazdewich[1], N Ladhani[2], J Pendergrast[1] and Y Lin[2]

[1]University Health Network [2]Sunnybrook Health Science Center, Toronto, Canada

Background: Hemolytic disease of the fetus and newborn (HDFN) occurs when maternal Ig-G alloantibodies cross the placenta and mark the fetus' red blood cells (RBCs) for destruction. Neonatal presentation ranges from mild jaundice, to anemia, and rarely hydrops fetalis and death. During pregnancy, treatments include observation and/or intrauterine transfusions (IUT). Neonatal treatment includes observation, phototherapy, intravenous immunoglobulin (IVIG) and /or neonatal transfusions.
Aims: The objectives of this study were to: (1) Determine the prevalence of RBC antibodies at a single center, (2) Evaluate the fetal and neonatal outcomes of these pregnancies.
Methods: Between 2000–2017, a retrospective audit of alloimmunized pregnancies was conducted at a single center that performs 4200 deliveries annually. Data collected included maternal and neonatal demographic data, clinical data (pregnancy, delivery, and post-partum) and laboratory results. A diagnosis of HDFN was defined by any one of the following; (1) maternal receipt of an intrauterine blood transfusion; (2) neonatal receipt of intensive phototherapy (grade 2 or above), (3) neonatal receipt of a simple RBC transfusion or an exchange transfusion.
Results: 128 mothers and 136 neonates were alloimmunized with 162 allo-antibodies. Anti-E (N = 51, 31%), c (N = 26, 16%), D (N = 24, 15%) and K (N = 14, 9%) were the most frequent clinically significant antibodies identified. Prenatally, 12% (15/128) of patients were followed with bloodwork alone, 70% (89/128) were followed with Doppler surveillance, 9% (12/128) had abnormal ultrasound results, while 2% (2/128) required IUT. Post-partum, 71% (97/136) of neonates required no treatment, 28% (38/136) required phototherapy (28% mild and 13% intense), and 11% (15/136) received at least one blood product (IVIG or RBC transfusion). Thirteen percent of the neonates (17/136) fulfilled the HDFN criteria; the majority with Rh (13/17; 76%) or Kell (3/17) antibodies.
Summary/Conclusions: Although recent scientific literature postulates that cases of HDFN caused by anti-Rh are declining, our results suggest that Rh antibodies remain the main culprit for the most severe cases of HDFN. Future prospective studies are required to better validate these results.

P-697
FERRITIN SCREENING FOR PATIENT BLOOD MANAGEMENT IN PREGNANCY

P Crispin[1,2,3], B Stephens[4], E McArthur[2] and F Sethna[5]

[1]Haematology, Canberra Hospital, Woden [2]Medical School [3]John Curtin School of Medical Research, Australian National University [4]Obstetrics, Canberra Hospital, Canberra, [5]Obstetrics, Canberra Hospital, Woden, Australia

Background: Most guidelines recommend screening for anaemia in pregnancy with haemoglobin and not specifically with ferritin, despite the prevalence of iron deficiency in young women. This may in part be due to uncertainty in interpretation in the context of the physiological changes of pregnancy. Anaemia at the time of delivery is major risk factor for transfusion.
Aims: To determine the value of ferritin screening at different stages of pregnancy in order to guide patient blood management strategies.
Methods: Data were extracted from antenatal and pathology databases for women during pregnancy at an Australian tertiary referral hospital. Haemoglobin and ferritin levels were retrieved where available and results stratified by trimester. Multiple pregnancies and premature deliveries were excluded. The value of testing at each stage of pregnancy for the prediction of anaemia at presentation (within two days of delivery) was determined. Rates were compared by Chi-squared or Fisher exact tests. Data analysis was repeated following a patient blood management intervention targeting iron replacement in pregnancy.
Results: There were 153 women with a ferritin in first trimester and a pre-delivery haemoglobin recorded, with 48 (32.7%) having a ferritin of <30 μg/l and 6 (4%) anaemia pre-delivery. A ferritin <30 μg/l in the first trimester was associated with an increased risk of anaemia prior to delivery (P = 0.019, Fisher exact test). A receiver operator characteristic curve for ferritin in first trimester predicting anaemia at delivery had an area under the curve of 0.80 (95%CI 0.59–1). A ferritin of 30 μg/l had a sensitivity of 0.83 and sensitivity of 0.67. There were 545 women with a haemoglobin in trimester one and pre-delivery. While a low haemoglobin in first trimester was predictive of anaemia at the time of delivery (P = 0.002), at a haemoglobin of 110 g/l it had a sensitivity of only 0.23 and specificity of 0.69. Of the women with a low ferritin in first trimester, only three were anaemic at the time of the sample. There were 138 women with iron stores assessed in trimester two and a haemoglobin pre-delivery, with 10 having anaemia at delivery. Ferritin did not predict later anaemia (P = 1, Fisher exact test) and receiver operator curve did not identify a significantly better ferritin cut-off. Anaemia (Hb<105 g/l) in second trimester did not predict anaemia prior to delivery.
During the iron replacement intervention there were 118 women with a ferritin in first trimester, with 36 (30.5%) having a ferritin <30 μg/l. Three (only one with low ferritin) were anaemic at the time the test was taken and two prior to delivery. Ferritin in first trimester was not associated with pre-delivery anaemia during the period of active iron replacement.
Summary/Conclusions: Screening women for iron deficiency in the first, but not second, trimester of pregnancy identified women at risk of anaemia at delivery, with the association lost following implementation of an active iron replacement patient blood management strategy. These results support screening for iron deficiency in first trimester with serum ferritin, even within a "low risk" population.

P-698
PROACTIVE DETECTION AND TREATMENT OF ISOLATED IRON DEFICIENCY IN PREGNANCY IMPROVES HAEMOGLOBIN LEVELS AT DELIVERY

C S Booth[1], J McCullagh[2], N Sharma[3], C Denison[4], E Carpenter[5], L Anna[6], C Donohue[7], H Brian[8] and S Allard[1]

[1]Haematology, Royal London Hospital, London, UK [2]Haematology, Whipps Cross Hospital [3]Haematology, Newham University Hospital [4]NHS Blood and Transplant [5]Haematology, Kings College Hospital [6]Haematology [7]Anaesthetics, Royal Free Hospital, London [8]Statistics, NHS Blood and Transplant, Birmingham, United Kingdom

Background: Anaemia in pregnancy is associated with adverse outcomes for mother and baby and may lead to an increased risk of requiring a blood transfusion perinatally. Iron deficiency is the commonest cause. UK guidelines from the Royal College of Gynaecology (RCOG), British Society for Haematology and National Institute for Health and Care Excellence recommend screening for anaemia at booking and 28 weeks and starting empirical oral iron replacement if haemoglobin (Hb) is below the normal range for gestation (<110 g/l in 1st trimester or <105 g/l in 2nd-3rd trimester). Measuring ferritin is not recommended unless there is an inadequate response to iron. This approach will fail to detect women who are iron deficient but not anaemic, who are at risk of developing anaemia later in pregnancy. Up-front measurement of ferritin and treatment of iron deficiency could prevent anaemia.
Barts Health NHS Trust serves a population of 2.5 million in East London where there is a high prevalence of iron deficiency due to dietary and ethnic factors. Approximately 14,000 women deliver each year across three hospitals. At Royal London Hospital (RLH), routine ferritin testing on each antenatal blood sample was introduced in 2014. Iron tablets are given to any woman with ferritin less than 30 μg/l. Newham (NUH) and Whipps Cross (WXH) Hospitals follow standard RCOG guidelines.
Aims: This retrospective observational study aimed to assess the impact of proactive detection and treatment of iron deficiency on haemoglobin and anaemia rates in pregnancy by comparing the 3 hospitals.
Methods: Data were collected retrospectively on all women delivering at RLH, NUH and WXH between 1st and 7th October 2015. Hb and ferritin levels were recorded at booking, 28 weeks, in labour and postnatally and compared using analysis of variance. The number of women requiring red cell transfusions was recorded. At RLH, prescription of oral iron in iron deficient women was assessed.
Results: There were 298 deliveries. Anaemia was common, rising from 10–14% at booking to 10–33% at 28 weeks. At RLH, 46% were iron deficient at booking and 85% at 28 weeks, though less than 25% of these women were anaemic. 68% of those iron deficient at booking and 90% at 28 weeks were given iron. At delivery, mean Hb was significantly higher at RLH (124 g/l) compared to WXH (118 g/l) or NUH (116 g/l) (P = 0.0007) and fewer women were anaemic (6% versus 18% and 17% respectively). 13 women received red cell transfusions, 8 following major obstetric haemorrhage. Only 3 of these had been anaemic in labour. Postnatally there was no significant difference in mean Hb levels between the sites.
Summary/Conclusions: Isolated iron deficiency without anaemia is common in pregnancy. Treatment with oral iron was associated with higher Hb at the time of delivery. This did not correlate with reduced transfusion rates or higher postnatal Hb, as blood loss in labour is unpredictable and transfusion uncommon unless there is major obstetric haemorrhage. However, improving iron stores and Hb may have additional benefits for maternal and foetal health and wellbeing which should be the focus of future studies.

P-700

EFFICACY OF LOW AND HIGH DOSE PROPHYLACTIC PLATELET TRANSFUSION THERAPY IN HAEMATO-ONCOLOGY PATIENTS

R Sharma[1], Y Dhiman[2], P Malhotra[3], R Hans[2] and N Marwaha[2]

[1]Transfusion Medicine [2]Transfusion Medicine [3]Internal Medicine, PGIMER, Chandigarh, India

Background: It is important to determine an optimal platelet dose in thrombocytopenic patients for the judicious use of this scarce resource. This can be achieved by transfusing platelets in different doses and comparing their post transfusion response indictors

Aims: This prospective study was performed to compare the efficacy of low and high dose with standard dose of Single Donor Apheresis Platelet (SDAP) transfusions in terms of platelet transfusion response indicators - Corrected Count Increment (CCI) and Percent Platelet Recovery (PPR) and their correlation with patient's clinical profile

Methods: A total of 28 stable, non-refractory hemato-oncology patients were enrolled in the study after fulfillment of inclusion criteria. The study was approved by the Institute Ethics Committee. Patients received apheresis platelets as low dose $(1.5 \times 10^{11}$platelets /unit), medium dose $(3 \times 10^{11}$ platelets/unit) and high dose $(>4 \times 10^{11}$platelets/unit) at different time points in a sequence of standard, low and high dose as and when a request was received based on his/her pre transfusion platelet count and clinical profile. The post transfusion counts were assessed after 20–24 h of transfusion and post transfusion response indicators were calculated in terms of platelet increment, corrected count increment (CCI), percent platelet recovery (PPR). Transfusion free interval and the bleeding events were also recorded for different doses

Results: Post transfusion response indicators CCI and PPR were comparable for standard dose (CCI=12553 $\pm$ 7598, PPR=36.11 $\pm$ 24) and low dose (CCI=12279 $\pm$ 10842, PPR=35.00 $\pm$ 31.7). Post transfusion increments were comparable with standard (22318.18 $\pm$ 12159) and high dose (22636.3 $\pm$ 18062), however CCI (P = 0.006) and PPR (P = 0.008) were better with standard dose and were statistically significant. Higher post transfusion increments were observed with high dose as compared to low dose, however CCI (P = 0.04) and PPR (P = 0.05) were better with low dose and were statistically significant. The transfusion free interval after the standard dose, low dose and high dose was 3.71 $\pm$ 3.4 days, 3.36 $\pm$ 4.4 days and 7.24 $\pm$ 7.9 days respectively, however, the difference was not statistically significant. Donor exposure to patients was significantly (P = 0.000) reduced to 17.5% owing to the splitting of platelet products to form customized doses for the transfusion

Summary/Conclusions: Standard dose of apheresis platelets is the best choice for adequate post transfusion response in hemato-oncology patients however, the possibility of low dose as an alternative to standard can be considered in stable thrombocytopenic patients owing to the comparable post transfusion response indicators (CCI and %PPR) in the two groups

P-701

IMPACT OF PRE-OPERATIVE SUPPLEMENTAL OF FIBRINOGEN CONCENTRATE ON BLEEDING AND TRANSFUSION REQUIREMENTS IN CARDIAC SURGERY

E Khalaf Adeli

Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran, Tehran, Iran

Background: Cardiopulmonary bypass (CPB) induces a multifactorial coagulopathy due to an extensive consumption of coagulation factors especially fibrinogen. There are contradictory reports about effects of preoperative supplemental fibrinogen in patients without hypofibrinogenemia.

Aims: The aim of this study was to investigate the effect of pre-operative supplemental of fibrinogen concentrate on bleeding and transfusion requirements in cardiac surgery.

Methods: Totally 78 patients scheduled elective CABG or valvular surgery, were included in a clinical trial study between March 2017 and November 2017. Patients were randomly assigned to the fibrinogen and control groups. In the fibrinogen group patients received 2 grams of fibrinogen dissolved in 50 mL of normal saline over a 15 min period 30 min after induction of anesthesia. In the control group the patients were received the same volume of normal saline during the same period of time. Post-operative bleeding was recorded as the overall mediastinal drainage or other drain in surgical site during 24 h after surgery. Amount of transfused packed red blood cells, fresh frozen plasma, and platelets during first post-surgery day were also documented.

Results: The mean volume of bleeding was significantly lower in fibrinogen group compared with control group (168 $\pm$ 12 ml vs 344 $\pm$ 37 ml) (P = 0.001). Furthermore, the mean volume of FFP and platelet concentrate which used in fibrinogen group was significantly lower in fibrinogen group compared with control group (P < 0.05). However, we didn't found any significant differences in RBC consumption between groups

Summary/Conclusions: Preoperative supplementation with fibrinogen results in reduction in postoperative blood loss and transfusion requirements during cardiac surgery.

P-702

FRESH FROZEN PLASMA: UNDER–DOSED AND OVER–TRANSFUSED

H Shaikh[1], S Shaikh[1], D Lee[2] and P Mewawalla[2]

[1]Division of Internal Medicine, Allegheny Health Network [2]Division of Hematology and Cellular Therapy, Allegheny Health Network Cancer Institute, Pittsburgh, Pennsylvania, United States of America

Background: Despite the widespread use of fresh frozen plasma (FFP), it is interesting that there are no randomized controlled trials establishing indications of FFP transfusion. Based on the guidelines from ASH and AABB, and experts' opinion, the indications of plasma transfusion agreed upon are: actively bleeding trauma patients in the setting of multiple coagulation factor deficiencies (massive transfusion, disseminated intravascular anticoagulation, etc.), emergent reversal of warfarin with active intracranial bleeding, and during plasma exchange. However, a consensus on the dosing of FFP has been observed, which is 10 to 20 ml/kg of recipient weight.

Aims: The objectives of this study were to evaluate consistency of appropriate dosing, correlation with coagulation tests and common settings of FFP transfusions.

Methods: A retrospective review was conducted at a tertiary care facility, which included patients receiving FFP between January 2016 to June 2017. More than 1000 transfusion orders were placed in the stated time period. Based on the studies published on FFP and after meeting with the statistician, we decided on a sample size of 200 $\pm$ 20. 201 events were randomly selected and analyzed by age, weight, number of units ordered with each transfusion, indication of transfusion, pre-transfusion and post-transfusion INR, and if multiple orders of transfusion were placed on the same day. The dose of plasma was calculated by 20 ml/kg body weight and each unit of plasma being 250 ml.

Results: Among 201 events, 616 units of FFP were transfused. Median age of the recipients was 59 years (range 20–88). Most common indication was INR $\geq$ 1.6 with bleeding or pre-procedure (n = 170), followed by massive transfusion (n = 7), plasma exchange (n = 2) and unknown (n = 22). Of the total transfusions, only 3.48% (7/201) were of adequate dose based on weight. Among those transfused for supra-therapeutic INR, only 41.79% corrected to post-transfusion INR < 1.6 and 36.8% had more than one order of transfusions on the same day. And 12.4% (25/201) had pre-transfusion INR <1.6.

Summary/Conclusions: While it is commonplace to transfuse FFP based on coagulation studies (e.g., INR), there is no data to establish a correlation between the two. This and the fact that majority of transfusions were inadequately dosed can explain why more than half of the cases did not correct to INR < 1.6 and around one third required multiple transfusions. Moreover, FFP transfusions do not come without risks, commonly transfusion-related circulatory overload, allergic reactions, transfusion-related acute lung injury and development of antibodies.

Therefore, we strongly recommend that medical staff be educated on the indications as well as appropriate dosing of FFP. This also highlights the need for clear guidelines for FFP transfusions.

Abbreviations: ASH (American Society of Hematology), AABB (American Association of Blood Banks)

P-703

SAFETY AND EFFICACY OF GRANULOCYTE TRANSFUSION IN HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS - A SINGLE CENTRE EXPERIENCE

S Ojha[1], M Poojary[1], N Khattry[2] and S Rajadhyaksha[3]

[1]Transfusion Medicine [2]Medical Oncology, Tata Memorial Centre-ACTREC, Navi Mumbai [3]Transfusion Medicine, Tata Memorial Hospital, Mumbai, India

Background: Despite usage of broad spectrum antibiotics and antifungal drugs, bacterial and fungal infections continue to be cause of life threatening severe

neutropenia in patients of Hematopoietic Stem Cell Transplantation (HSCT). Neutrophils play an integral role in host defense against bacterial and opportunistic fungal pathogens. Neutrophil production by the marrow and an adequate number of blood and tissue neutrophils are the key predictors of recovery from infections. Hence, granulocyte transfusion therapy is a possible way to bridge a gap between marrow suppression and neutrophil recovery unresponsive to appropriate antimicrobial therapy.

Aims: To determine safety and efficacy of granulocyte transfusion therapy in allogeneic HSCT patients with neutropenia related infections.

Methods: Retrospective analysis was done to determine safety and efficacy of granulocyte transfusion in 14 HSCT patients with severe neutropenia related infections unresponsive to appropriate antimicrobial agents. Granulocytes were donated by healthy donors stimulated by subcutaneous 5 µg/kg G-CSF plus 8 mg dexamethasone orally on Cobe Spectra cell separator machine. The response was analyzed in terms of clinical response and survival of patient at 42 days after first granulocyte transfusion during that particular neutropenia episode. The high-dose transfusion included all subjects in the transfusion arm who received a mean dose of >2.8 × 10⁸/kg per transfusion (equivalent to >2 × 10¹⁰/bag for an average 70 kg patient). The rest were included in low-dose transfusion arm (received mean dose </ = 2.8 × 10⁸/kg per transfusion).1 h and 24 h Absolute Neutrophil Count (ANC) increment in patients receiving high dose and low dose granulocyte transfusions were compared by Mann-Whitney test. $P < 0.05$ was considered significant.

Results: All 14 patients received a mean of 2.92 granulocyte transfusion (range, 1–7) and a mean dose of 3.59×10^8/kg granulocytes (range, 0.22 to 11.6×10^8/kg). Out of total 42 transfusion episodes, 24 had high-dose granulocyte transfusion and 18 had low-dose granulocyte transfusion. 1 h and 24 h post transfusion ANC increments were significantly higher in high-dose transfusion arm. 9 patients (64.28%) responded favorably to the granulocyte transfusions and 10 patients (71.42%) survived at 42 days after first granulocyte transfusion. Granulocyte transfusions were well tolerated with adverse reactions seen in only 1 patient.

Summary/Conclusions: Granulocyte transfusion therapy is an effective adjuvant therapeutic method in HSCT patients with neutropenia related infections resistant to appropriate antimicrobial agents. However, the heterogeneity of patient population, type of infection, antimicrobial therapy and dosage of granulocyte concentrates including outcome parameters make it difficult to propose accurate recommendations.

P-704

THE IMPACT OF RED BLOOD CELL AGE ON PRODUCT UTILISATION IN THE CHRONICALLY TRANSFUSED OUTPATIENT POPULATION (ABC-TOP TRIAL)

O Prokopchuk-Gauk[1], J McCarthy[2], J Hendry[2] and M Shabani-Rad[2]

[1]Pathology and Laboratory Medicine, Royal University Hospital, Saskatoon [2]Calgary Laboratory Services, Calgary, Canada

Background: Recent studies in acutely ill hospitalized patients have demonstrated that that red blood cell (RBC) age has no impact on mortality. However, adverse patient outcomes are known to increase as the cumulative number of transfusions received rises. Chronically transfused medical outpatients comprise a significant proportion of transfusion recipients annually, with this population largely underrepresented in the literature.

Aims: Our goal was to prospectively evaluate the impact of RBC age on product utilisation in a cohort of chronically transfused medical outpatients randomized to receive fresh (≤ 7 day old) or aged (22–42 day old) RBC. The primary outcome was to evaluate overall RBC transfusion rates in the fresh versus aged blood recipients. We hypothesized that use of fresh RBC in chronically transfused patients would lead to a decrease in overall RBC transfused.

Methods: Institutional ethics approval was obtained. Enrolment to this double-blind randomized controlled feasibility study was by invitation. Inclusion criteria included adult patients (≥ 18 years of age) receiving outpatient chronic red cell transfusions (≥ 2 red cell units per month for at least 3 consecutive months) in an ambulatory care clinic within the Calgary Zone. Patients with an established pre-requisite for fresh or irradiated RBC, chronic hemodialysis, or those with an acute decompensation of chronic disease were excluded. Parameters of usual pre- and post-transfusion bloodwork were followed. The total duration of enrollment was 1 year. The unpaired, two-sided t-test was used for statistical calculations, and based on the intention-to-treat principle.

Results: A total of 17 participants were enrolled, with n = 8 in the fresh and n = 9 in the aged RBC groups. Underlying participant diagnoses included myelodysplastic syndrome (59%), myelofibrosis (18%), and palliative acute myeloid leukemia (12%).

The mean duration of enrolment was 282 days (range 61–365 days), with 11 participants completing the full year (n = 5 fresh, n = 6 aged). A total of 226 RBC units were given during 135 transfusion events in the fresh RBC group, compared with 399 RBC units during 198 transfusion events in the aged RBC group. The calculated mean (±SD) number of RBC units transfused per 30 days of participant enrolment was 3.6 (±1.3) in the fresh RBC versus 5.7 (±2.5) in the aged RBC groups (P = 0.014). There was no significant difference in the mean (±SD) number of days between transfusions received among groups, with 13.7 (±9.3) days versus 12.4 (±5.8) days in the fresh versus aged RBC groups (P = 0.286); or the pre-transfusion hemoglobin of 84.3 (±3.7) g/l and 77.8 (±6.6) g/l in the fresh and aged RBC groups (P = 0.163).

Summary/Conclusions: We demonstrated a statistically significant decrease in the RBC units transfused in chronically transfused participants receiving fresh RBC, with an average reduction in utilisation of 2.1 RBC units per participant per month. Limitations of this study include the small sample size, variability in participant underlying clinical profile, and a greater overall proportion of irradiated RBC transfusion in the aged blood group due to site inventory management requirements. A larger study completed in a multi-center design is required to confirm these findings. (NCT02393508)

P-705

Abstract has been withdrawn

P-706

PREOPEARATIVE ANEMIA IS ASSOCIATED WITH INCREASED INTRA-OPEARTIVE MORTALITY IN PATIENTS UNDERGOING CARDIAC SURGERY

AZ Al-Riyami[1], B Baskaran[2], S Panchatcharam[3] and H Al-Sabti[4,5]

[1]Hematology [2]Anesthesia, Sultan Qaboos University Hospital [3]Studies and Research, Oman Medical Specialty Board [4]Surgery, Sultan Qaboos University Hospital [5]Oman Medical Specialty Board, Muscat, Oman

Background: During the last years, several investigators described pre-operative anemia to be associated with adverse short-term outcome. The risk of pre-operative anemia in patients undergoing heart surgery has not been described precisely. In all reports, the need of more studies in this field was expressed. There are no studies from the region that assessed the incidence nor the outcome of pre-operative anemia in patients undergoing cardiac surgery.

Aims: This study aimed to investigate the incidence of pre-operative anemia in patients undergoing cardiac surgery in our institution and to study its association with patient outcomes.

Methods: Retrospective review of clinical, laboratory and transfusion data of patients underwent cardiac surgery at the Sultan Qaboos University Hospital was performed. Patients were divided into anemic and non-anemic groups based on the Hb level pre-surgery. Anemia was defined based on WHO definition as Hemoglobin (Hb) < 12 g/dl in males and < 13 g/dl in females. Patients' demographics and clinical variables were compared between the anemic and non-anemic patients using Chi-square test and independent t-test. Factors influencing preoperative mortality were analyzed using multivariate binary logistics regression method. A p-value of <0.05 was considered statistically significant.

Results: Total of 599 patients (70% females, 30% males) were operated during the study period. Majority of the patients (69%) underwent Coronary Artery Bypass Surgery. Pre-operative anemia was found in 76% and 27% of males and female patients respectively. The rates of intra-operative red blood cell (RBC) transfusions were higher among anemic patients when compared to non-anemic patients (76% vrs 53% respectively, P < 0.001).

Anemic patients had a higher risk of intra-operative mortality when compared to non-anemic patients (7% vrs 3%, P = 0.023). Patients having anemia though had a worse risk profile before surgery when compared to non-anemic patients; with higher incidence of Diabetes Mellitus (54% vrs 39%, p < 0.001), Heart Failure (52% vrs 29%, P < 0.001), arrhythmia (17% vrs 9%, P = 0.004), cerebrovascular disease (10% vrs 5%, p 0.015) and cardiogenic shock at presentation (6% vrs 1%, P = 0.002). However, taking these risk into account in the logistic regression analysis, pre-operative anemia remains a risk factor for intra-operative mortality (P = 0.03, Odd Ratio 2.79, 95% CI 1.09–7.19). Moreover, pre-operative anemia was found to be a risk factor for early re-admission post-surgery (Odd Ratio 1.92, 95% CI 1.04–3.54).

Summary/Conclusions: Pre-operative anemia in patients undergoing cardiac surgery is independently associated with increased risk of intra-operative mortality, higher rates of intra-operative RBC transfusions and early re-admission rates post-surgery.

P-707

A DESCRIPTIVE STUDY OF HB LEVELS IN THE USE OF RED BLOOD CELL PRODUCTS ISSUED BY SOUTH AFRICAN NATIONAL BLOOD SERVICE (SANBS)

R Swanevelder[1] and K van den Berg[2]

[1]ICT, SANBS, Roodepoort [2]Medical, SANBS, Port Elizabeth, South Africa

Background: Although allogeneic red blood cell (RBC) transfusion is often a life-saving intervention, it also comes with certain risks. In search of cost-efficient and appropriate transfusion protocols optimising patient outcome, several studies assessed transfusion practises based on inter alia the use of haemoglobin (Hb) triggers. For most medical indications a restrictive transfusion strategy (Hb ≤ 7.0 g/dl) was associated with reduced infection risk without compromising patient outcome. South Africa delivers health care services through a two-tiered system of public and private facilities with an underlying perception of higher utilisation in better resourced private facilities compared to the lower resourced public facilities. Since June 2017 SANBS captured Hb information on blood product requests enabling us to benchmark transfusion practises against recommended transfusion strategies.
Aims: We evaluated transfusion practices and Hb triggers among SANBS blood recipients.
Methods: RBC requisitions received in blood banks are recorded on Meditech™, the SANBS operational system. Hb levels, demographic and clinical information for requests between July and December 2017 were extracted from the SANBS Business Intelligence system. Summary statistics and chi-squared tests were used to describe patient population and blood usage and assess significance of findings. Blood usage is expressed as number of units per transfusion event where a transfusion event includes transfusion activities within 72 h of receiving a cross-match specimen.
Results: During the study period 160 553 patients received 408 228 red cell products. Seventy-five per cent of the patients were treated in public facilities and received 62% of the red cell products. Public patients older than 4 years received 1.77 RBC's per transfusion event compared to 2.03 RBC's for private patients of similar age (p < 0.0001). Per transfusion event, males received 1.88 RBC's compared to 1.86 RBC's for females and older recipients received more units than younger recipients (1.36 units for recipients 4 – 12 years increasing to 2.01 in recipients older than 50). Hb levels were available on 84% of the requisitions, of which, 3% had Hb levels >12.0 g/dl. The average Hb was 7.2 g/dl but differed significantly between public and private sector (6.7 vs 8.05 g/dl; P < 0.0001). In both public and private facilities more units were given at lower Hb levels decreasing steadily as Hb increased. Overall, private facilities ordered more units for similar Hb levels than public facilities. By discipline, trauma departments issued the most units per event (2.36) followed by cardio-thoracic surgery (2.22). Medical departments used 30% of the blood with 1.88 units per transfusion event.
Summary/Conclusions: Overall, transfusion triggers in South Africa fall within the guidelines of restrictive transfusion practice. Transfusion practices in the public sector seems to be more aligned to restrictive protocols than in private sector but both sectors follow a scaled approach requesting fewer units at higher Hb levels with the exceptional high Hb levels probably relating to patients with specific risk factors. Having patient Hb information available to SANBS enables us to develop targeted strategies and is our first attempt to gain an understanding of patient blood management in South Africa.

P-708

PATIENT BLOOD MANAGEMENT STRATEGIES ASSOCIATED WITH REDUCED TRANSFUSION RATES IN ELECTIVE ORTHOPAEDIC SURGICAL PATIENTS

L Pickles[1], C Akers[1], J Burke[2], C Plunkett[3], S Liew[3] and A Davis[1]

[1]Haematology [2]Anaesthetics [3]Orthopaedics, Alfred Health, Melbourne, Australia

Background: Patient blood management is an important part of patient care with the intention of improving patient outcomes. The Alfred Hospital is a major tertiary referral hospital in Metropolitan Melbourne, with one of Australia's busiest emergency and trauma centres and a variety of state-wide specialty services. In 2009 a

retrospective audit of transfusion in elective primary hip and knee arthroplasty was performed and provided a baseline for further auditing.
Aims: To implement patient blood management strategies in elective orthopaedic surgical patients to improve patient care by optimising pre-operative haemoglobin, minimising intra-operative blood loss and reducing unnecessary transfusion post-operatively.
Methods: The transfusion team worked with the orthopaedic and anaesthetic groups to develop a pre-operative haemoglobin optimisation algorithm to optimise patient's haemoglobin prior to surgery, mainly in regard to correction of iron deficiency. The algorithm was introduced in 2012 and is ongoing. Transfusion nurses collected 12 months of data from March 2012 and 36 months of data from 2015 – 2017. Over this time frame the algorithm was reviewed and modified in response to results from audits and changes in available guidelines to improve outcomes. For example, ferritin testing was routinely added for all patients to ensure we did not miss those patients who were iron deficient but not yet anaemic. The team has also provided information in the anaesthetic department Enhanced Recovery After Surgery (ERAS) pathway regarding the use of tranexamic acid and single unit transfusion policy.
Results: Baseline audit data in 2009 on 17 primary hip and 10 primary knee replacements showed transfusion rates of 30% (8/27). In 2012, post introduction of the algorithm, the transfusion rate remained at 35% (72/205). Post further refinements, including additions to ERAS and universal ferritin testing the transfusion rate dropped to 17% (32/184) in 2015. In 2017 the rate reduced further to 5% (11/204). During this time the use of tranexamic acid has increased from 42% in 2015 to 79% in 2017. The single unit transfusion rate has remained similar, 22% in 2015 and 18% in 2017. Follow up of patients after iron replacement and prior to surgery is currently not optimal, with few patients being retested. However, the majority of patients requiring transfusion are those with anaemia associated with other chronic diseases rather than those who were iron deficient.
Summary/Conclusions: Our patient blood management strategies have been associated with increased recognition and correction of pre-operative anaemia and iron deficiency in the orthopaedic surgery group. We have also noted an increased use of tranexamic acid peri-operatively along with significantly reduced transfusion rates over 5 years. Limitations of this data include its retrospective nature, incomplete compliance with the algorithm and the inability to attribute the reduction in transfusion rate to any particular blood management strategy. As a result of these positive findings, this approach has also been introduced to other major surgical groups. Ongoing audit and review is required in order to continue to improve patient blood management.

P-709

TRANSFUSIONS IN PEOPLE WITH HAEMATOLOGICAL MALIGNANCIES – RESULTS OF A REPEAT UK NATIONAL COMPARATIVE AUDIT WITH IMPROVEMENT IN PRACTICE

LJ Estcourt[1,2], M Karakantza[3], J Grant-Casey[1], D Lowe[4] and J Birchall[5]

[1]NHS Blood and Transplant [2]Radcliffe Department of Medicine, University of Oxford, Oxford [3]NHS Blood and Transplant, Leeds [4]Astraglobe Ltd, Congleton [5]Welsh Blood Service, Cardiff, United Kingdom

Background: Red cell and platelet transfusions are essential in the management of people with haematological malignancies and bone marrow failure disorders. Up to 65% of platelet components and 25% of red cell components issued are given to haematology patients, and most are used in the elderly. As the UK population is ageing, with a predicted doubling in people aged 85 years by 2041, only using red cell and platelet transfusion to those likely to benefit is imperative to minimise side effects, limit costs, and maintain the blood supply.
Aims: The aim of this national audit was to identify areas where practice has improved compared to the audit in 2016, and to identify areas that require further improvement.
Methods: All hospitals in UK were invited to participate in these audits of red cell and platelet transfusions in adults (≥16 years) with haematological malignancies or a myeloid failure disorder. The initial audit was undertaken in January 2016 and assessed the use of platelets and red cells against nationally agreed standards. Following feedback of results to all participating hospitals a repeat audit was performed in July 2017.
Patients with chronic anaemia were excluded from red blood cell (RBC) transfusion standards which used a haemoglobin threshold alone, as this group may require an individualised transfusion threshold.
Results: A total of 153 hospitals from the UK participated in the 2017 audit and provided information on 1553 platelet transfusions and 3830 RBC transfusions. 148 hospitals also participated in the 2016 audit.

The majority of patients included in this audit were over sixty years of age (median 73 years). Myelodysplasia, largely a disease of older people, was the commonest haematological diagnosis (29.7%).

Chronic anaemia was the commonest reason for a RBC transfusion (58%; 2187/ 3780). Most platelet transfusions were prophylactic (79%, 1223/1553), and within this group 50% were given to patients with chronic bone marrow failure. An additional 9% (138/1553) were given to prevent bleeding prior to a procedure.

When comparing practice for the 148 hospitals participating in both audit rounds, there has been an improvement in the use of a restrictive red cell transfusion policy (Hb 70 g/l and no additional risk factors) from 19% to 24% (P = 0.004). There was an increase in the use of a single unit RBC transfusion approach in inpatients (37% to 50%; P < 0.001) and outpatients (13% to 24%; P < 0.001). Despite only 12% of inpatients having an Hb measured when they received >1 RBC unit.

76% of prophylactic platelet transfusions were considered appropriate in reversible bone marrow failure, compared to 72% (459/638) in 2016 (P < 0.001). 94% (1144/ 1218) of prophylactic platelet transfusions were single unit transfusions, compared to 93% (1277/1379) in 2016.

Summary/Conclusions: Overall, there has been an improvement in practice since 2016. This is particularly evident in areas where change in practice can be achieved more readily and where there have been national campaigns to improve practice, such as the single unit transfusion policy.

P-710

A STUDY OF BLOOD COMPONENT USE AND CLINICANS' KNOWLEDGE AND PERCEPTIONS OF TRANSFUSION AT A TERTIARY REFERRAL HOSPITAL IN GHANA

A Dhariwal[1], E Allotey[2], A Fisher[3,4] and I Bates[5]

[1]Haematology, St George's University Hospitals NHS Foundation Trust, London, United Kingdom [2]Haematology, University of Health and Allied Sciences, Ho, Ghana [3]Haematology, Leeds Teaching Hospitals Trust [4]Institute of Cancer and Pathology, University of Leeds, Leeds [5]International Public Health, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Background: Whilst blood transfusion remains a life-saving treatment in sub-Saharan Africa, difficulties with blood supply and safety persist. Many countries, including Ghana, have not reached the WHO-recommended target of 10 donations per 1000 population, and the background prevalence of transfusion-transmitted infections is higher than in more developed countries. In this context, the appropriate clinical use of blood components, supported by national guidelines, is vital.

Aims: We undertook a study to assess the compliance of clinicians with the National Blood Service of Ghana (NBSG) guidelines for the clinical use of blood components at a tertiary referral hospital in Ghana, and to assess clinicians' knowledge and perceptions of transfusion, in order to identify any potential areas for intervention to improve the clinical use of blood components.

Methods: Retrospective data were collected for patients at Volta Regional Hospital who had been transfused between 1st Sept and 30th Nov 2017 from the blood bank, patient folders, and electronic record. Using the guidelines, a checklist to assess appropriateness of each transfusion was devised in collaboration with NBSG. Based on interviews with clinicians, a questionnaire was devised to assess clinicians' knowledge and perceptions of transfusion.

Results: Data were gathered for 313 transfusions in 232 patients. 162 of 313 transfusions (52%) were appropriate, and 136 were not appropriate (43%.) In 15 episodes, appropriateness was unknown (5%.)

About 144 of 282 transfusions of whole blood/ packed cells were appropriate (51%), and 126 were not appropriate (45%.) In 12 episodes, appropriateness was unknown (4%.) Of the 31 FFP transfusions, 27 (87%) were not appropriate, and 16 (52%) were used for unrecognised indications including hypoalbuminaemia.

The 44/50 questionnaire responses (response rate 88%) were received. Respondents indicated they felt knowledgeable about the indications and complications of transfusion, and felt confident making transfusion decisions. However, significant gaps in knowledge were identified. Respondents provided haemoglobin thresholds for transfusion that differed from the NBSG guidelines, with a large range of individual variation. 48% of respondents listed incorrect indications for FFP, and only 2 of 44 (5%) of respondents were familiar with the NBSG guidelines.

Summary/Conclusions: In conclusion, 43% of transfusions within the 3-month period were not appropriate. Whilst confident in the clinical use of transfusion, most clinicians were unaware of the national guidelines and gaps in knowledge relative to the national guidelines were identified. Efforts to optimise appropriate use of blood components should be one component of a national strategy to improve the safety and availability of blood transfusion in Ghana. Increased development of hospital-based transfusion committees and targeted education to clinicians may have a role in supporting these efforts.

P-711

AGE OF BLOOD DOES NOT IMPACT OF THE FREQUENCY OF BLOOD TRANSFUSION IN MYELODYSPLASTIC SYNDROME

P Crispin[1,2,3], M D'Souza[1] and J D'Rozario[1]

[1]Haematology, Canberra Hospital, Woden [2]John Curtin School of Medical Research [3]Medical School, Australian National University, Canberra, Australia

Background: Stored blood deteriorates with age. Recent studies have verified the safety of blood stored for longer periods compared with fresh blood. Older blood is known to have reduced post transfusion red cell recovery following transfusion.

Aims: To assess the effect of red cell storage duration on post transfusion haemoglobin increments and transfusion intervals in myelodysplastic syndromes (MDS).

Methods: Patients with MDS who had transfusions between 1995 and 2012 were identified from the hospital pathology database. Data on transfusions and haemoglobin levels prior and subsequent to transfusion were collated. A transfusion episode was considered to be all units transfused on consecutive days. A pre-transfusion haemoglobin was defined as the lowest reading on the day of or the day prior to transfusion and a post transfusion haemoglobin as the first haemoglobin reading after the transfusion, provided it was within one week. The inter-transfusion interval was defined as the time between the start of two consecutive transfusion intervals. Blood was considered old if any of the units transfused in a transfusion episode were more than 14 days from collection. Further sensitivity analysis was conducted evaluating transfusions with only fresh (14 days or less from storage) and old red cell units.

The effect of age on post transfusion haemoglobin and transfusion in intervals was analysed using a linear mixed model in SPSS V20 (IBM). ANOVA was used in subsets with fixed inter-transfusion intervals. Results were considered statistically significant with P < 0.05.

Results: There were 130 MDS patients evaluated, receiving 1629 transfusions, with a mean age of 66 years and 78% male. Red cells were a mean of 16 days (range 1– 42) old at the time of transfusion. The post transfusion haemoglobin increment was 9.23 g/l per unit, and did not differ between fresh (8.8 g/l) and old (9.7 g/l) blood (P = 0.23). Inter-transfusion intervals were 20 days and 19 days for fresh and old blood respectively (P = 0.26). There was no difference in secondary analysis when transfusion episodes with only old or only fresh units were compared for haemoglobin increment per unit red cells or inter-transfusion intervals.

Summary/Conclusions: Red cells stored for longer than 14 days prior to transfusion were comparable in terms of haemoglobin responses and the intervals between transfusions to fresh red cells.

P-712

BLOOD TRANSFUSION REQUIREMENT AFTER ALLOGENEIC BONE MARROW TRANSPLANTATION: RISK INDICATORS

TM De Luca, L Lopez, M Szelagowski, S Yantorno, J Napal and J Milone
Hospital Italiano de La Plata, La Plata, Argentina

Background: Allogeneic Bone Marrow Transplant is a useful alternative for many patients (pts) with hematological diseases, but it is associated with high morbidity and mortality. There are different risk factors involved such as age, comorbidities, HLA disparity, disease status, conditioning intensity, high risk malignancy, pre-transplant anemia etc. In addition, patients with a poor evolution usually fall into a high consumption of transfusions, then it is important to know if these indicators are related to the consumption of blood components during the post-transplant period.

Aims: To analyze blood transfusion consumption in relation to different risk indicators.

Methods: We analyzed 103 medical records of transplanted pts between 2011 and 2017. They were divided according to Pre-transplant Hemoglobin (ptHb) (<10 mg/dl vs > 10 mg/dl), disease status (CR vs noCR), Score HCT-CI (Low vs Intermediate/ High), Conditioning (MAC vs RIC), kind of donor (Histoidentical vs Haploidentical vs Unrelated), ABO incompatibility (Major vs no Major), Age (<40 vs > 40) and according to Disease Risk Index - DRI (Low/Intermediate vs High/Very High).

The blood transfusion requirement was analyzed in 3 consecutive periods of 60 days (0–60, 60–120, 120–180 and global) comparing the different groups by a multivariate analysis using a multiple regression test.

Results: We evaluated 103 pts, with a mean age of 37 years (16–68), 52 women. According to their pathology, pts were: AML 32 (31%), ALL 28 (27%), MDS 6 (6%), NHL 3 (3%), HL 14 (13%%), MCL 10 (10%), MF 4 (4%%), AA 6 (6%).

Multivariate analysis showed that the difference between pts divided according to ptHb as significant when analyzing the transfusion requirement in the periods 0–60, 60–120 and global. The mean transfusion blood units for pts with <10 mg/dl was 9.1 in the 1st period, 4.6 in the 2nd, 3.1 in the 3rd, and 12.8 in the global. And for pts with >10 mg/dl it was 3.7 in the 1st, 1.3 in the 2nd, 1.0 in the 3rd, and 8.6 in the global (P = 0.0001, P = 0.03, P = 0.19, and P = 0.0026). In addition, age was also significant in the 0–60 period, with a mean transfusion of 5.1 for pts under 40 and 6.3 for those over 40 (P = 0.02). The other variables were not significant in any period.

Summary/Conclusions: The variables that are associated with morbi-mortality in the allogeneic transplant setting are known; however, not all of them seem to be related to the blood transfusion requirement.

In our experience, ptHb was an independent risk factor for blood transfusion requirement during a period of 6 months post-transplant, with a 10 mg/dl cut-off point. Age had an impact in the first 2 months.

P-713

Abstract has been withdrawn

P-714

IMPACT OF ROTATIONAL THROMBOELASTOMETRY (ROTEM®) ON BLOOD PRODUCT UTILIZATION IN A CARDIAC SURGERY PROGRAM – IMPLICATIONS FOR THE MANUFACTURER?

J Trudeau[1], L Sham[2] and T Petraszko[3]

[1]*Anesthesiology and Perioperative Care, Vancouver General Hospital, Vancouver, BC* [2]*Transfusion Medicine, Vancouver General Hospital* [3]*Canadian Blood Services BC/Y, Vancouver, Canada*

Background: Bleeding management in cardiac surgery remains challenging. Rotational thromboelastometry (ROTEM®) is a whole blood coagulation test that has been introduced into many cardiac surgery programs in attempt to improve blood product utilization.

Aims: We undertook a retrospective review of blood utilization during two distinct time periods when ROTEM was used at our institution in cardiac surgery. We hypothesized that the use of ROTEM would be associated with fewer red cell and plasma transfusions.

Methods: Blood product utilization was retrospectively analyzed during 4 time periods: T1: Nov 1, 2013 – Nov 2, 2014 = A one year time frame prior to ROTEM testing in the operating room; n = 767; T2: Nov 3, 2014 – May 1, 2015 = A 6 month trial of ROTEM testing and a point of care (POC) platelet function test (Plateletworks®); n = 377; T3: May 2, 2015 – Nov 1, 2016 = An 18 month period with no POC testing available; n = 1077; T4: Nov 2, 2016 – Nov 1, 2017 = A one year period with re-introduction of ROTEM (no Plateletworks®); n = 623. During T2, patients were managed according to a published transfusion algorithm. During T4, ROTEM-guided bleeding management guidelines were provided, but treatment was at the discretion of the treating anesthesiologist. For the purpose of analysis, patients were allocated to high risk cardiac (combined CABG and valve, multiple valve, aortic or redo surgery), n = 1046; or low risk cardiac (CABG, single valve, or minimally invasive surgery), n = 1798.

Results: For both high risk and low risk cardiac surgery, time frames during which ROTEM was used were associated with significantly less frozen plasma (FP) use (intraoperative FP use from T1 to T4 = 0.91 vs 0.26 units, p

Summary/Conclusions: At our institution, time frames that included ROTEM use were associated with a significant increase in fibrinogen replacement and decreased use of FP in both low and high risk cardiac surgery. Red cell use decreased in the low risk cardiac surgery group. ROTEM use was associated with fewer large volume intraoperative resuscitations (≥6 red cells), potentially reflected in decreased factor VIIa use. From a supplier perspective, it is clear that ROTEM guided transfusion results in a significant practice change toward more use of fibrinogen replacement. It remains unclear whether this change in practice had a positive impact on patients.

P-715

A CLINICAL AUDIT OF PLATELET TRANSFUSION PRACTICES IN CHRONIC LIVER DISEASE PATIENTS IN A TERTIARY CARE HOSPITAL IN NORTHERN INDIA

B Kakkar and M Bajpai

Transfusion Medicine, Institute of Liver and Biliary Sciences, New Delhi, India

Background: Patients with chronic liver disease (CLD) have a high risk of bleeding due to underlying coagulopathy and thrombocytopenia. These patients require transfusion support for various therapeutic and prophylactic indications.

Aims: The aim of our study was to perform a clinical audit of platelet transfusion practices in chronic liver disease (CLD),patients admitted in our hospital and to compare the current platelet transfusion practices against the British Society of Haematology (BSH) guidelines for platelet transfusion.

Methods: A retrospective three-month audit of platelet transfusion practices was conducted from July 2017 to September 2017 in CLD patients. All the platelet transfusion requests received during the study period were retrieved and reviewed. The records were evaluated to determine the total number of transfusion requests received, indications for transfusion and their transfusion triggers followed by comparison with the standard guidelines.

Results: During the study period, a total of 603 platelet transfusion requests were received for 285 patients (240 males, 84.2%; 45 females, 15.6%; age range 3 months to 80 years). Of these 285 patients, 39.6% (113/285) patients received repeated transfusions. Maximum number of requests were received from the liver intensive care unit (26.3%) followed by emergency services (16.5%) and high dependency unit (15.1%).

Around 76.8% of the requests received were for prophylactic transfusion (mean platelet count - $49 \times 10^3/\mu l$), while 19.4% were for therapeutic transfusion (mean platelet count - $32 \times 10^3/\mu l$). The most common indication for transfusion was thrombocytopenia (36.3%), followed by active bleeding (19.2%) and correction of coagulopathy based on thromboelastography (14.6%). On comparing the transfusion triggers with the BSH guidelines, the percentage of inappropriate transfusions for patients with thrombocytopenia, active bleeding and correction of coagulopathy were 71%, 19% and 70%, respectively.

Summary/Conclusions: Chronic liver disease patients are known to have thrombocytopenia as well as platelet function defects. High rate of non-compliance was seen in platelet transfusions given to our patients. Due to lack of standard guidelines for platelet transfusion in CLD patients, the current guidelines for transfusion thresholds may not be suitable in them. Therefore, there is wide scope of research to develop guidelines for appropriate use of platelet transfusions in these patients.

P-716

PATIENT BLOOD MANAGEMENT IN SURGERY – RESULTS OF A REPEAT UK NATIONAL COMPARATIVE AUDIT WITH IMPROVEMENT IN PRACTICE

S Allard[1,2], K Pendry[3], T Richards[4], J Grant-Casey[5], D Lowe[6], D Highton[7] and A Kotze[8]

[1]*NHS Blood and Transplant* [2]*Barts Health NHS Trust, London* [3]*NHS Blood and Transplant, Manchester* [4]*University College Hospital, London* [5]*NHS Blood and Transplant, Oxford* [6]*Astraglobe Ltd* [7]*National Hospital for Neurology & Neurosurgery, London* [8]*The Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Patient Blood Management (PBM) is an evidence based patient centred approach to transfusion practice with emphasis on active anaemia management, minimisation of blood loss and appropriate blood use.

Aims: We repeated a large national comparative audit in 2016 to assess improvements in PBM practice from a previous audit in 2015.

Methods: The initial audit was undertaken over a 3mth period between Feb and April 2015 assessing practice in the application of pre-operative, intra-operative and post-operative PBM measures in a range of surgical patients likely to need transfusion. Following feedback of results to all participating hospitals a repeat audit was undertaken over a further 3mth period between Sep and Nov 2016.

Results: Data on 3266 cases were available for analysis, submitted by 156 sites across the UK. 138 of these sites also took part in the 2015 audit with 3105 cases in round 1 and 2950 cases in round 2. The commonest type of surgery in both audits was elective orthopaedics surgery followed by surgery for fractured neck of femur and then cardiac surgery.

Overall, there has been an improvement in PBM practice since 2015. This is particularly evident in areas where change in practice can be achieved more readily. When comparing practice for the 138 sites participating in both rounds, there has been an

improvement in the use of a restrictive approach to postoperative transfusion from 23% to 34% (P < 0.001) and an increase in the use of a single unit transfusion approach post-operatively from 37% to 50% (P < 0.001). Tranexamic Acid use has increased from 32% to 42% (P < 0.001). In contrast, there has been a smaller, although still significant (P = 0.01), improvement in the management of pre-operative anaemia with the relative proportion managed appropriately improving to 50% in 2016 compared to 46% in 2015.

Overall, only 11% of patients receiving a post-operative transfusion were found to have had all appropriate PBM measures attempted in 2016, compared to 7.5% in 2015 (P = 0.002).

Summary/Conclusions: Key barriers that need to be overcome include adequate resources to support the infrastructure to deliver effective management and a restructuring of the pre-operative pathway to allow for timely investigation and management. There are also difficulties in resolving the roles of primary and secondary care in pre-operative optimisation of anaemia, and within secondary care in setting up services to manage patients effectively.

It is encouraging to see that there has been progress in the implementation of PBM since 2015, particularly in areas highlighted in NICE Clinical Transfusion Guidelines and Quality Standards. Further work is required to deliver timely pre-operative anaemia management in particular and to ensure consistent implementation of all appropriate PBM measures.

P-717
A PILOT NATIONAL AUDIT ON PATIENT BLOOD MANAGEMENT

A Ang[1,2], N Chia[3], S Lee[4], E Lew[5], B Ng[6], L Ng[7], S Tan[8], S Tien[1] and J Chay[2]
[1]Haematology, Singapore General Hospital [2]Blood Services Group, Health Sciences Authority [3]Anaesthesia, Khoo Teck Puat Hospital [4]Laboratory Medicine, National University Hospital [5]Anaesthesia, KK Women's and Children's Hospital [6]Anaesthesia, Ng Teng Fong General Hospital [7]Anaesthsia, Changi General Hospital [8]Anaesthesia, Tan Tock Seng Hospital, Singapore, Singapore

Background: Blood Services Group (BSG) serves as Singapore's national blood service, and had been actively promoting patient blood management (PBM) implementation in all public hospitals since 2016. This was endorsed by the hospitals' Senior Management and Transfusion Committees (HTCs). A series of measures were undertaken nationwide to facilitate PBM implementation, including the distribution of PBM-related recommendations, conducting educational talks and increasing the awareness via lectures and discussions held by an international PBM expert. It was also agreed that from 2016 onwards, all public hospitals would participate in an annual national audit coordinated by BSG to benchmark their efforts in implementing PBM, with the purpose of encouraging improvements and sharing of good practices.

Aims: The first national PBM audit was carried out as a pilot in 2016, and its findings are presented here.

Methods: As early as 2013, a consensus was reached among BSG and the public hospitals on the selection of 2 PBM performance measures for the national audit: 1) percentage compliance to the documentation of clinical indications for RBC prior to transfusions; 2) percentage compliance to pre-operative anaemia screen 14 to 45 days before pre-selected elective surgeries. Performance measure 1) was selected to encourage appropriate RBC transfusion. Performance measure 2) was chosen to promote improvements in pre-operative anaemia screening and management. The pilot audit was conducted retrospectively covering a 2-week period from 3 to 16 Oct 2016, with the data being self-reported by the hospitals. BSG analysed the data and surveyed the hospitals for their relevant PBM initiatives, and shared the audit outcome and good practices with all the hospitals' Senior Management and HTCs.

Results: 7 public acute care hospitals with 550 to 1700 beds (including 2 tertiary and 1 specialty hospitals) participated in the pilot audit. The compliance for performance measure 1) ranged widely from 60 to 100% (median 86%), and 1 hospital did not submit data as they were unable to retrieve data for this audit. Hospitals which incorporated mandatory indications in their electronic transfusion orders had better compliance. The variations were likely also due to differences in data collection methods as documentation in case notes might not be captured. Hospitals were encouraged to incorporate indications as mandatory fields in their electronic transfusion orders, and to include decision-support systems to guide appropriate transfusions. The compliance for performance measure 2) also ranged widely from 56% to 100% (median 80%), and 1 hospital submitted an alternative metric: 76% of their patients who received perioperative transfusions had proper preoperative anaemia screening and management. Hospitals with established preoperative anaemia screening and management workflow had better compliance, and good practices from one

hospital were shared with the rest. Hospitals were advised to establish such workflows and to postpone non-urgent surgeries for proper evaluation and treatment of reversible causes for anaemic patients.

Summary/Conclusions: It is feasible to conduct a national PBM audit which is useful for the nationwide promotion and benchmarking of efforts in PBM implementation. We will continue with the national audit annually and include perioperative RBC transfusion rates for selected major surgeries in future audits.

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KNOWLEDGE, ATTITUDE AND PRACTICE OF PATIENT BLOOD MANAGEMENT AMONG SURGICAL AND OBSTETRIC MEDICAL OFFICERS IN COLOMBO, SRI LANKA

M Krishnapillai[1] and S Jayasekara[2]
[1]National Blood Centre, Colombo, Sri Lanka [2]National Blood Transfusion Service, National Blood Centre, Colombo, Sri Lanka

Background: Patient blood management has become one of the widely discussed topics of transfusion medicine. Establishment of patient blood management minimizes the unnecessary transfusions and related complications and ensures good clinical practice. While the transfusion practitioners highlight the importance of patient blood management, it depends on the clinicians to actively implement the concepts of patient blood management clinically.

Aims: The aim was to assess the level of knowledge, attitudes and practice of surgical and obstetric medical officers on patient blood management.

Methods: A cross sectional descriptive study was conducted at the National Hospital and De Soysa Maternity Hospital, Colombo, Sri Lanka among 136 medical officers working in the Surgical, and Obstetric wards. Data was collected from self administered structured questionnaire and statistically analyzed with the SPSS software and Microsoft Excel.

Results: Among the 136 participants, only 4.41% (6) of them did not appreciate the correlation between anemias diagnosed preoperatively and related perioperative morbidity and mortality. 62.5% (85) of the clinicians considered blood transfusion as an option to treat preoperative anemia in elective surgeries. While analyzing the knowledge on treating deficiency anemia, 58.8% (80) suggested blood transfusion as a treatment modality. 38.9% (53) of them suggested that blood transfusion is necessary in treating deficiency anemia if it was detected a few days before surgery. While analyzing the triggers for red cell transfusion, 47.01% (54) of them suggested transfusion for patients about to undergo elective surgeries with hemoglobin level of 9 g/dl.

When questioned about transfusing patients with a hemoglobin level of 6 g/dl, 67.6% (92) of them did not appreciate single unit transfusion and reassessing the hemoglobin level before transfusing another unit. Among the whole study population, 69.1% (94) agreed that they did not have adequate knowledge about patient blood management and 90.4% (123) liked to learn more on patient blood management.

Summary/Conclusions: Patient blood management seemed to be relatively a new topic for most of the medical officers. Majority agreed with their inadequacy of knowledge on this subject. It's important to implement methods to educate the clinicians on patient blood management in order to improve the transfusion practice and patient outcome.

P-719
FRESH FROZEN PLASMA STORAGE DURATION ASSOCIATED WITH SMALL INCREASED IN-HOPSITAL MORTALITY RISK

MS Ng[1,2], K Hay[3], R Middelburg[4], J Suen[1], J Tung[2] and J Fraser[1]
[1]Critical Care Research Group, Faculty of Medicine, University of Queensland [2]Research and Development, Australian Red Cross Blood Service [3]QIMR Berghofer Medical Research Institute, Brisbane, Australia [4]Centre for Clinical Transfusion Research, Sanquin Research, Leiden, Netherlands

Background: Storage-induced changes in fresh frozen plasma (FFP) have been posited to lead to decreased transfusion efficacy and safety. To date, the effects of FFP storage duration on mortality has only been investigated in one study of cardiac surgery patients (Van Straten, J Thorac Cardiovasc Surg, 2011).

Aims: This study aimed to determine the relationship between FFP storage duration and in-hospital mortality.

Methods: Secondary analyses were conducted on patient level data previously collected for an individual meta-analysis studying the effects of packed red blood cell storage duration. Studies reporting FFP storage duration were included in the analysis. Two-stage meta-analyses were performed to derive pooled effect estimates of FFP storage duration on mortality. Patient-level mixed effects logistic regression models were also fitted. Models were adjusted for age, gender and volume of FFP transfused.

Results: The FFP storage duration analysis included 3625 patients across 4 studies, conducted in orthopaedic surgery, acute medicine, intensive care and cardiac surgery patients. Each additional month of FFP storage was associated with a small enhanced risk of in-hospital mortality (OR 1.05, 95% CI 1.01–1.08, P = 0.01). Effect estimates from the patient-level mixed effects model were consistent, but did not remain significant at the 5% level (OR 1.03, 95% CI 1.00–1.06; P = 0.09).

Summary/Conclusions: This study updates existing information on the clinical FFP storage duration effects by including a wide range of patient subtypes. There was an increased risk of in-hospital mortality with longer storage of FFPs. Before considering FFP shelf life alterations, further investigation is warranted to address potential confounding factors such as patient subgroup, country and recruitment year.

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HOME BASED SCIG (SUBCUTANEOUS IMMUNE GLOBULIN) PROGRAM IMPROVES QUALITY OF LIFE, MEDICAL MANAGEMENT AND HEALTH ECONOMY OUTCOMES FOR CHRONIC IVIG (INTRAVENOUS IMMUNE GLOBULIN) USERS

S Zolfaghari, J Hendry, J McCarthy and M Shabani-Rad

Department of Pathology and Laboratory Medicine, Calgary Laboratory Services/University of Calgary, Calgary, Canada

Background: Home-based SCIG administration is increasingly becoming more popular among chronic IVIG users. Therefore, it is very important to ensure that this alternative route is as effective as IVIG therapy especially for patients, who receive the higher doses of this product as immunomodulatory therapeutic modality. Although both IVIG and SCIG therapy are approved in the treatment of primary and secondary immunodeficiencies (PID and SID respectively), the use of SCIG as alternative route instead of IVIG is under debate for neuromuscular disorders.

Aims: Our goal was the assessment of clinical outcomes, patient satisfaction and cost effectiveness of SCIG among patients requiring immune globulin therapy for replacement and immunomodulatory treatments.

Methods: This study is an observational retrospective study conducted in Calgary Zone (CZ) through CLS's SCIG program. Adult chronic IVIG user patients who were interested in SCIG program referred to this program by their attending physicians following criteria had been approved by CZ IVIG advisory group in 2015. All patients were also reviewed by CLS medical team for informed consent, medical and physical eligibility. Patients with PID and SID were accepted to SCIG program after completion of immune deficiency work-up completed by immune deficiency experts. Non-immune deficient patients should have had medical reasons for referral to SCIG program; loss of IV access, history of severe headaches/aseptic meningitis or continuous hemolysis with IVIG. All patients' clinical information was entered into IVIG/SCIG database which used for analysis. A survey was developed by TM team to assess the patients' satisfaction after being in the program for 3 months. Cost advantages were calculated based on Daymed clinic encounters when patients getting IVIG.

Results: The SCIG clinic received 119 referrals from September 2015 to December 2017. The eligible cases (n = 111) included 50 PID, 35 SID and 26 neuromuscular patients. PID patients mainly included Common Variable Immunodeficiency patients (CVID); n = 41 (82%). Patients with SID (32% of SCIG patients) included the ones who has developed humoral immune deficiency due to the treatment of underlying lymphoma/leukemia, multiple myeloma or SCTs (Stem Cell Transplants). The majority of neuromuscular SCIG patients (23% of total Pts) included Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Multifocal Motor Neuropathy (MMN) and Myasthenia Gravis (MG). Seven out of 8 dropped out patients were from neuromuscular group. Patient survey revealed 92% satisfaction rate and expression of positive impact in the quality of patients' life. In addition, shift of 111 patients from Daymed IVIG clinics toward of home-based SCIG program came with estimated annual cost saving of $670,000 as well as opening of more outpatient spots for others required care.

Summary/Conclusions: This study confirmed that patients with PID and SID benefit from SCIG therapy, allowing patients a better medical management by providing steady IgG levels and significant improvements in life quality and job security. Moreover, SCIG seems to be a reasonable alternative for neuromuscular patients suffering from IVIG's medical complications. Economic savings could easily compensate and justify the operational expense for the program.

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MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE (MSBOS) AT A TERTIARY CARE ONCOLOGY HOSPITAL IN INDIA

AM Gupta[1], A Tendulkar[2] and P Waghmare[1]

[1]Department of Transfusion Medicine, Tata Memorial Hospital [2]Department of Transfusion Medicine, Tata Memorial Centre, Mumbai, India

Background: Despite over 11 million blood donations in India, blood is still in short supply. Blood transfusion services are challenged to maintain a fine balance between the supply of this limited resource and an ever-increasing demand. Blood ordering before surgery is clearly excessive. The most important policy to reduce this over ordering is the 'Type and Screen' (T & S) whereby units are not cross matched until an actual need for transfusion occurs. Another policy is MSBOS which is an institution-specific list of the most commonly performed surgical procedures that suggest the extent of pre-transfusion testing to be performed before the case begins. Many International and national guidelines are available for the MSBOS, but there is paucity of data for oncology patients. Therefore a revised MSBOS is required exclusively for oncology patients.

Aims: *Primary aim*: Revising MSBOS at our institute.
Secondary aims: 1. Predicting transfusion requirements in their respective surgical disciplines. 2. Evaluate the crossmatch to transfusion ratio (C/T) ratio.

Methods: Retrospective data was retrieved and analyzed to assess transfusion requirements and pre-operative blood cross-match requisitions in surgical patients. Data from 03/07/2015 to 31/07/2016 was evaluated. Patients less than 18 years of age were excluded. Each surgical procedure was grouped into different procedure categories determined by surgical subspecialty and relevant anatomical operative site. A detailed data was collected with respect to age, gender, organ and type of surgery, pre-operative blood orders, Hb prior to and after surgery, pre-intra-post-operative requirement of RBC transfusion, FFP (fresh frozen plasma) and platelet transfusion.

Results: A total of 6,664 surgical events were studied but 659 surgeries got postponed or cancelled leaving 6,005 surgical events for analysis. A total of 14,934 RBC units were cross-matched before the surgeries but only 2,262 RBC units were transfused giving a very high C/T ratio of 6.6. Nearly 200 surgeries have been studied with respect to C/T ratio, Transfusion probability, Transfusion Index and various other parameters. A revised MSBOS has been proposed for optimum utilization of blood services.

Summary/Conclusions: An algorithm has been formulated which can guide preoperative blood ordering for any oncology surgical procedure. Implementing an updated, institution-specific MSBOS has substantial advantages that include (1) decreasing the number of pre-operative blood orders considered to be unnecessary, (2) reducing the C/T ratio, and (3) decreasing overall costs without evidence of impact on patient safety. Implementation of the recommended MSBOS is a safe, effective and financially beneficial strategy.

P-722

THE ROLE OF STEROID PREMEDICATION ON ADVERSE TRANSFUSION REACTIONS IN THE OUTPATIENTS: TO USE OR NOT?

C Chang[1,2], T Lee[1,2] and F Chu[1,2]

[1]Department of Clinical Pathology, Far Eastern Memorial Hospital [2]Taiwan Society of Blood Transfusion, New Taipei City, Taiwan, China

Background: Despite accumulating investigations were conducted, premedication before transfusion remains controversial to prevent adverse transfusion reactions (ATRs). And there is lack of evidence concerning the efficacy of steroid premedication on prevention of ATRs.

Aims: To investigate whether premedication use of steroids prevents outpatients from having ATRs.

Methods: From May to December 2017, outpatients with transfusion were registered. Clinical data were retrospectively obtained for chi-square test and multivariate regression analysis, including disease categorizations, premedications and the presence of ATRs. A P value less than 0.05 was statistically significant.

Results: During the study interval, a total of 2,295 blood units were transfused in 404 outpatients with 1,062 transfusion events. Of these, transfusions were mostly prescribed by the hema-oncologist (81.0%), followed by the nephrologist (9.3%) and gynecologist (6.1%). The overall premedication rate was 92.4%, including the use of antipyretics (16.5%), antihistamines (68.4%) and steroids (34.3%). The most common used regimen of premedication was diphenhydramine only (43.5%), followed by the steroid only (22.7%) and acetaminophen plus diphenhydramine (13.7%). Eleven ATRs were reported, including 8 febrile non-hemolytic transfusion reactions (FNHTRs) and 3 minor allergic reactions. Univariate and multivariate regression analyses revealed that there was no statistical significance concerning premedication of acetaminophen (P = 0.995) or diphenhydramine (P = 0.930) before in prevention of ATRs in the outpatients. Furthermore, premedication of hydrocortisone may decrease the risk of developing ATRs in the outpatients, but there was no statistical significance (OR: 0.690, 95% CI: 0.143–3.322, P = 0.643).

Summary/Conclusions: It seemed that steroid premedication was not significantly efficacious in preventing ATRs in the outpatients. Prospective studies are warranted for further research and establishment of transfusion strategies in the future.

P-723

THE USE AND MISUSE OF PLATELET TRANSDUSION IN A REGIONAL HOSPITAL IN TAIWAN

J Chien[1], K Li[2], S Juang[3], T Zheng[1] and T Ho[4]

[1]Department of Laboratory Medicine [2]Department of Hematology and Oncology [3]Department of Research, Taichung Tzu-Chi Hospital, Buddhist Tzu Chi Medical Foundation [4]Department of Medical Laboratory Science and Biotechnology, Central Taiwan University of Science and Technology, Taichung, Taiwan, China

Background: Platelet transfusion is one of the major therapeutic support of thrombocytopenia. Every year approximately of 170,000 platelet concentration and 245,000 Apheresis Platelets/ Leukocyte-Reduced Apheresis Platelets(LRP) products are transfused in Taiwan and the transfusion numbers have been rising over past several years.

Aims: According to AABB guideline and recommendations, it was suggested prophylactic platelet transfusion with platelet count less than 50×10^9 cells/l in major elective neuraxial surgery and less than 10×10^9 cells/l to reduce the risk for spontaneous bleeding. This research was focused on the clinical platelet transfusion and to provide evidence for the appropriate use of platelet in the hospital.

Methods: A retrospective review of all patient who transfused with platelet components reported in Taichung Tzu-Chi Hospital. Total of 1604 patients was included in 2017 and total of 1162 platelet apheresis, 397 LRP and also 540 platelet concentrations were transfused. In our hospital, the physician required to document the reasons for blood transfusion. Group characteristics were compared using X^2 test. The multivariable logistic regression model was applied to estimate odds ratios and 95% CI for the incidence of transfusion reaction.

Results: In the total of 1604 patients who transfused platelet products, there was 427 (26.6%) individuals were hematology and oncology-related disease, followed by Chest disease 302 patients (18.8%). From our result, patient's platelet counts between $1–50 \times 10^9$ cells/l, 521 (53.0%) were transfused within 4 units and platelet counts between 100×10^9 cells/l, 188 (39.4%) were transfused within 4 units. However, Patient's platelet counts over 200×10^9 cells/l, 26 patients were also transfused with platelet products within 1–4 units without active bleeding. Those patients may not be necessary for platelet transfusion and may consider as overuse of platelets.

Summary/Conclusions: Early studies of spontaneous bleeding increased the bleeding risk significantly only at platelet counts below 5×10^9/l. A high proportion of platelet units were transfused prophylactically to reduce the risk of bleeding. However, platelet transfusion also associated with risk of transfusion reaction in thrombocytopenia patient. Although a good proportion of platelet transfusion was considered appropriate, there was still few misuse and overuse has to justify. Our results may help to reduce platelet inappropriate use and also improve transfusion quality.

P-724

MULTIFACETED PATIENT BLOOD MANAGEMENT MEASURES REDUCE RED CELL TRANSFUSION IN SURGERY

S Lee[1], N Binte Said[2], R Ho[1], G Singh[3], S Tang[4], R Sanjeeva[5], G Moshi[1], B Ng[5] and L Tan[1]

[1]Department of Laboratory Medicine [2]Department of Oncology Nursing [3]Department of Orthopaedic Surgery [4]Department of Surgery [5]Department of Anaesthesia, National University Hospital, Singapore, Singapore

Background: Patient Blood Management (PBM) is a multidisciplinary, evidence-based approach to optimizing the care of patients who might need a blood transfusion. National recommendations were instituted in the last several years, which all hospitals were encouraged to adopt.

Aims: This study aims to examine the impact of PBM implementation on red cell (RBC) transfusion rates in surgeries performed in a tertiary hospital.

Methods: Perioperative RBC transfusions rates (number of cases transfused/total number of cases x 100%) occurring between 3 days pre-operation to 3 days post-operation for six surgeries, coronary artery bypass grafting (CABG), total knee arthroplasty (TKA), total hip arthroplasty (THA), nephrectomy, colectomy and hysterectomy, were studied. Baseline transfusion rates before intensive implementation of PBM were measured in June 2016. Post-implementation transfusion rates were measured in a randomly selected two-month period in 2017. PBM planning phase occurred from 2014 and 2015, and these measures were intensively implemented from July 2016 onwards: (1) early pre-operative screening for anemia, (2) rapid access pre-operative anemia management clinic, (3) use of tranexamic acid when indicated, (4) use of Intraoperative Cell Salvage for high blood loss surgeries, (5) introducing reminders of evidence-based transfusion guidelines into the electronic ordering system at the time of RBC ordering, (6) hospital-wide audit of appropriateness of RBC transfusions. Extensive engagement with surgeons and anaesthetists occurred through talks and meetings to raise awareness of PBM. To measure the take up rate of PBM, two indicators were recorded: (i) proportion of patients whose pre-operative anemia was managed, (ii) mean pre-transfusion hemoglobin of post-operative transfusions as a surrogate of adoption of evidence-based transfusion thresholds.

Results: The number of surgeries in the baseline/post-implementation periods were 33/40 CABG, 26/48 TKA, 12/11 THA, 4/9 nephrectomies, 7/11 colectomies, 27/50 hysterectomies. Transfusion rates for CABG and THA were significantly lower post-implementation compared to baseline (CABG: 57.5 vs 87.9%, 95% CI of difference 9.74–47.36, P = 0.005; THA: 18.2 vs 66.7%, 95% CI of difference 8.08–71.97, P = 0.022). TKA, nephrectomies and hysterectomies all showed trends towards lower transfusion rates post-implementation compared to baseline, i.e. 2.1 vs 11.5%, 11.1 vs 25.0%, 6.0 vs 14.8%. Transfusion rate for colectomies increased from 14.3% to 36.4%, but sample size was small. All surgeries combined, the proportion whose pre-operative anemia was managed increased from baseline 6.1% to 50.0% post-implementation (95% CI of difference 24.48–58.73, P < 0.0001) and mean pre-transfusion hemoglobin decreased from baseline 8.4 g/dl to 7.8 g/dl post-implementation (95% CI of difference -0.59 ± 0.21, P = 0.0061). For CABG, these differences remained significant: proportion whose pre-operative anemia was managed increased (0% vs 35.7%; P = 0.015), while mean pre-transfusion hemoglobin decreased (8.4 g/dl vs 7.7 g/dl; P = 0.003) and mean number of RBC units transfused per transfused patient decreased (4.3 vs 3.3).

Summary/Conclusions: Implementation of multifaceted PBM is able to reduce transfusion rates across different types of surgery. Proportion of pre-operative anemia managed increased and mean pre-transfusion hemoglobin decreased, reflecting adoption of PBM measures. The next phase would focus on ensuring as many patients as possible are managed accordingly, and to study outcomes such as infection rates and resource utilization.

P-725

THE ABO INCOMPATIBILITY IN BONE MARROW ALLOGENEIC TRANSPLANT. RETROSPECTIVE ANALYSIS OF 91 PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

L Lopez, T De Luca, F Cillero, J Napal and J Milone

Hematologia, Hospital Italiano La Plata, La Plata, Argentina

Background: Bone marrow allogeneic transplantation is a well-known treatment for a wide variety of hematological diseases. During the post-transplant period, patients generally receive support through transfusions of blood components. A risk factor associated with the greater consumption of these, is the presence of incompatibility ABO between donor and recipient. In addition, in some studies, it has been related

to an increased risk of Graft-versus-Host Disease (GVHD), and a lower survival after transplantation. There are 3 types of ABO incompatibilities, each one is associated with different complications that occur during the post-transplant period, in addition to those already mentioned. In Major ABO incompatibility prevails Hemolytic Anemia, Pure Red Cell Aplasia, and the delay in the engraftment of red blood cells, neutrophils and platelets. In Minor ABO incompatibility, Hemolytic Anemia and Passenger Lymphocyte Syndrome. And in bidirectional ABO incompatibility, the combination of both.

Aims: To establish an association between the presence of ABO Incompatibility with the blood transfusion requirement of red blood cells, neutrophils engraftment and platelets, change of ABO group, incidence of GVHD and Global Survival, as well as reporting the occurrence of immunohematological complications.

Methods: A total of 91 clinical histories of patients undergoing allogeneic transplantation were analyzed between 2011 and 2017. They were divided into 3 groups according to their ABO incompatibility: Isogroup, Minor ABO and Major/Bidirectional ABO incompatibility. The blood transfusion requirement was analyzed for consecutive periods of 60 days (0–60, 60–120 and 120–180) and the groups were compared using a one-way analysis of variance (ANOVA). The same method was used to evaluate the change of ABO group, and the engraftment of neutrophils and platelets. The prevalence of acute and chronic GVHD was analyzed by the Chi-square test, and Global Survival was evaluated using Kaplan Meier curves by comparing the groups by log-rank test.

Results: Ninety-one patients were evaluated, with an average age of 36.5 years (16–62), 45 women. The patients according to their pathology were: AML 31 (34%), ALL 28 (30%), MCL 10 (11%), MDS 5 (6%), NHL 3 (4%), HL 14 (15%). The patients with Major/Bidirectional ABO incompatibility were 27 (31%) and patients with Minor ABO Incompatibility were 16 (17%). The median number of days until neutrophil engraftment was: 19.5 for isogroup, 17.5 for Minor ABO and 18 for Major ABO (p0,7). And of platelets was: 21 in Isogroup, 20 in Minor ABO and 21 in Major ABO (p0,32). The ABO group change was detected with a median of 65 days for Minor ABO and 83 for Major ABO (p0,9). The median of transfusion on the 1st period (0–60) was: 4.7 in Isogroup, 4.1 in Minor ABO, and 5.8 in Major ABO. On the 2nd period (60–120): 2.4 in Isogroup, 0.4 in Minor ABO, and 2.2 in Major ABO. And on the 3rd period (120–180): 1.5 in Isogroup, 0.3 in Minor ABO, and 1 in Major ABO (p0,9, p0,9, p0,5). The Global Survival at 12 months was 51% for Isogroup, 50% for Minor ABO and 58% for Major ABO (0,7), with a median follow-up of 12 months. A patient with AML who received a transplant with Major ABO incompatibility was diagnosed with Pure Red Cell Aplasia.

Summary/Conclusions: In our experience, the presence of the ABO incompatibility was not a factor that has an impact on the transfusion requirement, nor on the engraftment of neutrophils and platelets, nor on survival. In this series of patients we observed a higher prevalence of acute and chronic GVHD in patients transplanted with some ABO incompatibility (p ns).

P-726

Abstract has been withdrawn

P-727

BC PRIMARY IMMUNE DEFICIENCY WORKING GROUP – PROMOTING APPROPRIATE AND EVIDENCE-BASED USE OF IMMUNE GLOBULIN

P Danesin[1], D Morrison[2], K Dallas[3], A Beauchamp[1], S Darnel[1] and A Tavaszi[1]

[1]BC Provincial Blood Coordinating Office [2]Hematopathology, Children's and Women's Hospital [3]Hematopathology, St Paul's Hospital, Vancouver, Canada

Background: Immunoglobulins (IG) are expensive blood products made from pooled human plasma. IGs are globally in short supply, and Canada is one of the highest users of IG in the world. Utilization data from the BC Provincial Blood Coordinating Office (PBCO) Central Transfusion Registry (CTR) shows that IG use in BC had an 11% increase from fiscal year 2014/15 to 2015/16. Immunology comprises the largest speciality and accounts for 46% of Provincial IG use. The condition Primary Immune Deficiency Disease (PIDD) accounts for 64% of IG used for immunology patients and the growth of utilization year over year has been significant. To address increases and support optimal care, the PBCO established a PIDD Working Group (WG) in 2016. The WG consists of Immunologists, Hematopathologists, data analysts, technologists and other healthcare professionals.

Aims: To develop a PIDD Toolkit to provide standardized tools and resources to support physicians in managing care for PIDD patients. The tools include Diagnostic and Treatment algorithms which have proven to be key components to the success of the current BC Rheumatology and Neuromuscular Programs.

Methods: A comprehensive review of literature and CTR data for IG use in PIDD was done in collaboration with the WG. The WG identified gaps and opportunities in the current process to form the basis of the contents of the PIDD toolkit. Data analysis showed variations across regional, institutional and physician level in terms of the amount of IG prescribed to patients, despite Provincial IG Guidelines, which prompted the need for treatment and diagnostic algorithms to support general physicians to determine when to refer a suspected PIDD patient to an immunologist. The WG highlighted the importance of ensuring patient-centered care and early establishment of patient-centered goals and outcomes in the treatment process. A need for access to diphtheria, tetanus and pneumococcal antibody testing for accurate diagnosis was also identified. The WG collaborated with BC Centre for Disease Control (BCCDC) to expedite an approval process for diphtheria and tetanus testing and is working with the BC Clinical Support Services (BCCSS) to streamline the process for pneumococcal antibody testing.

Results: Development of a PIDD Toolkit; a Diagnostic Algorithm; a Treatment Algorithm; a Dosage Calculator; an Adjusted Dose Calculator; updated Provincial IG Utilization Recommendations; and easily accessible up to date References. Collaboration with BCCDC to obtain preapproved diphtheria and tetanus testing for all BC immunologists. Collaboration with BCCSS to establish an expedited process for pneumococcal antibody testing.

Summary/Conclusions: The PIDD Toolkit will be disseminated through the PIDD Working Group to the BC Society of Allergy and Immunology. Transfusion Medicine Services, Hematopathologists, and technical coordinators will receive the toolkit through BC stakeholder committees. The toolkit will be used to ensure accurate diagnosis of PIDD and appropriate treatment with IG. There will be ongoing re-evaluation of adoption and use of the current algorithms by ordering physicians through the regular review of CTR data and use of patient outcome evaluations. To provide timely and easily accessible access, the PBCO is developing a PIDD Toolkit App. The expected launch date is May 2018.

P-728

THE EPIDEMIOLOGY OF MULTIPLE BLOOD COMPONENT TRANSFUSION: A SYSTEMATIC REVIEW

I Perelman[1,2], S Khair[2], E Dermer[2], A Tinmouth[1,3], E Saidenberg[1,3] and D Fergusson[1,2]

[1]Clinical Epidemiology, Ottawa Hospital Research Institute [2]University of Ottawa [3]Ottawa Hospital, Ottawa, Canada

Background: Patient care and blood product allocation within the hospital can be optimized by better understanding the prevalence of patients that receive co-transfusions of multiple blood products (multi-transfusions), as well as the characteristics and outcomes of these multi-transfusion recipients. However, there is a lack of literature describing the epidemiology of multi-transfusion, as most studies concentrate on a particular blood product and its utilization.

Aims: The purpose of this systematic review was to describe the prevalence of multi-transfusion, and as a secondary objective, to determine any patient characteristics and outcomes associated with multi-transfusion.

Methods: The databases Medline, EMBASE, and the Cochrane Library of Systematic Reviews were searched. Observational cohort and cross-sectional studies of adult or pediatric hospital patients that reported on multi-transfusion incidence or prevalence, or on patient characteristics and outcomes associated with multi-transfusion, were included. A descriptive synthesis of studies was performed.

Results: A total of 37 studies were identified and included, of which 34 (92%) reported on multi-transfusion prevalence. It was found that multi-transfusion prevalence varied greatly by patient population and by the specific combination of blood products given in the multi-transfusion, but changed little over time. Multi-transfused patients included those with burns, cardiac surgery, liver transplant, cancer, infectious diseases, trauma, patients requiring massive blood transfusions, and ICU patients. Five studies found associations between multi-transfusion and adverse health outcomes for cardiac surgery and liver transplant patients; however, these findings are likely confounded by indication. The overall quality of evidence was very low, given a fair-to-poor individual study quality, inconsistent multi-transfusion estimates, and significant confounding by indication.

Summary/Conclusions: A knowledge of multi-transfusion trends and of multi-transfusion recipients is needed to help improve patient care and patient blood management. Physician awareness of the risks and benefits of multi-transfusion can help optimize transfusion decision-making, leading to appropriate transfusion practice

and avoidance of unnecessary transfusions. Our research showed that in certain patient groups, as many as 99% of patients are multi-transfused. Yet, little is really known about these patients. Further research is needed in several areas to gain a better understanding of the epidemiology of multi-transfusion, including more studies on multi-transfusion in hematologic cancer patients, and studies looking for patient characteristics that can better predict the need for multi-transfusion.

P-729

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P-730

VALUE OF CONTROL OF HEMOSTASIS SYSTEM IN ITT AND DISSEMINATED INTRAVASCULAR COAGULATION SYNDROME

BB Bakhovadinov[1] and G Ashurova[2]
[1]Raisa Gorbacheva Memorial Institute for Children Oncology, Hematology and Transplantation, St. Petersburg State Medical University, Saint Petersburg, Russian Federation [2]Dushanbe City Maternity Hospital N3, Dushanbe, Tajikistan

Background: There are disorders of hemostasis system in clinical practice that lead to bleedings menacing to life. Major bleedings in obstetric practice among 50% of women are caused by hemostasis disorders in the form of disseminated intravascular coagulation syndrome (DICS). In such cases the destiny of a patient depends on timely diagnostics of pathology of hemostasis system, and its effective treatment using modern programs of medicamental and infusion-transfusion therapy (ITT).
Aims: To identify and treat complications related to hemostasis system in acute massive bleedings and to identify ways to improve the ITT program performance.
Methods: We analyzed treatment results of 75 pregnant women with the acute massive bleedings connected to disturbances of hemostasis system. The duration of bleeding was ranged from 1.5 to 6 h. Most patients had serious post hemorrhagic anemia - hemoglobin of 55 ± 18 g/l (at an initial indicator of 116 g/l), erythrocytes $-1.7 \pm 0.3 \times 10^{12}$/l, hematocrit 16 ± 3.2%, number of thrombocytes made up $112 \pm 0.2 \times 10^9$/l. We observed elongation of blood coagulation by 13 ± 1.5 min to full coagulation, time of plasma recalcification 147 ± 12.7 s, activated partial thromboplastin time 69 ± 2.5 s, depressions prothrombin ratio72 ± 7.5%, thrombotest to II-III degrees, the fibrinogen maintenance of 0.9 ± 0.1 a g/l, rising retraction of a bloody clot 64.9 ± 9.1% and fibrinolytic activity was 27 ± 7.9% that all meant that patients had disseminated intravascular coagulation syndrome. The presence DICS was identified in 81.54% of observations. The principle of ITT meant the restoration of blood volume, organa a blood flow and restoration of deficiency of plasma procoagulants single- through transfusion of fresh frozen plasmas (FFP) in a dose of 25–30 ml/kg in a combination to saline solutions (a parity 1:2), a cryoprecipitate of 6 - 12 doses. Transfusion of FFP was carried out with a great speed to 1000 ml within 30 min. When necessary, we repeated the transfusion of FFP in 8–12 h in dose of 15 ml/kg. After achieving hemostatic effect in the presence of clinical signs of hemic hypoxias, we transfused washed packed red blood until cupping of clinical signs of hypoxia irrespective of hemoglobin and hematocrit level. Decrease of fibrinolytic blood activity was reached by intravenous introduction of contrical – 100–150,000 units or Gordoxum-500,000–1,000,000 units 15–30 min prior to transfusion of FFP. In the presence of thrombocytopenia below 50×10^9/l we carried out transfusion of 1–2 medical doses of thrombocytes concentrate. Also, we used prednisolonum in a dose of 1.5–2 mg/kg, correlation of acidosis. At detection of hypercoagulative phase of an acute DICS we transfused drop heparin introduction in a dose of weight 35–50 µn/kg, of rheologic nature. We did not have lethal cases.
Results: At acute massive bleedings in obstetric practice connected to DICS it is possible to achieve positive treatment results through transfusions of sufficient volumes of FFP in combination with saline solutions. The transfusion of eritro containing components was carried out after achievement of hemostatic effect in the presence of clinical implications of anemia.
Summary/Conclusions: At acute massive bleedings in obstetric practice connected to DICS it is possible to achieve positive results of treatment through transfusions of sufficient volumes of FFP in combination with saline solutions. The transfusion of eritro containing components is carried out after achievement of hemostatic effect in the presence of clinical implications of anemia.

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Abstract has been withdrawn

P-732

MANAGEMENT OF SEVERE SEPSIS

N Adinolfi, M Mottola, B Federico, O De Cenzo, R Ciotola, V Mininni and B Zuccarelli
Immunohematology Service, A.O.R.N.dei COLLI, Napoli, Italy

Background: Severe sepsis, defined as the presence of infection and organ dysfunction, is one of the main factors of morbidity and hospital mortality(20–60%) and its incidence is steadily increasing(9% annually). It helps to trigger the DIC, acquired syndrome characterized by activation of intravascular coagulation up to the formation of intravascular fibrin. The definition has in it all the clinical consequences that characterize the syndrome: organ damage due to the process thrombotic-ischemic and hemorrhagic diathesis. In patients with sepsis, the management of the DIC can be problematic because it may require the infusion of large amounts of blood products resulting overload circle, increased fluid loss trans capillary, worsening of pulmonary compliance and gas exchange.
Aims: The aim of our study was to assess the impact of the rate of infusion of FFP on survival and resolution in a shorter time of DIC/sepsis.
Methods: The use of FFP has been evaluated in a prospective cohort of 34 patients affected by DIC related sepsis admitted to the TYPE(Intensive Care Post-Operative), from 1 January to 31 December 2017. Patients with a diagnosis of acute DIC and laboratory investigation showed: lengthening of clotting time, platelet count, presence of FDP and D-dimer, abnormal plasma levels of coagulation inhibitors. Patients with a diagnosis of acute DIC and laboratory investigation showed: lengthening of clotting time, thrombocytopenia, presence of FDP and D-dimer, abnormal plasma levels of coagulation inhibitors. Of these patients, 6 received plasma by slow infusion continuous(1 ml/min),the remaining 28 were transfused slowly at first(5 ml/min) to monitor the appearance of any reactions and subsequently the infusion rate was increased to 10–20 ml/kg/h.
Results: Of the 6 patients treated with slow continuous infusion, the average stay was assessed in 36gg (15–90 gg)and with a survival of 80%. While for the other 28 patients, the average stay was 11 gg (7–15 gg), the survival of 91.3%.
Summary/Conclusions: On the one hand, this study has highlighted the inadequate use of FFP likely due to the habits and personal convictions resuscitators that led to the need to enact new corporate guidelines in order to allow operators (surgeons, resuscitators and immunohematologist)to act in synergy. Second, the heterogeneity, the relative small size of the populations studied together with methodological limitations spurred us to formulate a prospective study with our resuscitators in order to improve the diagnosis and treatment of DIC and create a project for the management of severe sepsis and septic shock.

P-733

PROLONGED IMMUNE HEMOLYTIC ANEMIA AFTER MINOR-MISMATCHED LIVER TRANSPLANTATION

S Joshi, S Bakdash, P Figueroa and S Sapatnekar
Section of Transfusion Medicine, The Cleveland Clinic, Cleveland, United States of America

Background: Passenger Lymphocyte Syndrome (PLS) is an alloimmune phenomenon that classically occurs in ABO minor-mismatched stem cell and organ transplantation but may occur with minor-mismatch involving other blood group systems. Antibodies against recipient antigens from allograft- derived plasma cells and lymphocytes may cause severe hemolysis in the recipient. PLS is considered a self-limiting disorder lasting the duration of survival of graft-derived lymphocytes.
Aims: To describe the clinical and serological features of a case of prolonged hemolysis due to PLS in the setting of non-ABO antigen-mismatched liver transplantation.
Methods: Clinical case management, chart and literature review.
Results: A 57 year-old-man with hepatitis C, end-stage liver disease and type-2 diabetes, underwent orthotopic liver transplantation from an ABO-identical, deceased donor. The patient had no record of red cell antibodies and had required no allogeneic transfusions within the preceding 3 months or during transplant surgery. On postoperative day 3, a routine type and screen revealed a new positive Direct Antiglobulin Test (DAT), new anti-D and anti-C in the plasma and eluate, and new anti-S the plasma alone. The patient's red cells typed D+C+S-. On Transfusion

Medicine staff review, these findings were deemed suspicious for donor-derived anti-bodies. Enquiries initiated by the Transfusion Service with the organ procurement agency confirmed donor history of anti-D, anti-C and anti-S. Concurrently, the patient's hemoglobin dropped by 4 g/dl with laboratory features of hemolysis and no evidence of hemorrhage. In the context of his immunohematological findings, this clinical presentation was found to be consistent with PLS. The patient received high-dose corticosteroids, intravenous immunoglobulin and rituximab for PLS in addition to his transplant-related immunosuppression, and eventually, a prolonged course of maintenance corticosteroids. These measures failed to control his symptoms of hemolysis, for which he required frequent transfusions (approximately 2 units of RBCs every 14 days) over the next few months. Red cell antibodies persisted in the plasma and eluate. Seven months after transplant, as a result of poor glycemic control, transfusion-dependency and development of transfusional siderosis, a splenectomy was performed. After splenectomy, there was a dramatic reduction in transfusion requirements, with just 2 transfusions in the next 6 weeks, and none thereafter. However, plasma antibodies were present for at least four months and the DAT remained positive for at least 55 months more. Over four years later, the patient has remained transfusion-independent with a hemoglobin consistently above 11.5 g/d. However, he continues to demonstrate evidence of compensated hemolysis of likely, a multifactorial etiology. His graft function is robust, and he shows no evidence of Post-Transplant Lymphoproliferative Disorder.

Summary/Conclusions: In the setting of non-ABO minor-mismatched organ transplantation, PLS has the potential for prolonged hemolysis. Patients with new red cell antibodies following transplantation must be evaluated for this condition. The inclusion of donor antibody status as part of the donor blood type report would facilitate early recognition of this under-appreciated complication.

P-734
EXTENDED ANTIGEN-MATCHING STRATEGIES TO PREVENT ALLOIMMUNIZATION AMONG HEMODIALYSIS PATIENTS

T Lin[1,2], S Hung[3], Y Yang[4] and T Chiang[4]

[1]Department of Medical Laboratory Science, I-Shou University [2]Department of Medical Research [3]Division of Nephrology, Department of Internal Medicine [4]Department of Laboratory Medicine, E-Da Hospital, Kaohsiung, Taiwan, China

Background: Blood transfusions are frequently used in the management of patients with hemodialysis-related anemia. According to a retrospective study, the overall prevalence of alloimmunization after blood transfusion at E-DA hospital was 0.83% (253/30324). However, a significantly higher RBC alloimmunization rate of 3.88% (39/1005) was found in hemodialysis patients (P < 0.001). It is well known that the development of erythrocyte alloantibodies complicates transfusion therapy for chronically transfused patients. It will result in difficulty and delay in obtaining compatible blood, and induce hemolytic transfusion reactions in hemodialysis patients with alloantibodies.

Aims: A strategy could provide RBC antigen-matched transfusion for hemodialysis patients to reduce alloimmunization.

Methods: A retrospective study was first conducted by reviewing blood request records at the Blood Transfusion Unit of E-Da Hospital for hemodialysis patients from 2005–2010. An extended RBC antigen-matching protocol was then applied for 628 non-alloimmunized hemodialysis patients between 2012 and 2017. With the extended RBC antigen-matching protocol, patients and donors were phenotyped for "Mia" and E antigens and then use the information to select RBC units lacking for antigens that not expressed by the recipients.

Results: The anti-"Mi^a" antibody was demonstrated to be the most common alloantibodies encountered (48.7%) followed by the anti-E antibody (36.8%) in hemodialysis patients. The RBC antibodies most commonly associated with alloimmunization in our population were directed agaThe RBC antibodies most commonly associated with alloimmunization in our population were directed against Mi.III and E antigens. Before the implementation of the extended RBC antigen-matching protocol, the anti-"Mia" antibody was demonstrated to be the most common alloantibodies encountered (48.7%) followed by the anti-E antibody (36.8%) in hemodialysis patients. In this study, the prevalence of MiIII and E antigens among 628 hemodialysis patients were 3.07% and 42.8%, respectively. During 2012 to 2017, with extended blood type- matching for 'Mia' and E antigens in the non-alloimmunized hemodialysis patients, not a single patient produced alloantibody after receiving blood transfusion.inst Mi.III and E antigens. In this study, we have performed immunohematology studies for "Mia" and E antigens in 628 hemodialysis patients. The prevalence of MiIII and E are 3.07% and 42.8%. We recommend administering blood with extended blood type- matching for 'Mia' and E antigens in the non-

alloimmunized hemodialysis patients. It was demonstrated no patient produced alloantibody after receiving blood transfusion during 2012 to 2017.

Summary/Conclusions: Extended blood type matching beyond ABO and D has long been proposed as a strategy to reduce alloimmunization. We found extended matching strategies for 'Mia' and E antigens in hemodialysis patients could significantly decrease alloimmunization ratio comparing to that before implementation of the transfusion protocol. It is concluded chronic transfused patients could be highly benefited from the extended blood typing strategies for the most common associated antigens.

P-735
CLINICAL EFFICACYOF SINGLE AND SIMULTANOUS DOUBLETRANSFUSIONS OF AMOTOSALEN/UVA LIGHT PATHOGEN-REDUCED PLATELET UNITS

R Ayupova[1], U Sultanbaev[2], S Madzaev[3] and E Zhiburt[3]

[1]Deputy Chief Doctor [2]Blood Bank of Bashkortostan, Ufa [3]Pirogov National Medical Surgical Center, Moscow, Russian Federation

Background: Platelet transfusions are an important tool for the prevention and treatment of bleeding in thrombocytopenia and/or thrombocytopathy. The current national guideline of platelet transfusion recommends a therapeutic dose of 200–250 × 10^9 platelets per 1 m^2 of the recipient body surface. Specific indications for transfusion of platelets are determined by the attending physician on the basis of the clinical picture and the causes of thrombocytopenia, the degree of its expression, the localization of bleeding and the volume and severity of the forthcoming procedure. One unit of platelets must contain more than 200 × 10^9cells. Accordingly, two therapeutic units of platelets are transfused simultaneously to adult patients if appropriate. To minimize the risk of pathogen transmission, particularly bacterial contamination, pathogen inactivation of platelet units was implemented in our center.

Aims: To compare the clinical efficacy of single and simultaneous double transfusion of pathogen-reduced platelets.

Methods: Data regarding the clinical efficacy of transfusion was collected from 14.01.2016 to 30.09.2016 from 15 hospitals at the Bashkortostan Republic, covering 915 transfusions of pathogen-reduced platelets (INTERCEPT Blood System, Cerus Corporation, Concord, USA). In 84 cases, one patient was simultaneously transfused with two therapeutic units of platelets. The results were processed using descriptive statistics with a significance level of 0.05.

Results: Fridays, simultaneous double transfusions occurred 1.4 times more often than single doses (P < 0.05), and Wednesdays, 1.9 times less often (P < 0.05). To stop bleeding, 72 transfusions were performed (7.9%), in the other 843 cases, platelets were used to prevent bleeding. The recipients of single and double transfusions did not show differences in the following indices:

surface area of the body,

the average number of transfusions in the history,

the proportion of the first transfusions of platelets,

the frequency of preventive and therapeutic transfusions,

effectiveness of stopping bleeding,

corrected platelet gain.

The platelet count before transfusion with double units was 21.0% lower (P < 0.05) than in the group of single transfusions. This ratio was leveled for the concentration of platelets after transfusion. The corrected platelet increment after 24 h (CCI) in the study groups did not differ. The number of platelets in the platelet container did not correlate with CCI in both, single and double transfusions. CCI directly correlated with the concentration of platelets before transfusion as for single, so for dual transfusions (P < 0.001). A direct correlation of CCI and baseline platelet concentration suggests an increased consumption of transfused platelets with the lowest initial cell concentration. Accordingly, it is necessary to search for the boundary value of the initial concentration of platelets, at which prophylactic transfusions are excessive.

Summary/Conclusions: There is no evidence of differences in the efficacy of dual and single transfusions of pathogen inactivated (Amotosalen/UVA) platelet concentrates. The direct correlation of CCI and the initial concentration of platelets indicates the limited diagnostic significance of CCI as an indicator of the effectiveness of platelet transfusion.

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P-736

BUFFY COAT GRANULOCYTES ARE A VIABLE ALTERNATIVE TO APHERESIS GRANULOCYTES

S Basu[1], A Bajpayee[1] and M Chandy[2]

[1]Transfusion Medicine [2]Clinical Haematology, Tata Medical Center, Kolkata, India

Background: Granulocyte transfusions are used in hemato-oncology patients and often prove life saving in patients with profound neutropenia. Granulocyte apheresis is expensive and requires a suitable donor. At our centre when granulocytes are indicated, we often use buffy coat granulocytes (BCG) as an alternative to apheresis granulocytes (AG). In this study, we retrospectively reviewed BCG transfusions undertaken at our centre, over a twenty months period.

Aims: To study the quality of BCG products and assess the outcomes of BCG transfusion.

Methods: During this period 12 patients received a total of 26 BCG transfusions. Buffy coat granulocytes were prepared using quadruple TAB-SAGM bag with the TACE II machine, from group specific, cross match compatible donors. These donors met all the criteria for blood donation and were non-reactive for infection markers (HBV, HCV, HIV, malaria, syphilis). The units were processed into components (platelets, packed red cells, plasma and buffy coat bags). Group specific buffy coat bags, cross match compatible with the patient were identified. Depending on availability of donors, a total of 216 buffy coat bags were used to prepare 26 BCG products. The product was irradiated and transfused within 8 h of preparation. The indications were ANC <0.5 × 10^9/l with drug resistant invasive bacterial/fungal infection.

Results: The gender distribution was 7 male and 5 female and the age ranged from 8- 67 years. Of these 12 patients, five patients received BCG transfusions for 3 consecutive days, four patients received BCG transfusions for 2 consecutive days and three patients each received BCG transfusion for 1 day only. The granulocyte content in the pooled BCG product ranged from 0.7 × 10^{10}–1 × 10^{10} and the RBC contamination ranged from 191–239 ml. Post transfusion counts (after 24 h) were performed to assess absolute neutrophil count (ANC)

Summary/Conclusions: Buffy coat granulocyte transfusions are useful in managing drug resistant neutropenic patients. These are relatively inexpensive, can be easily prepared and are a viable option when a granulocyte apheresis donor is not available.

P-737

RATIONAL USE OF PLATELETS FOR DANGUE/MALARIA EPIDEMICS

Y Patel

Lab Medicine, Global Hospital and Research Centre, Mumbai, India

Background: Critical shortage of platelets during dengue epidemic leads to preferential transfusion of platelets.

Aims: To overcome platelet shortage during Dengue/Malaria epidemic in India.

Methods: Six hundred patients with high grade fever tested positive for Dengue/Malaria were admitted and screened for Malaria, Dengue (Ns IgM and IgG), CBC for Atypical lymphocytes(ATL), Platelet Count,Mean Platelet Volume(MPV). And Platelet function Tests

Results: Three hundred and thirty-six patients had low platelet counts, 276 showed Atypical Lymphocytes (ALT), 182 had high mean platelet volume (MPV) and 94 had Normal MPV. CBC samples were tested every ten hours, revealed that the patients with high MPV, increased platelet counts over the period of next 24 to 36 h, also their smear showed reduction in ATL. However, patients with thrombocytopenia associated with ATL and normal platelet volume, worsened and started developing petechiae, these required immediate platelet transfusion. Thrombocytopenia patients with normal platelet volume associated ATL were also Dengue NS 1 and IgM positive, indicating active recent Dengue infection.

Summary/Conclusions: All Dengue, Malaria Cases with low platelets need not be transfused. Patients with Positive NS1, IgG, IgM, ATL having thrombocytopenia platelets not responding to production of large platelets, should be given immediate platelet transfusion. Such patients constitute to only about 27.9% as seen in this study, thereby releasing the remaining 70% platelets, as rational use requirement for the needy.

P-738

BLOOD TRANSFUSION PRACTICE FOR THYROIDECTOMY IN NIGERIA

A Afolabi[1] and F Fasola[2]

[1]Surgery [2]Haematology, College of Medicine, University of Ibadan, Ibadan, Nigeria

Background: There are variations in transfusion practice among surgeons for different procedures and for same procedure. The variations may be due to differing opinions on the threshold level of hemoglobin below which a patient needs blood transfusion, differences in surgical and anesthetic techniques, differences in case gradation and preoperative anemia. Despite shortage of blood, a large of number blood units is tied down for surgical procedure that may not require it. This may reflect perception or uncertainty of the surgeon on the relationship between the blood loss and subsequent transfusion

Aims: This study was carried out to evaluate transfusion practice for thyroidectomy in a tertiary hospital in Nigeria

Methods: A 12 years retrospective analysis of patients, who underwent thyroidectomy in our Hospital, was conducted. Information on the following was retrieved: demographic characteristics, pre and post operation haematocrit, the number of blood crossmatched and blood transfused. Indices used to determine the efficiency of blood ordering and utilization system included: crossmatch to transfusion ratio (C/T ratio), probability of a transfusion (%T), transfusion index (TI). The number of units to be crossmatched for thyroidectomy was determined using Maximal Surgical Blood Order Schedule (MSBOS = 1.5 × TI).

Results: Existing data of two hundred and sixty-five patients who had elective thyroidectomy from 2002 to 2014 was collected and used for this study. About 84.9% of the patients were female. The mean age of the patients was 40.75 ± 12.57 years. The commonest clinical diagnosis observed among the patients was simple multinodular (49.1%) followed by simple solitary nodular (16.2%). About 94.9% of the patients had their blood crossmatched while only about 17.6% had blood transfused. Pre- operation haematocrit of the patients was 37.6 ± 4.0% while the post-operation haematocrit was 35.78 ± 4.42%. Indices used to determine the efficiency of blood ordering and utilization showed that: Cross-match to Transfusion ratio (C:T ratio) was 5.3:1, Transfusion Probability (%T) was 19.3% and Transfusion Index (TI) was 0.24. Maximal Surgical Blood Order Schedule (MSBOS) to estimates the amount of blood that will be needed for the procedure was 0.36. The association between blood transfusion and type of operation was statistical significant.

Summary/Conclusions: This study shows that there was excess blood arrangement for thyroid surgery as suggested by CT ratio < 2.5, %T less than 30% and TI < 0.5. This would have led to avoidable burden on the blood bank staff and resources. The need for blood transfusion in patients for surgery of the thyroid was a function of the type of thyroidectomy performed, besides that, the MSBOS suggests that grouping of patient and saving group compatible blood without crossmatch is not likely to have detrimental effect on the quality of care of patients for thyroid surgery. Anaemia was uncommon among patients both preoperatively and postoperative which further corroborates the need for a change in transfusion practice of the surgeons.

Haemorrhage and Massive Transfusion

P-739

AVAILABILITY AND USE OF GROUP O, RHD–NEGATIVE RED CELLS IN EMERGENCY ADMISSIONS WITH CRITICAL BLEEDING: DATA FROM THE AUSTRALIAN AND NEW ZEALAND MASSIVE TRANSFUSION REGISTRY

HE Haysom, R Sparrow, M Tacey, Z McQuilten and E Wood

Department of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

Background: In emergency admissions that require massive transfusion (MT), guidelines recommend transfusion of blood group O RhD-negative (ONeg) red blood cells (RBCs) until the patient's blood group is known. Due to the low frequency of ONeg blood group, supply may be exhausted. Limited data exist on the use of ONeg RBCs in emergency admissions, including how frequently RhD-incompatible units are given, particularly, emergency transfusion management of females of childbearing potential. The Australian and New Zealand Massive Transfusion Registry (ANZ-MTR)

captures clinical and laboratory data on patients who have had MT (≥5 RBCs in any 4 h period) for any type of critical bleeding during their hospital admission.

Aims: To describe: 1) use of ONeg RBCs when MT occurred within 2 h of hospital admission and 2) the proportion of RhD-negative females <50 years who received RhD-incompatible RBCs.

Methods: All patients who received a MT within 2 h of hospital admission at participating hospitals during 2011 to 2015 were included. Variables included patient sex, age, time of issue of first blood component, bleeding context, number and blood group of RBCs transfused compared to patient blood group. Data were analysed using statistical software (Stata).

Results: 1359 MT cases met the inclusion criteria, all from metropolitan hospitals. Of these, 889 (65%) were admitted out-of-hours (i.e. weekends and/or before 8am or after 6 pm). The most common bleeding contexts were trauma (569; 42%), gastrointestinal (234; 17%), vascular (214; 16%), and obstetric (66; 5%). Of 77 (5.7%) ONeg patients, 48 (62%; 30 male, 18 female) received exclusively ONeg RBCs, 26 (34%; 20 male, 6 female) received both ONeg and ORhD-positive RBCs, and 3 (4%; 3 male) received only ORhD-positive RBCs. The median (inter-quartile range [IQR]) RBCs transfused within 4 h in these three groups were 6 (5–10), 12 (6–20) and 9 (7–16), respectively. Of the non-ONeg patients, 753 (59%) received at least one unit of ONeg RBCs and 49 (4%) received exclusively ONeg RBCs. For patients who received exclusively ONeg RBCs, 92% had MT duration of under 2 h and received a median 6 (IQR: 5–8) RBCs, while 48 (30 male) were RhD-positive. Examining the 198 females aged <50 years (mean age, 35 ± 9y), 72 (36%) were trauma admissions and 66 (33%) were obstetric. Twenty-six were RhD-negative; of these 12 RhD-negative females (11 ONeg) received exclusively ONeg RBCs, and 13 other RhD-negative females received exclusively RhD-negative RBCs. Only one RhD-negative female received RhD-positive RBCs. She was a trauma patient aged 43, transfused 40 RBCs in 4 h and died within 10 h.

Summary/Conclusions: In this cohort from the ANZ-MTR, 61% of massively transfused patients received at least one ONeg RBC. A small but important proportion were transfused exclusively with ONeg RBCs. Transfusion of RhD-matched RBCs was not achieved for 38% of ONeg patients and for 31% of all RhD-negative patients. There was only one case of an emergency admission RhD-negative female <50 years who did not receive RhD-matched RBC units. Our findings suggest that transfusion laboratory inventories largely met RhD-negative RBC requirements for emergency admissions requiring massive transfusion.

P-740

MASSIVE HEMORRHAGE PROTOCOL SURVEY OF 150 HOSPITALS IN CANADA: MARKED VARIABILITY IN PROTOCOLS

V Chin[1], S Cope[2], C Yeh[3], K Pavenski[4], T Thompson[2], B Nascimento[1] and J Callum[1]
[1]Sunnybrook Health Sciences Centre [2]Ontario Regional Blood Coordinating Network [3]University of Toronto [4]St. Michael's Hospital, Toronto, Canada

Background: Massive hemorrhage protocols (MHP) are key to ensuring patients receive standardized, state-of-the-art, and coordinated care to achieve the best possible outcomes. Previous surveys have shown variability in protocols including activation criteria, transfusion ratios, and laboratory testing. In addition, retrospective reviews have found that poor protocol compliance is associated with inferior outcomes.

Aims: The aim of this survey was to determine the proportion of hospitals across Ontario with a formal MHP and where implemented, the underlying components of the protocol. We hypothesized that MHPs are still lacking in many Ontario hospitals; and when present, protocols would be highly variable. The survey was performed in preparation for launching a Provincial wide, standardized, MHP.

Methods: The survey was sent to all hospitals (n = 150) with a transfusion service. Hospitals failing to respond by the deadline were emailed to encourage completion. Hospitals failing to respond to email were contacted by phone to encourage reporting (or provide a negative affirmation that they did not have a MHP). The survey included questions regarding activation criteria, communication, laboratory testing, transfusion pack configurations, hemostatic adjuncts, temperature, blood transport containers, anticoagulant reversal, and quality improvement metrics.

Results: Overall survey completion rate was 133 of 150 hospitals (87%) (the remaining providing negative affirmation that they did not have a protocol). A MHP was in place at 97 of 150 (64%) hospitals and the protocol was most commonly termed the "Massive Transfusion Protocol" (60%). Activation criteria were present in 85%; most commonly activated based on volume of blood loss (70%) and the number of units transfused (60%). Activation was triggered most commonly through a call to the transfusion laboratory (78%) and/or locating (25%). Blood work was most

commonly drawn at the discretion of the physician (37%) or at predefined intervals (31%; majority every 60 min). The most common routine laboratory tests performed were CBC (87%), INR (84%), aPTT (77%), and fibrinogen (75%). Fibrinogen testing was available at 88 of 133 reporting hospitals. Median targets of hemostatic resuscitations were: platelets $>50 \times 10^9/l$, INR<1.8, fibrinogen >1.5 g/l, and hemoglobin >70 g/l. Protocol required patient temperature monitoring in 65% and specified reversal plan for patients on anticoagulants in 59%. At 36% of sites all patients are initially managed with O-RhD negative blood. 45% of sites issue blood in predefined packs (vs. 55% based on physician orders). Hemostatic agents in the protocols included: tranexamic acid (70%), PCCs (14%), fibrinogen (13%), and rVIIa (4%). Quality metrics were tracked in 32% of hospitals; most commonly proportion of activations with wastage and appropriate activations.

Summary/Conclusions: MHPs are still lacking in at least 1/3 of hospitals in Ontario. There is marked variability in all aspects of the reported MHPs across Ontario. The variability may be due to differences in capacity of each reporting hospital, the lack of supporting literature to allow for uniform practice, and knowledge gaps. The lack of tranexamic acid as part of the protocol at 30% of hospitals and the lack of consistent laboratory testing in 37% suggest there are considerable gains to be made with a uniform Province wide protocol.

P-741

ANALYSIS OF MASSIVE TRANSFUSION BLOOD PRODUCT USE IN A TERTIARY CARE HOSPITAL

Y Lim
Laboratory Medicine, Ajou University School of Medicine, Suwon, Korea

Background: Massive blood transfusion (MT) requires significant efforts by the Blood Bank in the preparation of different blood products used in MT. In Ajou University Hospital (AUH), a 1180 bed tertiary care hospital, all blood products are provided by the Blood Bank. Following the opening of the Trauma Surgery Center (TSC) in October 2015, four units of dedicated emergency O Rh Positive red cells (emergency O RBCs) have been available in the Blood Bank for emergency use. Since March 2016, emergency O RBCs have been held in and released directly from TSC for emergency patients before their ABO Rh blood typing has been determined.

Aims: To analyze blood product use in MT since March 2016 when emergency O RBCs were available directly from the TSC.

Methods: MT was defined as a transfusion of 10 or more RBCs within 24 h. In the case of patients who were continuously transfused blood products for more than 24 h, only the number of products transfused in the first 24 h was included. Medical and transfusion records of MT cases were extracted from the hospital information system and reviewed. Total RBCs, fresh frozen plasma (FFP), platelets (PLTs -single donor platelets (SDP) or random platelet concentrates (PC)) issued from AUH Blood Bank between March 2016 and November 2017 were reviewed. SDP was considered equivalent to 6 units of PC. The percentage of products transfused during MT was compared with the overall percent of products transfused. Also the percentage of emergency O RBCs transfused was compared with total units transfused per patient and was defined as use of emergency O RBCs%.

Results: There were 345 MTs during the 21 month survey period (16.4 cases/month). A total of 53,268 RBC were transfused during that period of which 6,233 RBC (11.7%) were used in MT. For routine non-MT RBC transfusions 33.4% were group A, 26.1% group B, 30.6% group O and 9.9% AB. In MT RBC transfusions 29.5% were group A, 28.6% B, 33.9% O and 8.0% AB. During the same period 4717/19376 (24.3%) FFP, 170/347 (49%) cryoprecipitate and 4473/94166 (4.8%) PLTs were used in MT. The ratio of RBC:FFP:PLT use were 1:0.76:0.72 in MT and 1:0.36:1.77 in total transfusion. Emergency O RBCs were used in 125/345 (36.2%) MT cases with a total of 461 emergency O RBC used in these cases which was only 7.4% of total RBCs and 19.8% of O RBCs for MT. The average number of emergency O RBCs units transfused per patient varied from 1 to 18 and use of emergency O RBCs% varied between 2.0–100% (20.8 ± 18.6%, mean ± SD).

Summary/Conclusions: Ongoing education of clinicians to minimise over use of emergency O RBCs in MT is required. Although emergency O RBC were quickly available a procedure to have thawed plasma more readily available in MT appears to be of more importance than availability of O RBCs because FFP was used more frequently in MT compared with total transfusions.

P-742

TRIGGERS APPLIED BY THE OBSTETRIC SPECIALISTS ON INITIATING BLOOD TRANSFUSION FOR POST-PARTUM HEMORRHAGE

M Krishnapillai[1] and S Sivachandran[2]

[1]National Blood Centre [2]Obstetrics and Gynecology, De Soysa Maternity Hospital, Colombo, Sri Lanka

Background: Post-partum hemorrhage (PPH) is identified as the leading cause for the maternal deaths worldwide. Guidelines from the recognized institutions state that blood transfusion should be initiated on the clinical judgment but there are no well-defined fixed criteria to initiate the blood transfusion.

Aims: Aim was to analyze the clinical and biochemical parameters and triggers considered by the obstetric specialists to commence blood transfusion in clinical practice.

Methods: A descriptive study was conducted among 52 Consultant Obstetricians practicing in Sri Lanka. Data was collected with self- administered questionnaire and analyzed with Microsoft excel and SPSS.

Results: The mean years of experience of participants practicing as clinical consultants were 8 years. Among them, 88.4% (46) participants agreed that they considered initiating blood transfusion depending on the rate of bleeding irrespective of estimated total loss, when there was an evidence of hypovolemia. All of them used 'increase in pulse rate above 100 or rise of pulse rate by 10 from base line' as an indicator. Only 11.1% (6) agreed that they considered blood transfusion on the rate of bleeding irrespective of the estimated total blood loss and clinical parameters. Regarding total blood loss in a patient with ongoing bleeding, all of them considered transfusion when total blood loss was above 1000 ml irrespective of clinical parameters and they considered transfusion with increasing pulse rate or dropping of blood pressure even if total loss is less than 1000 ml. All participants agreed that visual assessment of total blood loss was an inaccurate method to define PPH. All of them agreed that combination of clinical parameters was more reliable and effective method in assessing the need for transfusion than single parameters. Thirty-five (67.3%) participants agreed that pulse rate was the most reliable parameter followed by blood pressure and respiratory rate and 32.7% (17) of them suggested change in the respiratory rate followed by pulse rate and blood pressure would be more reliable. None of them suggested that they'd consider blood transfusion on the basis of clinical pallor or patients' consciousness status alone unless there was a defined blood loss or other evidence of hypovolemia and 86.5% agreed that they 'd wait for the hemoglobin assessment in a patient who was pale without considering the ongoing blood loss and normal clinical parameters. All participants agreed that the involvement of a Hematologist or a Transfusion physician would be beneficial in making the decision of blood component therapy. If a hematologist was not available, 59.6% (31) and 40.4% (21) agreed they'd have had initiated components transfusion with 4th unit and after 4th unit of red cells (before coagulation profile was available in low-risk patients). Only 13.5% had the facility for point of care testing and they agreed that it could be beneficial, but it was not necessary for them to manage obstetric hemorrhage, whereas 86.5% never had the facility to manage a patient with such test.

Summary/Conclusions: All the specialists agreed clinical judgment was the important determinant and there were some specific parameters used by each of them in initiating the blood transfusion.

P-743

FLUID MANAGEMENT AND DILUTIONAL COAGULOPATHY IN POSTPARTUM HAEMORRHAGE: A NATIONWIDE RETROSPECTIVE COHORT STUDY

A Gillissen[123], T van den Akker[3], C Caram-Deelder[1], D Henriquez[3], K Bloemenkamp[4], J Eikenboom[5] and J van der Bom[1]

[1]Center for Clinical Transfusion Research, Sanquin Research [2]Department of Clinical Epidemiology [3]Department of Obstetrics, Leiden University Medical Center, Leiden [4]Department of Obstetrics, University Medical Center Utrecht, Utrecht [5]Department of Thrombosis and Hemostasis, Leiden University Medical Center, Leiden, Netherlands

Background: In order to achieve volume expansion and prevent hypovolemic shock, administration of clear fluids has become an essential part of the management of postpartum haemorrhage. At the same time, large amounts of fluids may induce dilutional coagulopathy. We describe the change in coagulation parameters with increasing volumes given in the course of postpartum haemorrhage.

Aims: The aim of this study was to evaluate the association between restrictive and more liberal volume resuscitation management strategies and the development of dilutional coagulopathy during postpartum haemorrhage.

Methods: Nationwide retrospective cohort study of 1391 women experiencing post-partum haemorrhage who had received at least four units of red cells or fresh frozen plasma or platelets in addition to red cells. For 1038 women (75%), data were available for coagulation parameters and amount and timing of clear fluids. The amount of blood loss at the time of blood sampling was categorised in 7 groups: 1000–1500 mL, 1500–2000 mL, 2000–2500 mL, 2500–3000 mL, 3000–3500 mL, 3500–4000 mL and >4000 mL with 0–1000 mL as reference category. Coagulation parameters were allocated to the category representing amount of blood loss at sampling. Subsequently the amount of clear fluids administered at the time of blood sampling was calculated and classified into three fluid administration strategies, based on the RCOG guideline: < 2000 mL, 2000–3500 mL and > 3500 mL. Thus, coagulation parameters were first grouped based on amount of blood loss at sampling and then subdivided over the three fluid administration strategies for further analyses. Outcomes included haemoglobin, haematocrit, platelet count, fibrinogen, aPTT and PT levels.

Results: Between the lowest and highest category of fluid administration, median haemoglobin level decreased from 10.1 g/dl (IQR 8.5–11.6) to 8.1 g/dl (IQR 7.1–8.4), median platelet count from 181×10^9/litre (IQR 131–239) to 89×10^9/litre (IQR 84–135), and aPTT prolonged from 29s (IQR 27–33) to 38s (IQR 35–55) although being sampled at the same amount of blood loss. For fibrinogen, largest change was displayed for measurements in the reference category (blood loss 0–1,000 mL): 3.9 g/l (IQR 2.5–5.2), 2.6 g/l (IQR 1.6–3.7), 1.6 g/l (IQR 1.3–2.1) over the three fluid management categories. After transfusion of blood products the observed differences diminished.

Summary/Conclusions: In this large cohort of women with postpartum haemorrhage, administration of large volumes of clear fluids was associated with changes in coagulation parameters corresponding to dilutional coagulopathy.

P-744

EXPERIENCE WITH NATIONWIDE MASSIVE TRANSFUSION PROTOCOL (MTP) IMPLEMENTATION IN A TERTIARY INSTITUTION

Y Khng[1], C Lee[2,3], S Lim[1], K Lim[1], S Lee[1,2] and L Tan[1,2]

[1]Laboratory Medicine [2]Department of Haematology-Oncology, NCIS, National University Hospital [3]Yong Loo Lin School of Medicine, National University Singapore, Singapore, Singapore

Background: Massive transfusion protocols (MTP) are structured mechanisms for early blood product delivery during critical bleeding. This transfusion practice is increasingly used across different hospital specialties in early resuscitations to maintain perfusion and to correct consumptive coagulopathy prior to definitive hemostatic measures. Despite these benefits, MTPs may also result in wastage of costly blood products.

Aims: To review blood products usage and mortality of patients receiving MTPs from 2012–2017 in National University Hospital (NUH).

Methods: In NUH, MTP consist of 3 packages, including MTP1 and MTP3 which consists of 4 packed red cells (pRBC), 4 units of fresh frozen plasma (FFP) and 4 units of platelets pooled in 1 bag (pPLT). As for MTP2, additional 10 units of cryoprecipitate are added to the package. After MTP1 is issued, the attending physician will decide if MTP2 and MTP3 are required. Assessment of Blood Consumption (ABC) scores in trauma patients is used to guide MTP activation. We reviewed the indication of massive transfusions, patients' demographics and clinical data of all MTPs initiated.

Results: A total of 401 MTPs were activated. Of which 311(78%) were males, and the median age of the patients was 52 years (13 - 93 years). There were 185(46.1%) trauma cases, 89(22.2%)gastrointestinal hemorrhage, 47(11.7%) peri-operative hemorrhage, 20(5.0%) ruptured aortic aneurysm (AAA), 11(2.7%) peripartum hemorrhage and 49(12.3%) massive bleeding due to other causes. Overall, 261(65.1%) MTP1, 87 (21.7%) MTP2, 46(11.5%) MTP3 were activated, and 7(1.7%) cases required more than MTP3. A total of 10668 blood products were issued during this period accounting for 5.8% of the total blood product issued in our hospital from 2012–2017. 5036 (47.2%) of the blood products are issued to the emergency department, 1996(18.7%) to operating theatres, 3394(31.8%) to intensive care units and 242(2.3%) to general wards. 1557(14.6%) blood products were returned unused including 568 units of pRBC (5.3%), 121 units of pPLT (1.1%), 693 units of FFP (6.5%) and 175 units of cryoprecipitate (1.6%). 72(17.9%) MTP activation had 528(4.9%) blood products returned due to patient's death and accounts for 34% of blood products returned.

300(74.8%) patients survived more than 1 day after MTP activation, with 150 (50.0%) trauma, 61(20.3%) BGIT and 10(3.3%) ruptured AAA and others 79(26.3%). 37(9%) of patients who survived after activation expired within a month.

Summary/Conclusions: 14.6% of blood products activated after MTP were returned unused to the blood bank, and less than half was due to patient's death. Overall blood product wastage is much lower compared to Dunbar et al. at 50.3%, and with Balvers et al., a lower FFP wastage by 3.1%. Out of the returns, some can be re-issued provided it meets the stringent storage requirement policy by our hospital whereas some may be wasted due to improper storage and limited shelf life. There are limited clinical predictive scoring to aid decision to activate MTPs. MTPs are activated based on the clinical judgment of senior physicians in attendance which can be inconsistent. Education of clinicians for the prompt return of blood products to blood bank when MTPs ceases is crucial to reduce wastage.

P-745

STUDY ON OVER ACTIVATION OF MASSIVE TRANSFUSION PROTOCOL IN SINGAPORE

S pandey and J Chay

Blood Service Group, Health Science Authority (HSA), Singapore, Singapore

Background: Background; Massive Transfusion Protocol (MTP's) are used to maintain adequate circulation and haemostasis in critical Bleeding, especially trauma bleeding, using standardized and early delivery of blood products. For Trauma bleeding, the MTP recommends use of a validated massive transfusion predictive scoring system specifically the 'ABC' score 'to initiate MTP but for non-trauma bleeding, activation of the MTP is based on the clinical assessment and medical judgement of the medical team attending to the patient. Recently, concern has been raised that the use of MTP especially in non-trauma cases might be inefficient due to protocol over activation which may lead to transfusion reactions and blood wastage. There is also fears that high ratios of plasma and platelets transfused may lead to poorer outcome in non-massively bleeding patients who do not require MTP support.

Aims: We aim to investigate the rate of MTP over activation from the year 2010–2016. This report would arouse awareness regarding inappropriate activation of MTP which can be harmful to the patients.

Methods: All activated MTP's cases from different restructured hospitals in Singapore over a period of 6 years from December 2010- December 2016 were analysed. We used modified definition of massive transfusion of 9 units or more of red cells (reached MTP pack 3) transfusion within 24 h in adult patients. MTP cases were categorized in to Trauma, Surgical, medical and obstetric based on the type of haemorrhage. MTP de-escalations were decided by the medical or surgical team.

Results: From December 2010-Dec 2016, 1209 cases of MTP were initiated of which 37.4% were identified as trauma and 62.6% as non- trauma. Common diagnosis of non-trauma included obstetric (7%), medical mostly gastrointestinal bleeding (27%), surgical mostly cardiac op (28.6%). The MTP was found to be over-activated in 64% cases in general, but 62% of Trauma and 67.3% of non -trauma were over-activated where it did not reach pack 3 or used less than 9 units of red cells.

Summary/Conclusions: Our results indicate that majority (64%) of our MTP activated cases do not meet the definition of a massive transfusion and to reduce the wastage we recommend a) Improving Triaging for MTP cases, especially for non-trauma MTP over triage b) Consider Viscoelastic hemostatic point-of-care testing (POCT) to guide MTP and blood product transfusion (eg ROTEM),with possible de-escalation of MTP if vital signs are normal.

P-746

USE OF BLOOD TRANSFUSION AMONG ROAD TRAFFIC ACCIDENT VICTIMS ADMITTED TO THE DISTRICT GENERAL HOSPITAL, MATALE, SRI LANKA

A Godamunne

National Blood Transfusion Service, Narahenpita, Colombo, Sri Lanka

Background: Road traffic accidents (RTA) are a leading cause of death globally as well as in Sri Lanka and results in a large proportion in disability especially among young people. Ninety-percent of world's road traffic deaths occur in low- and middle-income countries. The gross disparities in injury outcomes relate to immediate post-crash and hospital management. Blood transfusion is a life-saving procedure in managing RTA victims. Thus, it is important to provide safe blood at the right time, to the right patient in right quantity.

Aims: The main objective of this research was to assess the proportion of RTA victims who receive blood transfusions and calculate the proportions of blood transfusions with the injury pattern.

Methods: This study was conducted as a descriptive cross-sectional study. All the consecutive RTA victims admitted to surgical wards at District General Hospital, Matale, Sri Lanka, over a period of three months were included into the study.

Results: Data from 387 road traffic accident victims were analyzed. The majority were in the 20–30 year age group. Seventy six percent of the patients were males. Motorcycles and trishaws were the most affected. First-aid was given to only 2% of patients. Limbs and head were the most affected areas of the body. Blood was transfused in 4% (14) of RTA victims and they all were males. Out of the patients who sustained grievous injuries, blood transfused in 7.1% of the victims. Blood transfused in 71.4% of victims who categorized as fatal in the ordinary cause of nature and 66.6% of necessarily fatal patients. However, none of the victims who sustained non-grievous injuries had transfusions. Seventeen red cell concentrate packs were issued to these 14 patients and none had gone into massive transfusion protocol.

Summary/Conclusions: As per this study, blood was transfused in 4% of road traffic accident victims. Out of the patients who sustained grievous injuries, blood transfused in 7.1% of the victims and it is 71.4% and 66.6% among the victims who sustained fatal in the ordinary cause of nature and necessarily fatal injuries respectively.

P-747

SAVING GROUP O RH D NEGATIVE RED CELLS IN A TRAUMA CENTRE

D McKeown[1], F Chowdhury[2], N Batrick[3] and J Graves[3]

[1]Blood Transfusion [2]Haematology [3]Emergency Department, Imperial College Healthcare NHS Trust, London, United Kingdom

Background: St Mary's Hospital became a Major Trauma Centre in 2010. Since its Go Live date the need for a satellite blood fridge was carefully monitored and in 2015 it was agreed a blood fridge was required. The remote blood fridge went live in January 2016 with an agreed stock of 6 group O Rh D positive and 6 group O Rh D negative units. However as group O D negative RBC usage remains constantly higher than availability, maintaining an adequate supply of group O Rh D negative units for emergency patients with unknown blood group remains challenging for the blood service. To try save group O Rh D negative units we reviewed our code red demographics over a six month period to assess if we could further reduce our stock of group O negative units in the satellite fridge.

Aims: To ensure appropriate blood stock is available in the emergency department for code red (trauma) calls.

Methods: Based on St Mary's Major Trauma Registry data all the code red calls during the period 01/07/2017–31/12/2017 were reviewed to identify the demographics of the trauma victims. We then cross examined the data against our blood transfusion laboratory system to identify the numbers of male and female trauma victims and their Rh D status.

Results: There were sixty three code red calls between 01/07/2017–31/12/2017. Of these 51/63 (80%) code red calls were for males and 12 (20%) for females, 9/12 females were of child bearing age but 11/12 females were subsequently identified as Rh D positive. The majority of male trauma victims (47/51 i.e. 92%) were subsequently identified as Rh D positive.

Summary/Conclusions: The risk of giving female or male trauma patients Rh D incompatible units is low. Therefore we plan to reduce our stock of group O Rh D negative units to 4 units and increase the group O Rh D positive emergency stock to 8 units.

P-748

BLOOD TYPING IN PRE-HOSPITAL CARE – COMPARISON OF TESTS FOR WALKING BLOOD BANK

M Bohonek, D Kutac and T Markovina

Hematology and Blood Transfusion, Military University Hospital Prague, Prague, Czech Republic

Background: Massive bleeding is the second most common cause of death of trauma patients and the main cause of death in wartime injuries. The death occurs

within 6 h if the treatment is inadequate. The fatal outcome can be largely avoided by applying Damage Control Resuscitation (DCR) procedures that reduce bleeding and optimize coagulation, including a surgical approach. Essential part of this strategy is hemostatic resuscitation, with the implementation of 1:1:1 transfusion protocol or transfusion of whole blood. For active pre-hospital care, including a combat situation under fire, the DCR concept is modified to Remote DCR procedures (RDCR). Its an integral part is the accelerated haemostatic resuscitation, "Blood Far Forward", where trained medical personnel applies blood products or blood derivatives, including fresh whole blood, collected on-site. "Walking Blood Bank" was named after this.

Aims: For safe blood collection and transfusion by the Walking Blood Bank, it is necessary to have a robust, usable assays for determining and verifying the blood group, at least in the AB0 system. With the participation of members of the special forces of the Czech Army, we conducted a check of selected blood group bed-side tests to assess their usability for pre-hospital care during combat deployment.

Methods: Evaluated test kits: MDmulticard® ABO-D, Grifols, Spain, ABTest card®, DIAGAST, France, One man kit Eldon Card, ELDON, Denmark, ABO set MP, EXBIO, Czech Republic. Three CLS specialists were selected who, after training, performed a blood group typing using all the evaluated test-kits. As such, each examiner examined 5 blood samples and individually evaluated the parameters: test preparation time (sec), test time (sec), total test time (sec), readability (1 - 5 points, 1 = worst, 5 = best), ease of testing (1 - 5), practicality of the test from the point of view of its field use (1–5), influence of the environment on the performance and reading of the test (1–5), robustness (1–5), durability of the result (1–5). Examinations were conducted on the ground. Of all the values, the arithmetic average was used to compare the individual experiments.

Results: Test preparation time: Grifols 24.33. Diagast 27.4. Eldoncard 62.73, Exbio 31.8. Time of typing: Grifols 451.6, Diagast 62.66, Eldoncard 119.93, Exbio 88.7. Total time: Grifols 451.6, Diagast 62.66, Eldoncard 119.93, Exbio 88.7. Readability: Grifols 3.26, Diagast 4.8, Eldoncard 4.33, Exbio 4.66. Ease of testing: Grifols 4.44, Diagast 4.4, Eldoncard 2.66, Exbio 3.0. Practicality: Grifols 3.46, Diagast 4.53 Eldoncard 2.66, Exbio 2.2. Influence of the environment: Grifols 3.8, Diagast 5, Eldoncard 2.66, Exbio 2.2. Robustness: Grifols 4.33, Diagast 4.1, Eldoncard 5.0, Exbio 3.33. Durability of result: Grifols 5.0, Diagast 5.0, Eldoncard 1.86, Exbio 1.0.

Summary/Conclusions: ABTest card® Diagast appears to be the most appropriate test. The test has the best rating for virtually all parameters, and the examiners have appreciated its user-friendly features. Surprisingly, the Eldon Card diagnostic kit, which is currently the most widespread field trial test-kit in the NATO.

P-749
BLOOD TRANSFUSION MANAGEMENT OF AN EARLY POSTPARTUM HAEMORRHAGE (PPH). CASE REPORT

M Coelho

Immuno-Haemotherapy, Hospital Santa Maria, Lisbon, Portugal

Background: PPH is the leading cause of pregnancy-related deaths worldwide. Its rapid diagnosis and early treatment are critical. PPH is defined as blood loss of more than 500 ml within 24 h after vaginal delivery or >1000 ml after caesarean delivery. Uterine atony is the major cause of PPH; other causes include surgical incisions, lacerations and the presence of coagulopathy. Unfortunately, although several risk factors exist, often PPH occurs without warning.

Aims: How to control a massive post partum haemorrhage using medical and surgical strategies.

Methods: Woman, 25 years old, obese (IMC 36.73), diabetes mellitus type I insulindependent, 40 weeks pregnancy of a macrosomic fetus (5.68Kg). She presented with Hb 14.0 g/dl and 12.0 g/dl pre and after caesarean delivery respectively (given: oxytocin 5U bolus and 15U continuous perfusion, plus 0.4 mg Misoprostol rectal). Two hours after delivery the patient became hemodynamic instable with a severe PPH (Hb 6.9) and was submitted to an urgent treatment to stop the bleeding, in the stepwise progression: Bimanual uterine compression (loosing 1000 cc of blood/compression), Tranexamic Acid (1 g iv–10 min followed by 1 g, iv/8 h), replacement of blood components (5 RBC and 4 platelet concentrates, 6 units of fresh frozen plasma) and Clotting Factors (9 g of fibrinogen concentrates-FC and 1.500UI of prothrombinic complex concentrates) according the Point of Care (POC) (ROTEM) results and our PPH algorithm.

Results: Surgery intervention was needed to control massive bleeding: hysterectomy plus right adnexectomy. (Puerpera transferred to intensive care unit) In the next day, surgical hemostasis control was needed again (5RBC, 2PC and 2 g FC were given). After a clinical diagnosis of PPH an effective multidisciplinary team management involved communication, resuscitation, investigation (clinical and laboratorial),

monitoring and goal-directed treatment. Mechanical, pharmacological, transfusional and surgical measures were used to stop the bleeding.

Summary/Conclusions: Fibrinogen level play a main role in any obstetric bleeding. Management of coagulopathy associated with PPH is crucial in transfusional medicine and based on POC and other laboratorial tests (Ca+, coagulation). A multidisciplinary team must be involved since the beginning of PPH to provide an early recognition of correct diagnosis and a goal-directed treatment based on a PPH algorithm. According to European Society of Anesthesiology/2017, an escalating PPH management protocol must include uterotonic drugs, surgical and/or endovascular interventions and procoagulant drugs.

P-749a
AUDIT OF CRYOPRECIPITATE USE IN ACADEMIC CENTRE

K Pavenski[1,2], E Krok[3] and M Anderson[3]

[1]*Medicine and Laboratory Medicine, St. Michael's Hospital* [2]*Medicine and Laboratory Medicine, University of Toronto, Toronto, Canada* [3]*Laboratory Medicine, St. Michael's Hospital, Toronto* [4]*Laboratory Medicine, St. Michael's Hospital, Toronto, Canada*

Background: Cryoprecipitate (CRYO) transfusion is used to treat bleeding in patients with fibrinogen deficiency. CRYO is indicated in bleeding patients when a fibrinogen level is less than 2 g/L. Each unit of CRYO contains a minimum of 150 mg of fibrinogen and 10 units of CRYO is expected to increase fibrinogen by 0.5 g/L in an average-sized, bleeding adult.

Aims: CRYO utilization has been increasing year to year in Canada and in our institution and we wanted to assess how it was being used.

Methods: A retrospective review of patients transfused with CRYO from November 1–30, 2017 in a single tertiary centre was performed to determine where and why CRYO is being used. All CRYO doses were prepared by thawing and pooling 10 units of CRYO into one bag. Pooled CRYO expires after 4 h at room temperature. We collected data on patients' demographics, diagnoses, bleeding status, blood component use and pre and post fibrinogen levels.

Results: Over 1 month, 34 doses of CRYO were ordered for transfusion. 2 CRYO (6%) doses were not used and were discarded (fibrinogen >2.2 and 2.3 g/L) while 32 CRYO doses were transfused to 18 patients. Of the 18 patients who received CRYO: 15 males (83.3%) and 3 females (16.7%), male median age: 54 yrs and female median age: 48 yrs. Patients undergoing cardiovascular surgery accounted for 7/18 (39%) patients who received CRYO, trauma 5/18 (28%) and miscellaneous diagnoses 6/18 (33%). The reason for CRYO transfusion was coagulopathy and bleeding in 29 of 32 (91%) transfusions. 14 out of 32 transfusions (44%) were administered as part of the massive hemorrhage protocol. In 26/32 (81%) CRYO transfusions, the pre - transfusion fibrinogen level was less than 2.0 g/L. All patients who received CRYO also received other blood components.

Summary/Conclusions: CRYO is most commonly used in cardiovascular surgery patients. Most CRYO use (91%) is in patients with coagulopathy and bleeding which is appropriate. Wastage rate is low.

P-750
VALIDATION OF HEMOSTASIS AND COAGULATION ASSAYS; IN THE DIAGNOSIS OF DISCREPANT MILD HEMOPHILIA A

A Soleimany Ferizhandy[1] and S Amini Kafi-Abad[2]

[1]*Quality Control* [2]*Iranian Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran*

Background: The clinical hemostasis laboratory is a complex testing employs numerous coagulation assays and spans several different test methodologies. The activity of the factors coagulation protein can be measured by three methods: a one or two-stage clotting assay and a chromogenic assay. Adding further complexity, these test results are expressed in a wide variety of unique units (time and percentage).

Aims: The factor VIII activity of most individuals with mild hemophilia A is the same regardless of which method is employed. However, approximately 30% of patients show marked discrepancies in factor VIII activity measured with the different methods.

Methods: The objective of this study was to investigate the incidence of assay discrepancy in our center, assess the impact of alternative reagents on factor VIII activity assays and determine the usefulness of global assays of hemostasis in mild

hemophilia A. Citrated plasma samples (Vacutainer, Becton Dickinson, USA) from 87 males and seven female carriers of hemophilia A, with FVIII:C levels between 7 and 49 IU/dl by at least one method, were obtained following informed consent. Assay discrepancy was defined as a two-fold or greater difference between the results of the one-stage and two-stage clotting assays. Rotational thromboelastometry and calibrated automated thrombography were performed.

Results: Assay discrepancy was observed in 31% of individuals; 18% with lower activity in the two-stage assay and 29% with lower activity in the one-stage assay. The current international guidelines do not define the type of assay to be used in the diagnosis of mild hemophilia A and some patients could be misclassified as normal. In our study, 4% of patients would not have been diagnosed on the basis of the one-stage factor VIII assay.

Summary/Conclusions: There are international standards available in hemostasis; unfortunately, many of the analytes await the development of such standards and values for these analytes are derived from local or manufacturer's standards. Before a method can be introduced into clinical use, both analytical and clinical performances must be verified under the standard operating parameters of the laboratory. Laboratories should use both one stage and chromogenic (or two-stage) assays in the diagnosis of patients with possible hemophilia A. The use of a standardized validation protocol and reference interval determination will help to objectively evaluate the method performance.

P-751

Abstract has been withdrawn

P-752

EFFECTIVENESS OF DIFFERENT INFUSION–TRANSFUSION THERAPY SCHEMES IN MASSIVE GASTROINTESTINAL BLEEDING

BB Bakhovadinov[1], N Ashuraliev[2], M Kucher[3], N Mukhiddinov N.D.[2], A Vakhidov[2] and D Pevtsov[3]

[1]*Raisa Gorbacheva Memorial Institute for Children Oncology, Hematology and Transplantation, Pavlov First Saint-Petersburg State Medical University, Saint Petersburg, Russian Federation* [2]*Institute of Postgraduate Education in Health Care of the Republic of Tajikistan, Institute of Postgraduate Education in Health Care, Dushanbe, Tajikistan* [3]*Raisa Gorbacheva Memorial Institute for Children Oncology, Hematology and Transplantation, St. Petersburg State Medical University, Saint Petersburg, Russian Federation*

Background: Gastrointestinal (GI) bleeding is a common cause of emergency hospitalization in surgical departments, reaching 10% of overall hospital mortality. Therapy of acute massive bleeding in addition to timely surgical correction also requires the implementation of adequate infusion-transfusion therapy (ITT) in pre - and postoperative period. The issue of optimal volumes, quantitative and qualitative composition of ITT in acute massive blood loss still remains debatable.

Aim: Analysis of ITT effectiveness in massive GI bleeding treatment.

Methods: A comparative retrospective analysis of ITT effectiveness in complex GI bleeding treatment was performed in 60 patients who was admitted to the surgical inpatient department (group I) and in 60 patients who had received additional treatment conducted by specialized intensive care and transfusion team from blood centers (group II). Age of the patients was 56.5±17.32 years, 110 were male and 10 – female. Determination of blood loss amount was performed by Ryabov G.A. method (1994), Moore and Algowure-Bruber shock index. Statistical processing was performed using variation Fisher-Student statistics (Stat Soft Statistica 6.0).

Results: The total volume of blood loss in patients in group I was 2.86±0.15 (from 1.82 to 3.95 liters), in group II – 2.3±0.11 (from 1.52 to 3.30 liters) (Table 1).

Table 1. Comparative characteristics of infusion-transfusion therapy

Total amount of ITT in group I was 5 072.5 ml or 177.3% of blood loss volume, in group II – 7 002.3 ml and 304.4%, respectively. Analysis of the qualitative composition of transfusion agents showed that in group II, patients received significantly more red blood cells, FFP, crystalloid solutions and albumin. The share of synthetic colloids, including dextran-containing solutions in group I was 47.3% of total ITT volume, in group II – 17.1% (especially gelatin derivates). FFP was used in 9.9% (group I) and in 14.1% (group II), crystalloid solutions – in 28% and 40.7%, respectively. The study of hemostasis system showed developments of hypocoagulation phase of disseminated intravascular coagulation syndrome, hemodilution

coagulopathy mainly in patients of group I. 17 (group I) and 5 patients (group II) required surgical treatment. 8 patients had died in group I and 3 patients in group II.

Summary/Conclusions: The qualitative composition of ITT has a significant impact on the outcomes of treatment in massive GI bleeding. ITT which includes predominantly crystalloid solutions in combination with high doses of FFP and natural colloid solutions is more rational and effective compared to the scheme, which is based on the use of synthetic colloids.

P-753

Abstract has been withdrawn

P-754

HEMODILUTION COAGULOPATHY AT INFUSIONALLY–TRANSFUSION THERAPY OF OBSTETRIC BLEEDINGS

BB Bakhovadinov[1] and G Ashurova[2]

[1]*Raisa Gorbacheva Memorial Institute for Children Oncology, Hematology and Transplantation, St. Petersburg State Medical University, Saint Petersburg, Russian Federation* [2]*Dushanbe City Maternity Hospital N3, City Maternity Hospital N3, Dushanbe, Tajikistan*

Background: Obstetric bleedings continue to remain the leading reason of maternal mortality accounting to about 46% of lethal pregnancy outcomes. Hemorrhages and aggravating them coagulopathy bleedings are one of the reasons of maternal mortality.

Aims: The goal of this research is to specify pathogenetic mechanisms of hemostasis disorders at infusional hemodilution and also to provide characteristics of hemocoagulation disturbances.

Methods: We conducted a retrospective analysis of investigation data of 75 women in childbirth with bleedings whose age ranged from 19 to 39 years. We analyzed the condition of hemostasis system with help of developed hemostasiogramms that included tests characterizing angio-trombotcitic, coagulative links of hemostasis system, also anticoagulation, and fibrinolytic activity. Depending on character of volemic anomalies, the parturient woman were divided into two groups: the first group included 45 parturient women with indicators of deficiency of circulating blood volume – 19.11 ± 3.35 ml/kg, HB – 80.07± 3.62 g/l; Ht – 25.76± 3.28%, erythrocytes – 2.11± 0.76×10^{12}/l, the general fiber – 50.32 ± 3.19 g/l. The second group included 30 parturient women with deficiency of circulating blood volume of 26.11 ± 3.27 ml/kg, HB – 72.48 ± 3.44 g/l, Ht – 21.50± 2.61%, erythrocytes – 1.98 ± 0.38× 10^{12}/ l, the general fiber - 44.12 ± 2.61 g/l. Parturient women of the first group were subject to infusion-transfusion therapy (ITT) in volume of 48.9% of colloid, 46.5% - crystalloid solutions and a dextrose, fresh frozen plasma (FFP) −6.2%, 19.8% of concentrated erythrocytes. Total volume of ITT was 121.4% from the hemorrhage volume. Parturient women of the second group were subject to ITT in volume of 127.6% of deficiency circulating blood volume. 46.2% of deficiency was compensated by colloids, 46.8% - crystalloids, 24.8% of concentrated erythrocytes, FFP – 10.8%

Results: The comparison of results to indicators of healthy parturient women (control group n - 20) illustrated decrease of Ht on groups accordingly in 1.7 and 2.0 times, decrease of thrombocytes in 2.2 and 2.6 times, quantities of fibrinogen in 1.6 and 1.8 times, decrease of retraction of a clot in 1.7 and 1.8 times, elongation of activated partial thromboplastin time in 1.7–1.9 times, augmentation of MHO (IRN) to 2.2–2.5, decline of quantity of activity of factors of prothrombin complex on 48 and 59%, augmentation of fibrinolytic activity of blood, presence of products of degradation of fibrin and fibrinogen. Revealed results confirm connection of decrease of hemostatic potential of blood with volume of hemorrhage and conducted ITT, promoting development of hemodilution hemorrhages. Women of both groups had the ITT that was more or is less adequate in volume, though it was not possible to fully correct the hypovolemia, hence the volume of ITT should had been more in 1.8 times in volume than volume of circulating blood deficiency and be qualitative in composition structure including fresh frozen plasma as a carrier of plasma procoagulants.

Summary/Conclusions: The volume of ITT to parturient women of both groups was transfused without taking into account of deficiency of circulating blood volume, and also was of poor-quality that promoted depression of concentration and activity of plasma procoagulants, numbers of thrombocytes and promoted development of

hemodilution coagulopathy resulting from bleedings that in turn contributed to hemorrhage.

Adverse Events, incl. TRALI

P-755

PROSPECTIVE ASSESSMENT OF TRANSFUSION-RELATED IMMUNOMODULATION IN CARDIAC SURGERY PATIENTS

M Dean[1,2,3], A Perros[1,3,4], S Engkilde-Pedersen[1,3,4], K Rooks[1], F Chong[1], A Esguerra-Lallen[1,3,4], H Faddy[1,2,4], R Naidoo[5], J Tung[1,2,3,4], J Fraser[3,4], P Tesar[5], M Ziegenfuss[6], S Smith[5], D O'Brien[5] and R Flower[1,2]

[1]Research and Development, Australian Red Cross Blood Service, Kelvin Grove [2]Faculty of Health, Queensland University of Technology [3]Critical Care Research Group, The Prince Charles Hospital [4]School of Medicine, University of Queensland [5]Cardiothoracic Services [6]Adult Intensive Care Services, The Prince Charles Hospital, Brisbane, Australia

Background: Transfusion has the potential to modulate the recipient immune profile contributing to adverse outcomes collectively referred to as transfusion-related immunomodulation (TRIM). We developed a panel of assays to prospectively assess the impact of transfusion on the recipient immune profile using small blood volumes to align with the principles of patient blood management. Non-emergency coronary artery bypass grafting (CABG) patients were selected as the study population to investigate potential mechanisms associated with TRIM. Dendritic cells (DC) and monocytes are key immunoregulators and dysfunction may contribute to adverse outcomes, thus a number of assays are focused on these cells. Understanding the underlying mechanisms of TRIM and the impact of DC and monocyte dysfunction on mediating patient outcomes post-transfusion following is limited.

Aims: 1. Develop a panel of assays to prospectively investigate immune modulation using 10 mL of blood. 2. Assess immune profile at 5 time-points (admission, perioperative, ICU, day 3, day 5) in CABG patients (n=38) and investigate adverse patient outcomes in the sub-group of patients who received blood product transfusion (n=6).

Methods: We optimized a suite of assays to assess immune modulation using only 10 mL of blood: i) quantification of immune cell subsets (Trucount tubes), ii) quantification of DC activation/adhesion markers (Trucount tubes), iii) quantification of cytokines/chemokines in patient plasma (cytometric bead array), iv) assessment of gene expression in total leucocyte population (RNA extracted from whole blood) v) assessment of gene expression in isolated CD33+ myeloid cells, vi) characterize DC and monocyte activation and inflammatory response using an ex-vivo whole blood culture model in parallel with lipopolysaccharide (LPS) to model a bacterial complication. An association between inflammatory responses and adverse outcomes (prolonged intensive care unit (ICU) length of stay (LOS; >24 hrs) and prolonged ventilation time (VT; >8 hrs) for the overall patient cohort was assessed (Kruskal-Wallis, P<0.05). The impact on the DC and monocyte immune response and potential adverse outcomes in the transfused patient sub-group were assessed.

Results: CABG resulted in significant modulation of DC and monocyte immune responses with evidence of immunoparalysis. DC and monocyte cytokine dysfunction was associated with prolonged ICU LOS and VT. 16% (6/38) of patients received blood product transfusion (i.e. red cells, platelets). Preliminary analyses indicated that transfusion recipients were more likely to develop adverse outcomes with 67% having prolonged ICU LOS (vs. 34% of non-transfused patients) and 83% having prolonged VT (vs. 41% of non-transfused patients). In addition there was evidence of a differential immune response on day 3 and day 5 post-surgery in transfused patients.

Summary/Conclusions: We successfully developed a panel of assays to prospectively investigate the impact of transfusion on patient immune responses. Our preliminary data suggest that transfusion was associated with poor outcomes in CABG patients and we saw evidence of modulation of DC and monocyte responses. The panel developed here to prospectively assess changes in immune profile in CABG patients can be used in other clinical settings. Characterization of changes at the cellular level will facilitate improved understanding of the processes associated with TRIM.

P-756

TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD: BEST ELIMINATED WITH LASIX®? RESULTS OF A PILOT, DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL (TACO-BEL)

J Pendergrast[1,2], C Armali[1], C Cserti-Gazdewich[1,2], M Hansen[2,3], A Kiss[2,4], L Lieberman[1,2], Y Lin[2,5], N Parmar[6], D Scales[2,3], R Skeate[7] and J Callum[2,5]

[1]Laboratory Medicine Program, University Health Network [2]University of Toronto [3]Department of Medicine [4]Sunnybrook Research Institute [5]Department of Clinical Pathology, Sunnybrook Health Sciences Centre [6]University Health Network [7]Canadian Blood Services, Toronto, Canada

Background: Transfusion-Associated Circulatory Overload (TACO) is increasingly recognized as a cause of significant morbidity and mortality amongst transfusion-recipients, particularly those with a history of cardiac and renal disease. While diuretics are standard of care for the treatment of congestive heart failure, it is unclear whether they are safe and effective for the prevention of TACO. There is an urgent need for a well-conducted randomized controlled trial (RCT) to address this question.

Aims: To determine whether a double-blind RCT of pre-transfusion furosemide for the prevention of TACO in high-risk patients is feasible.

Methods: Pilot double-blind placebo-controlled RCT of 20 mg IV furosemide was performed in adult inpatients 65 years or older and scheduled to receive a single unit of RBCs during regular working hours. The primary outcome was the time required to have 80 patients complete the study protocol. Secondary feasibility outcomes included proportion of RBC transfusions meeting eligibility criteria (target ≥ 10%), proportion of eligible patients enrolled (target ≥ 25%), and proportion of eligible patients complying with study protocol (goal ≥ 80%). Clinical outcomes measured included the incidence of TACO using standard definitional criteria, related cardiac and respiratory complications, and the incidence of hyponatremia, hypokalemia, hypotension and acute renal injury.

Results: Nearly 10 months of enrollment was required before 80 patients completed the study protocol, a result of both fewer transfusions than expected meeting eligibility criteria (1.8% when analyzed at mid-trial) and of eligible patients consenting to participate (19.6%). Protocol compliance did not achieve 80% target primarily due to missing chart documentation by caregivers. Blinding was maintained through the study and during data analysis. Most enrolled patients were admitted for hematologic malignancy. 54% of enrollees had a history of cardiac disease, 30% had renal impairment and 33% were prescribed chronic diuretics. Treatment arms were well-balanced in regards to patient characteristics and transfusion therapy. A single case of TACO occurred in each arm of the study, for an overall incidence of 2.5% (95% CI 0.3–8.7%). Although volume status and chest imaging was not consistently performed in all patients, no difference was observed in post-transfusion change in vital signs or B-natriuretic peptide. No difference in cardiac or respiratory complications was observed, but there was a trend towards decreased 30-day mortality in patients randomized to pre-transfusion furosemide (5% v 17%, P = 0.09) which achieved statistical significance when extended to hospital length-of-stay (5% vs 24%, P =0.02). No difference between treatment arms was observed in regards to hyponatremia, hypokalemia, hypotension or renal injury.

Summary/Conclusions: The pilot protocol for pre-transfusion diuresis for the prevention of TACO will require modification to achieve target feasibility outcomes before a larger RCT can be performed. The dose of furosemide studied appeared to be safe and may be associated with improved clinical outcomes.

P-757

THE FREQUENCY OF RED CELL TRANSFUSIONS IN KELL ALLOIMMUNIZED FEMALES OF CURRENT AND FUTURE CHILD BEARING POTENTIAL

S Ning[1], P Morin[2], R Barty[2], Y Liu[2], N Li[2], A Elahie[2], M Zeller[2] and N Heddle[2]
[1]Department of Medicine [2]McMaster University, Hamilton, Canada

Background: Anti-K is an acquired red cell alloantibody with the ability to cause severe hemolytic disease of the fetus and newborn (HDFN) and fetal death. Previous studies report that 30–60% of anti-K antibodies detected during pregnancy may be related to red blood cell (RBC) transfusion; thus, provision of K negative units for women of current or future child bearing potential is the standard of care in many European countries. However, this practice is not mandated in Canada and the United States. A multinational retrospective study evaluating women with neonates suffering from severe HDFN reported that only 3% of alloantibodies were attributable to transfusion (Delaney M et al., 2017). These findings raise questions around the impact of transfusion as a cause of K alloimmunization. Furthermore, previous

studies have been limited to the obstetrical population and the incidence of anti-K alloimmunization in the pediatric population remains unknown.

Aims: Establish the frequency of RBC transfusion in females of current and future child bearing potential with anti-K antibodies.

Methods: This is a retrospective cohort study spanning Jan 1, 2007 – Jun 30, 2017 in Hamilton, Ontario, Canada. Kell-agnostic blood is provided to all patients at our institutions; exceptions include patients with a history of K alloimmunization and sickle cell patients. All females of current and future child bearing potential (age ≤ 50 during the study period) with anti-K antibodies documented during the study period were reviewed. Data was obtained via the Transfusion Registry for Utilization, Surveillance, and Tracking (TRUST) database, a comprehensive database containing blood product information on all transfused patients and demographic and clinical information on all hospitalized patients.

Results: From Jan 1, 2007 to Jun 30, 2017, a total of 345,052 units of RBCs were transfused at our institutions. Of these RBC transfusions, 36,836 units were transfused to 6,910 females age ≤ 50, with a median of 2 units (IQR 2, 5) per patient; 7,020 units were transfused to pediatric patients (age < 18), while 29,816 were transfused to adult patients (age ≥ 18). Group and screens were available following 23,366/36,836 (63.4%) of the RBC units transfused to females age ≤ 50. During the study period, there were a total of 239 females with detectable or previously detectable anti-K antibodies. Median age at time of antibody detection was 38 (IQR 28–44) and 22/239 (9.2%) patients were younger than age 18 at the time of initial antibody detection. Of the alloimmunized patients, 46/239 (19.2%) had at least one (median=5, IQR 3–11) RBC transfusion(s) preceding antibody detection.

Summary/Conclusions: RBC transfusion(s) preceded K alloimmunization in 19.2% of females with anti-K antibodies; an in-depth chart review of these patients is underway. Transfusion services without a policy to provide K-negative units to females of childbearing potential should consider clinical impacts of this practice and monitor for K alloimmunization post transfusion.

P-758
ACUTE HAEMOLYTIC TRANSFUSION REACTION DUE TO ANTI-MTA

V Claes[1], M Deleers[1], T Peyrard[2] and H El Kenz[1]
[1]CHU Brugmann, Brussels, Belgium [2]CNRGS, Paris, France

Background: Mta (MNS14) is a low-frequency antigen of the MNS system. Some rare cases of haemolytic disease of the foetus and newborn (HDFN) caused by anti-Mta have been reported in the literature, but this antibody has never been associated with a haemolytic transfusion reaction (HTR). An acute HTR was suspected in a 38-year-old patient of Congolese origin with sickle cell disease (HbSS) undergoing an exchange transfusion with four red blood cell (RBC) units prior to surgery.

Aims: To report the first HTR caused by anti-Mta.

Methods: Pretransfusion testing included ABO, Rh and Kell typing as well as an antibody screening test with an indirect antiglobulin test (IAT) (column agglutination technique, Bio-Rad). Posttransfusion samples were collected and tested using a direct antiglobulin test (DAT) with the patient's plasma. Transfused RBC units were crossmatched with the patient's plasma. In-house reagents were used for antibody identification and the testing of Mta and Wra phenotypes.

Results: Shortly after the start of transfusion of the third packed RBC unit, the patient developed shivering, nausea, dyspnea and pain in the lower limbs. Laboratory parameters showed signs of increased haemolysis. A positive crossmatch with one of the packed RBC units, in spite of a negative pretransfusion antibody screening test, suggested the presence of an antibody against a low-frequency antigen. The posttransfusion DAT was negative. Antibody identification showed anti-Wra (anti-DI3) and anti-Mta. The patient's RBCs were phenotyped as Wr(a−) and Mt(a−). The donor's RBCs were found to be Wr(a−) and Mt(a+).

Summary/Conclusions: Anti-Mta was most likely the cause of the transfusion reaction experienced by this patient. Negative DAT might be explained by rapid destruction of transfused Mt(a+) RBCs. A few cases of HDFN caused by anti-Mta have been published earlier, but this is the first reported HTR. This case highlights the inability of an antibody screening test to detect antibodies against low-frequency antigens, like anti-Mta. Routinely performing a full crossmatch test for patients with sickle cell disease receiving multiple transfusions, even in the presence of a negative antibody screening test, might add to the safety of the transfusion management of these patients.

P-759
CLINICAL SIGNIFICANCE OF ANTI-A/B IN MINOR INCOMPATIBLE WHOLE BLOOD AND PLASMA TRANSFUSIONS USING A MONOCYTE SUSPENSION ASSAY THAT DETECTS FC GAMMA- AND C3B-RECEPTOR MEDIATED ERYTHROPHAGOCYTOSIS

P Pandey[1], W Anani[1,2], T Pugh[3] and G Denomme[1,3]
[1]Blood Research Institute, Versiti/BloodCenter of Wisconsin [2]Department of Pathology, Medical College of Wisconsin [3]Immunohematology Reference Laboratory, Versiti/BloodCenter of Wisconsin, Milwaukee, United States of America

Background: Transfusion of low titer, Group O whole blood in emergency situations and plasma/apheresis platelet products is becoming an accepted clinical practice. Despite the provision of apparent low isohemagglutinin titer products, unforeseen adverse hemolytic events have been observed in some transfusion recipients. In vitro monocyte monolayer assay is an established pre-transfusion testing method to predict the clinical significance of red blood cell (RBC) antibodies by measuring monocyte mediated phagocytosis of antibody-opsonized RBCs. Monocytes phagocytose sensitized RBCs via IgG- and complement C3b- receptors. We have developed a fluorescence-based monocyte suspension assay (MSA) to assess ABO antibodies.

Aims: Evaluate the ability of a MSA to detect significant anti-A/B IgG- and C3b-mediated monocyte phagocytosis. We evaluated monocyte phagocytosis of RBCs sensitized with IgG anti-A having hemolysin activity, alone and in combination with fresh serum as a source of complement.

Methods: Monocytes were isolated from ACD blood of healthy donors by density gradient centrifugation and purified using CD14 positive selection. A 5% suspension of RhD+ RBCs were labeled with CFDA-SE. Labeled RBCs were sensitized as follows: i) anti-RhD IgG3 (BRAD3) sensitized R2R2, R1R1, and R1r RBCs, ii) BRAD3 plus murine monoclonal IgM anti-A (titer = 6000) with fresh individual Group A serum (n = 5) as a source of complement, and iii) Group O serum samples (n = 5; anti-A hemolysin titer ≤4) used to sensitize A1+ RBCs (titer 200) with and without fresh pooled A sera as a source of complement. Phagocytosis was performed by co-incubating sensitized RBCs with monocytes at 37°C for 30 min. Non-ingested RBCs were lysed using cold NH_4Cl. Flow cytometry was performed and fluorescence in FL1 channel (515–550 nm) was recorded. FcγR-mediated phagocytosis was confirmed by inhibition with IVIG (0.01 μg/ml to 1000 μg/ml).

Results: Phagocytosis was proportional to the density of RhD on RBCs (R2R2>R1R1³R1r). A single of source of monocytes had maximum phagocytosis from 84% to 92% (R2R2) over 5 independent experiments. The 50% inhibition of FcγR-mediated phagocytosis by IVIG (IC50) was achieved at 7±2 μg/ml (n = 3). RBCs with complement C3b activation using IgM anti-A alone showed ≤6% phagocytosis (n = 5). A 52% increase in phagocytosis was observed with BRAD3 plus IgM anti-A, and complement C3b sensitization vs BRAD3 alone. Complement C3b hemagglutination correlated with the percent increase in phagocytosis. The 5 IgG anti-A hemolysin sera did not show significant phagocytosis in the absence of complement C3b activation. A 6 fold increase in phagocytosis upon complement C3b activation was observed for 1 of 5 IgG anti-A hemolysin sera.

Summary/Conclusions: We have validated monocyte phagocytosis assay using monocytes in suspension (MSA). MSA can detect Fcγ- and C3b-receptor mediated phagocytosis in a dose-dependent manner. The MSA could be used to assess the biological significance of Anti-A/B in whole blood and plasma/apheresis platelet products used for ABO-minor incompatible transfusions.

P-760
CARDIAC STRESS BIOMARKERS AFTER RED CELL TRANSFUSION IN PATIENTS AT HIGHER RISK FOR TRANSFUSION ASSOCIATED CIRCULATORY OVERLOAD: A PROSPECTIVE OBSERVATIONAL STUDY

JL Callum[1,2], R Cohen[2], A Cressman[3], R Strauss[2], C Armali[2], Y Lin[1,2], J Pendergrast[1,4], L Lieberman[1,4], D Scales[2,5], R Skeate[6], H Ross[7] and C Cserti-Gazdewich[1,4]
[1]Laboratory Medicine and Pathobiology, University of Toronto [2]Department of Lab Med and Molecular Diagnostics, Sunnybrook Health Sciences Centre [3]Department of Medicine, University of Toronto [4]University Health Network [5]Department of Critical Care, Sunnybrook Health Sciences Centre [6]Canadian Blood Services [7]Ted Rogers Centre of Excellent in Heart Function, University Health Network, Toronto, Canada

Background: Transfusion-associated circulatory overload (TACO) is a leading cause of serious reactions. Little is known regarding the value of cardiac biomarkers as a

predictor of TACO, in differentiating TACO from other dyspneic reactions, or the optimal timing/thresholds. Although an elevation in the level of cardiac biomarkers is included in some diagnostic criteria for TACO, guidance on the timing of measurement, thresholds, or fold-rise from pre- to post-transfusion is not provided.

Aims: Prospectively evaluate the kinetics of cardiac biomarkers from pre-transfusion to 24 h post-transfusion.

Methods: Prospective observational study of inpatients at higher risk for TACO (age≥50) receiving 1 red cell unit. Cardiac biomarkers, brain natriuretic peptide (BNP), N-terminal pro-BNP (NT-proBNP), and high sensitivity troponin was measured at baseline, at 6–12 h (except troponin), and at 18–24 h post-transfusion. Primary outcome: critical rise (-CR) in biomarkers (>1.5-fold rise and exceeding a threshold) at 18–24 h.

Results: 51 patients analyzed; 29% had pre-existing cardiovascular disease, 73% had ≥1 cardiac risk factors, and 50% took cardiac/antihypertensive therapies. No reactions that met guidelines were observed; 8 (16%) developed rise in systolic pressure ≥30 mmHg and 4 (8%) reported dyspnea/cough. At baseline, BNP level was >100 ng/L in 59% and NT-proBNP was >300 pg/ml in 83%. Critical rises in biomarkers was common: 25% had a BNP-CR, 33% had a NT-proBNP-CR, and 2% had a troponin-CR at 18–24 h. Overall, 38% had at least one biomarker-CR and the NT-proBNP to BNP concordance was 84%. The highest biomarker yield was the NT-proBNP (>1.5 fold rise and >300 pg/ml) at 18–24 h. Critical rise of NT-proBNP at 18–24 h was associated with an elevation in systolic blood pressure after transfusion (5 of 15 patients with elevated NT-pro BNP vs. 2 of 32 patients without elevation in NT-proBNP had a rise in blood pressure; P=0.02).

Summary/Conclusions: In higher risk patients for TACO, baseline elevation in biomarkers is common and critical rises occur in a third. The optimal measurement interval as a surrogate marker for TACO is at 18–24 h post-transfusion. Larger studies are needed to clarify the risk of TACO for a given pre-transfusion biomarker profile and the correlation between TACO and rise in biomarkers post-transfusion.

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TRANSFUSION–ASSOCIATED CIRCULATORY OVERLOAD AMONG THE INPATIENT U.S. ELDERLY DURING 2011–2017

M Menis[1], R Forshee[1], H Izurieta[1], Z Kessler[2], B Kim[2], R Warnock[2], S Verma[2], S McKean[2], J Kelman[3] and S Anderson[1]

[1]FDA/CBER, Silver Spring [2]Acumen LLC, Burlingame [3]CMS, Baltimore, United States of America

Background: Transfusion-associated circulatory overload (TACO) is a serious complication that accounts for significant transfusion morbidity and mortality in the U.S.

Aims: To assess TACO occurrence and potential risk factors in the U.S. elderly transfused in the inpatient setting during the 2011–2017 study period.

Methods: Our retrospective claims-based study utilized large Medicare databases for January 1, 2011 through April 30 2017. Blood transfusions were identified by recorded procedure and revenue center codes. TACO was ascertained by recorded ICD-9-CM diagnosis code 276.61 and ICD-10-CM diagnosis code E87.71. Our study evaluated TACO rates (per 100,000 inpatient transfusion stays) among the elderly, overall and by calendar year, age, sex, race, blood components and number of units transfused. Fisher's exact tests were performed to compare TACO rates, and Cochran-Armitage tests were used to ascertain trends by calendar year, age, and transfusion volume.

Results: Of 12,344,025 inpatient transfusion stays for elderly Medicare beneficiaries, 9,905 had TACO recorded, an overall rate of 80.2 per 100,000 stays. The annual TACO rates during the 2011–2017 study period were 62.9, 68.0, 76.3, 80.1, 89.4, 106.2, and 110.3, respectively (P<0.001). TACO rates by number of units transfused were: 37.1 for 1 unit, 75.2 for 2–4 units, 124.1 for 5–9 units, and 160.0 for >9 units (P<0.001). TACO rates by blood component groups were: 84.6 for RBCs only, 66.7 for plasma only, 40.0 for platelets only, 71.1 for platelets and plasma, 204.0 for RBCs and plasma, 202.9 for RBCs and platelets, and 186.6 for RBCs, plasma, and platelets. Rates for age categories 65–69, 70–74, 75–79, 80–84, 85 and over were 55.7, 68.7, 78.4, 88.7, and 106.0, respectively (P<0.001). Females and males had TACO rates of 89.2 and 69.2 (P<0.001); whites and non-whites had rates of 84.0 and 62.9 (P<0.001).

Summary/Conclusions: Our multi-year population-based study on TACO occurrence is the largest-to-date among the U.S. elderly Medicare beneficiaries. It shows significantly increasing TACO occurrence trends over time, with greater number of units transfused, and with advancing age. The study suggests higher TACO risk for stays with RBCs transfused either alone or in combination with platelets and/or plasma. The findings also suggest significantly increased TACO risk in females and in whites,

which need further confirmation. The study was based on claims data, and thus limitations include potential under- or mis-recording of transfusion procedures and number of units, as well as lack of clinical detail to validate recorded TACO diagnosis.

P-762

DONOR DERIVED ANTI-JKA AND PASSENGER LYMPHOCYTE SYNDROME IN A LIVER TRANSPLANT RECIPIENT

R Jug, M Combs, N Bandarenko and J Poisson

Pathology, Duke Health, Durham, United States of America

Background: A 60-year-old O+ female with a negative pre-transplant red cell antibody screen (ABSC) developed a new red cell antibody post ABO-type compatible cadaveric liver transplant (9/9/2017) for non-alcoholic steatohepatitis. She received 3 units of red blood cells (RBCs) intra-operatively and 1 unit of RBCs on post-operative day (POD) 3 with no issues. Hemoglobin (HGB) levels dropped from 9.1 g/dl POD 3 to 7 g/dl on POD 10 prompting transfusion of an RBC unit, crossmatch (XM) compatible with most recent type and screen (T&S) sample. While blood was infusing, a new T&S was received which revealed a positive ABSC and a new anti-Jka. As a result, the transfusion was discontinued immediately. The patient was asymptomatic. Pre and post-transfusion direct antiglobulin tests (DAT) were positive (POD 10).

Aims: Determination of the clinical significance and source of new anti-Jka.

Methods: Patient's pre- and post-transplant DAT and hemolysis markers (e.g. total bilirubin (TB), lactate dehydrogenase (LDH)) were tested. Antibody elution from DAT-positive RBCs was performed using Hemobioscience ELUclear elution kit. The eluate was tested by PEG indirect antiglobulin test. The patient's predicted phenotype was determined using molecular microarray (Human Erythrocyte Antigen Bead-ChipTM, BioArray Solutions). Lymphoid microchimerism assay was conducted using polymerase chain reaction mediated amplification and subsequent size analysis of short tandem repeats to determine the peripheral blood recipient and/or donor cell composition.

Results: Pre-transplant and post-transplant DATs were negative until POD 10 when DAT was polyspecific 2+ (range 1–4+) IgG 1+, and C3 2+. RBC elution demonstrated anti-Jka. Pre-transplant/transfusion blood sample from the recipient demonstrated Jk(a+) phenotype. Anti-Jka was detected in organ donor plasma. Urinalysis showed 2+ bilirubin, serum TB was 2.3 mg/dl (N: 0.5–1.5 mg/dl), and LDH was elevated (269 U/L; N: 100–200 U/L). Lymphoid microchimerism performed POD 12 did not detect donor-derived T- and B-lymphocytes in peripheral whole blood or CD3+ fractions. Two months later, the DAT remained positive: Polyspecific 1+, with IgG w+, and C3 w+ (w+= very weak). RBC elution again demonstrated anti-Jka. LDH remained elevated (279 U/L) and HGB was 10.5 g/dl while TB was normal at 0.8 mg/dl.

Summary/Conclusions: The serological evidence of hemolysis, along with the patient's clinical course is consistent with a hemolytic transfusion reaction due to passenger lymphocyte syndrome (PLS) mediated by donor lymphocyte derived anti-Jka. This is the first report of PLS in a liver transplant recipient involving the Kidd blood group system. The presence of anti-Jka pre-transplant in the organ donor, followed by detection of anti-Jka in the Jk(a) antigen positive recipient suggests donor derived lymphocyte antibody production. Lymphoid PCR microchimerism analysis, however, did not detect donor lymphocytes circulating in the patient's blood. Poor or insufficient DNA quality/quantity may be related to the delay in sample collection following multiple transfusions. Two months post-op, the patient's HGB remains stable at 10.5 g/dl despite persistence of donor derived anti-Jka by elution.

P-763

RECURRENT REACTION TO RH IMMUNE GLOBULIN ADMINISTRATION IN A PERINATAL PATIENT RECEIVING ROUTINE ANTI-D PROPHYLAXIS

O Prokopchuk-Gauk[1], G Peters[2], G Clarke[3] and S Rutledge Harding[1]

[1]Pathology and Laboratory Medicine [2]Internal Medicine, Royal University Hospital, Saskatoon [3]Canadian Blood Services, Edmonton, Canada

Background: Administration of the polyclonal, plasma-derived anti-D product Rh Immune Globulin (RhIg) is part of routine care in the perinatal setting to prevent maternal Rh D alloimmunization. Significant adverse reactions to RhIg are rare.

Aims: We report a case of repeated Grade 2 allergic reaction following perinatal administration of RhIg to a Group O, Rh negative Caucasian woman during her second pregnancy. She had no allergy history, and an uneventful transfusion history, which included routine RhIg prophylaxis via intramuscular injection during her first pregnancy and one unit of red blood cells following post-partum hemorrhage.

Methods: A retrospective chart review was undertaken. The RhIg product administered was WinRho® (Aptevo BioTherapeutics LLC, USA). Different lot numbers of product were administered at each WinRho® exposure.

Results: A 26-year-old G2P1 woman presented to hospital with dehydration from severe gastroenteritis at 30 weeks gestational age. Following clinical stabilisation with intravenous (IV) fluid support, it was noted that she had not yet received RhIg during this pregnancy. Normal pre-transfusion vital signs were recorded and a standard dose of WinRho® 1500 IU was administered by IV push. Within seconds the patient described symptoms of chest constriction and dyspnea, flushing and light-headedness. Vital sign abnormalities recorded two minutes after WinRho® administration included marked tachypnea and hypoxemia on room air; blood pressure and heart rate were normal. Fetal bradycardia was documented during this event. She stabilized within minutes of applying oxygen and the administration of antihistamine and steroid medications. Epinephrine was not required. Results of investigations done eight weeks following this acute allergic reaction included normal serum IgA, haptoglobin, C3 and C4 levels. Allergy prick tests with undiluted WinRho® and intradermal tests at 1:100 and 1:10 yielded no reaction. Post-partum neonatal cord blood testing confirmed an Rh positive baby. According to a planned protocol, she received antihistamine pre-medication, followed by a graded-dose IV infusion of WinRho® 1500 IU over 1.5 h under observation. The infusion period was uneventful. However, 30 min after the infusion ended, the patient developed throat scratchiness and prominent swelling to the face and hands. IV steroids were administered immediately, causing all symptoms to resolve within an hour. No associated hypotension or hypoxemia was documented.

Summary/Conclusions: To our knowledge, this is the first case of repeat RhIg reaction to be published. These Grade 2 allergic reactions were reported the manufacturer, who ultimately concluded that there was no identifiable product-associated cause for the reactions. Potential explanations for the repeat reactivity may include an idiosyncratic donor-recipient reaction of unknown etiology; recipient presence of a rare protein deficiency and complimentary anti-protein antibody not yet identified; or unexplained reaction to a component or additive within the WinRho®. Strategies for minimizing future RhIg reactions include use of product from a different manufacturer, pre-medication with antihistamine and steroid medications, plus application of a graded-dose IV infusion protocol under close observation in a hospital setting. Finally, confirmation of an Rh negative fetal status by non-invasive methods antenatally may eliminate the need for RhIg administration altogether.

POST TRANSFUSION PURPURA (PTP) AND IMMUNE THROMBOCYTOPENIC PURPURA (ITP) IN THE SAME PATIENTS; CO-INCIDENCE OR MORE?

A Shokoohi[1], I Sabet[2], E Burrows[3], S Reddivari[1], J Birchall[1] and R Ahya[1]

[1]Clinical, Welsh Blood Service, Pontyclun [2]Haematology, CWM Taf University Health Board, Llantrisant [3]WTAILS, Welsh Blood Service, Pontyclun, United Kingdom

Background: Post transfusion purpura (PTP) is a rare complication of blood transfusion characterised by severe thrombocytopenia and refractoriness to platelet transfusion. PTP usually occurs 3–12 days after blood transfusion and is due to the presence of alloantibodies against Human Platelet Antigens (HPA). Immune Thrombocytopenic Purpura (ITP) is a more common autoimmune condition irrelevant to blood transfusion and due to abnormal autoantibodies with specificity for platelet membrane glycoproteins.

Aims: We present a new case of PTP in a patient with background chronic thrombocytopenia due to ITP. We are not aware of any other published reports where PTP has been diagnosed in a patient with ITP. Furthermore, we review another PTP case in whom a new diagnosis of ITP was made a few weeks after treatment for PTP.

Methods: A 75-year-old multiparous female was admitted with abdominal pain and acute rectal bleeding. She was on clopidogrel. An urgent endoscopy confirmed duodenal ulcer and oesophagitis. In admission she had HB:96 g/l and platelet:43 × 10⁹/l. She was transfused with two units of red cells and two units of platelet. There was poor increments after platelet transfusion but considering the history of chronic mild thrombocytopenia, it was deemed to be due to ITP. Patient was re-admitted 5 days after discharge with a further episode of abdominal pain, dark stool and purpura on her legs. FBC (10 days post transfusion of blood products in the first stay in hospital) confirmed platelet: 5 × 10⁹/l.

Results: In this admission, differential diagnosis of PTP or acute on chronic ITP was made and considering possibility of further GI bleeding, she was transfused another two units of platelets. She was also received IVIG x2gr with no response and therefore was offered methyl prednisolone x 2gr. A bone marrow examination did not show any dysplasia or other primary bone marrow changes and was in keeping with consumptive thrombocytopenia. Also a CT scan ruled out splenomegaly. Serological investigation confirmed presence of HPA-1a alloantibody and diagnosis of PTP. She received two units of HPA-matched platelets with very good increment. She also received another doses of IVIG. Despite some further drops in her platelets count before discharge, they were gradually increased and her platelets count four weeks after last treatment is 100 × 10⁹/l.

Summary/Conclusions: Based on our literature review, our case is the only confirmed PTP case with prior history of ITP. We are aware of only another case in whom ITP was diagnosed a few weeks after diagnosis of PTP. This was a 61-year-old female with multiple injuries following a road traffic accident. She received several blood components. Her normal platelet count in admission was dropped to 5 × 10⁹/l on day 15 post transfusions. She had extensive mucocutaneous bleeding symptoms and had no increments with further platelet transfusion. She also received IVIG X2gr with little clinical benefits. serological investigations confirmed HPA-1a alloantibody and she was treated with plasma exchange x 4. Three days after further dose of IVIG, her platelet count rose to 448 × 10⁹/l. One month later, however, she had platelet count of 43 × 10⁹/l and further investigation confirmed the diagnosis of ITP. There have been reports of association between HPA polymorphism and chronic ITP. In addition, there has been at least one published report of concomitant diagnosis of PTP with Heparin Induced Thrombocytopenia (HIT), another immune thrombocytopenia. it is possible that there is a common immunological susceptibility among patients with acquired immune thrombocytopenia.

TRANSFUSION–RELATED ACUTE LUNG INJURY (TRALI) AMONG THE INPATIENT U.S. ELDERLY DURING 2007–2017

M Menis[1], R Forshee[1], H Izurieta[1], Z Kessler[2], S McKean[2], R Warnock[2], S Verma[2], B Kim[2], J Kelman[3] and S Anderson[1]

[1]FDA/CBER, Silver Spring [2]Acumen LLC, Burlingame [3]CMS, Baltimore, United States of America

Background: Transfusion-Related Acute Lung Injury (TRALI) is a serious complication that accounts for significant transfusion morbidity and mortality in the U.S.

Aims: To assess TRALI occurrence and potential risk factors in the U.S. elderly transfused in the inpatient setting during the multi-year study period.

Methods: Our retrospective claims-based study utilized large Medicare databases for the January 1, 2007-April 30, 2017 study period. Blood transfusions were identified by recorded procedure and revenue center codes, whereas TRALI was ascertained via the ICD-9-CM diagnosis code 518.7 and ICD-10-CM diagnosis code J95.84. Our study evaluated TRALI rates (per 100,000 inpatient transfusion stays) among the elderly, overall and by calendar year, age, sex, race, blood components and number of units transfused. Fisher's exact tests were performed to compare TRALI rates, and Cochran-Armitage tests were used to detect trends by calendar year, age, and transfusion volume.

Results: Of 21,625,936 inpatient transfusion stays for elderly Medicare beneficiaries, 7,004 had TRALI recorded, an overall rate of 32.4 per 100,000 stays. The annual TRALI rates in 2007–2017 were 14.5, 17.9, 20.7, 25.2, 35.4, 39.6, 39.7, 44.9, 46.4, 46.8, and 51.1, respectively (P<0.001). TRALI rates by number of units transfused were: 16.4 for 1 unit, 21.3 for 2–4 units, 44.3 for 5–9 units, and 130.1 for >9 units (P<0.001). TRALI rates by blood component groups were: 24.1 for RBCs only, 36.8 for plasma only, 49.3 for platelets only, 102.7 for platelets and plasma, 78.1 for RBCs and plasma, 126.9 for RBCs and platelets, and 259.4 for RBCs, plasma and platelets. Rates for age categories 65–69, 70–74, 75–79, 80–84, 85 and over were 40.1, 37.5, 34.5, 28.0, and 23.5, respectively (P<0.001). Females and males had TRALI rates of 31.3 and 33.8 (P=0.001); whites and non-whites had rates of 33.7 and 25.8 (P<0.001), respectively.

Summary/Conclusions: Our eleven-year population-based study on TRALI occurrence is the largest-to-date among the U.S. elderly. It shows significantly increasing TRALI occurrence trends over time and with greater number of units transfused. In contrast, a significant decline in TRALI risk was identified with older age. The study also suggests increased TRALI risk with platelets transfused, especially in combination with RBCs and/or plasma, as well as possible effects of sex and race, which need further investigations. The study was based on claims data, and thus limitations include potential under- or mis-recording of transfusion procedures and number of units, as well as lack of clinical detail to validate recorded TRALI.

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Abstract has been withdrawn

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THROMBOTIC EVENT (TE) OCCURRENCE AMONG THE U.S. ELDERLY TRANSFUSED IN THE INPATIENT SETTING, AS RECORDED IN LARGE MEDICARE DATABASES DURING 2009–2015

M Menis[1], H Izurieta[1], Y Lu[1], S McKean[2], B Kim[2], Z Kessler[2], R Warnock[2], S Verma[2], J Kelman[3], S Anderson[1] and R Forshee[1]

[1]FDA/CBER, Silver Spring [2]Acumen LLC, Burlingame [3]CMS, Baltimore, United States of America

Background: Blood transfusion(s) may increase risk of serious thrombotic events (TEs) that can result in death. To our knowledge, there are no recently published population-based studies evaluating potential transfusion-related TEs among the U.S. elderly.

Aims: The objective of our study was to assess TE occurrence and potential risk factors among elderly Medicare beneficiaries, ages 65 and older, transfused in the inpatient setting during 2009–2015.

Methods: This retrospective claims-based evaluation utilized large Medicare administrative databases during January 2009 through September 2015 period, in coordination with the Centers for Medicare & Medicaid Services. Inpatient blood transfusion stays were identified by ICD-9-CM procedure and revenue center codes. TEs not present at the hospital admission were ascertained via ICD-9-CM diagnosis codes recorded during inpatient transfusion stays. Our study evaluated TE rates per 100 inpatient transfusion stays among elderly Medicare beneficiaries, overall and by age, gender, race, blood components and number of units transfused. The study used Chi-squared tests to compare TE rates and Cochran-Armitage tests to assess TE occurrence trends by calendar year, age, and number of units transfused.

Results: Among 5,380,239 inpatient transfusion stays for elderly beneficiaries, 226,966 had a TE diagnosis code recorded, for an overall rate of 4.2 per 100 stays: 132,884 (58.5%) had arterial TEs, a rate of 2.5; 86,129 (37.9%) had venous TEs, a rate of 1.6; and 7,953 (3.5%) had both types of TEs recorded, a rate of 0.1. The overall TE-case mortality was 19.7%. Annual TE rates (per 100) were 3.8 in 2009, 4.0 in 2010, 4.5 in 2011, 4.5 in 2012, 4.4 in 2013, 4.5 in 2014, and 4.1 in 2015 (P<0.001). TE rates by blood component groups were: 3.6 for RBCs only, 3.1 for plasma only, 3.7 for platelets only, 6.4 for platelets and plasma, 6.1 for RBCs and plasma, 6.3 for RBCs and platelets, and 10.7 for RBCs, plasma, and platelets. TE rates for age categories 65–69, 70–74, 75–79, 80–84, and ≥85 were 4.1, 4.4, 4.5, 4.3, and 3.9 respectively (P<0.001). Females and males had TE rates of 3.9 and 4.6 (P<0.05); whites and non-whites had TE rates of 4.2 and 4.4 (P<0.05), respectively. TE rates by number of units transfused were: 3.1 for 1 unit, 3.4 for 2–4 units, 6.0 for 5–9 units, and 10.4 for >9 units (P<0.001).

Summary/Conclusions: Overall, our large population-based investigation showed that among transfused inpatient elderly, the TE rates varied by calendar year, demographics, blood components and number of units transfused. The study suggests a potentially increasing TE occurrence trends over time and with greater number of units transfused. The findings also suggest higher TE rates for stays with platelets transfused in combination with plasma and/or RBCs as well as higher TE risk for males vs. females and for non-whites vs. whites. TE rates also significantly changed with advancing age, which needs further investigation. The study limitations include potential under- or misrecording of transfusion procedures, units, and diagnosis codes, as well as lack of clinical details to validate TEs. Future investigations are needed for further evaluation of underlying risk factors for TE occurrence.

Haemovigilance and Transfusion Safety

P-768

BIOLOGICS EFFECTIVENESS AND SAFETY INITIATIVE: INCORPORATING ISBT-128 CODES INTO OHDSI'S OMOP COMMON DATA MODEL TO BUILD A NATIONAL HEMOVIGILANCE SYSTEM TO MONITOR TRANSFUSION-RELATED ADVERSE EVENTS

J Obidi[1], K Chada[1], J Gruber[1], G Dores[1], E Storch[1], A Williams[1], J Banda[2], S Gombar[2], D Balraj[2], R Hayden[3], P Biondich[3], S Grannis[3], G Hripcsak[4,5], T Falconer[4,5], K Natarajan[4,5], D Dymshyts[6], S Dempster[7], C Reich[7], N Selvam[7], N Williams[7], S Anderson[1] and A Shoaibi[1]

[1]Center for Biologics Evaluation and Research, Office for Biostatistics and Epidemiology, U.S. Food and Drug Administration, Silver Spring [2]Stanford University, Stanford [3]Regenstrief Institute, Indianapolis [4]Columbia University [5]Observational Health Data Sciences and Informatics, New York [6]Odysseus Data Services, Cambridge [7]IQVIA, Durham, United States of America

Background: The U.S. FDA Center for Biologics Evaluation and Research (CBER) regulates whole blood and blood components used for transfusion among other biologics. One of CBER's goals is to protect blood recipients by monitoring transfusion-related adverse events (AEs), leading to the need to build a national hemovigilance system. CBER recently established the Biologics Effectiveness and Safety (BEST) Initiative, a component of the CBER Sentinel Program. The BEST Initiative, a distributed network of data providers, applies a common data model (CDM) and utilizes claims and electronic health record (EHR) data sources which capture health care exposures, treatment, and outcome data. The most detailed blood product data is included in the Information Standard for Blood and Transplant (ISBT)-128 coding system. ISBT-128 codes add specificity and granularity to the surveillance of blood products which other coding systems lack.

Aims: The aim of this study is to build the infrastructure for a national hemovigilance system using EHR data sources to monitor transfusion-related AEs by incorporating the ISBT-128 coding system into the Observational Medical Outcomes Partnership (OMOP) common data model (CDM) of the Observational Health Data Sciences and Informatics (OHDSI) consortium.

Methods: We explored three BEST EHR databases that cover approximately 24 million patient records from geographically diverse areas of the US. We added a library of 14,543 ISBT-128 codes to the OMOP CDM. We determined the type and frequency of ISBT-128 codes used in patient records from 2015–2017 within the blood banks of participating independent EHR data providers participating in the BEST Initiative. To identify additional blood and blood components, we also explored mapping standard terms used in blood banks prior to 2015 to ISBT-128 codes.

Results: f the three EHR data providers, two have completed review their database (site A and B). Of the 14,543 codes, the two sites consistently used approximately 100 ISBT-128 codes. Among the 5.5 million (database A) and 2.3 million (database B) patient records, the frequency of all utilized codes was 536,097 and 426,826 (respectively). The most commonly used codes were E0357 (AS-3 Red Blood Cells Leukocytes Reduced Irradiated) and E0401 (AS-5 Red Blood Cells Leukocyte Reduced). Within EHR database A, E0357 accounted for 33% of all ISBT-128 codes compared to less than 0.03% within EHR database B. The most frequent code used within EHR database B was E0401 which accounted for 26.7% of all the ISBT-128 codes compared to 0.66% within EHR database A. Red blood cells (63.4%, 62.0%) accounted for most blood components used in database A and B (respectively), followed by plasma (15.5%, 22.2%), and then platelets (17.2%, 13.7%).

Summary/Conclusions: Incorporation of ISBT-128 codes into the OMOP CDM has furthered CBER's capability to monitor the frequency of transfusion and transfusion-related AEs. We have demonstrated that ISBT-128 codes are captured within the BEST EHR databases. The addition of ISBT-128 codes is a critical part of the hemovigilance infrastructure that will afford FDA the ability to conduct active monitoring of transfusion-related AEs.

P-770

HAEMOVIGIL, A NEW SYSTEM TO PREVENT WRONG BLOOD IN TUBE (WBIT) AND TRANSFUSION ERRORS DUE TO PATIENT MIS-IDENTIFICATION: ONE YEAR EXPERIENCE AT A TERTIARY HOSPITAL IN INDIA

GR Wankhede[1] and S Pathak[2]

[1]Transfusion Safety, Jeevan Jyoti Blood Bank and Components, Nagpur [2]Transfusion Medicine, Max Super Speciality Hospital, New Delhi, India

Background: Transfusion is a multistep and multidisciplinary process, often subjected to human errors. Wrong blood in tube (WBIT) and failure to identify recipients before transfusion leads to devastating consequences, such as ABO incompatible transfusion. The latest Serious Hazards of Transfusion (SHOT) report mentions WBIT as the most frequent error; 60.5% of all near misses that caused three incorrect blood transfusions (IBCT) in 2016. Even without patient harm, time and effort is required to investigate these issues and patients are inconvenienced by sample re-collection and delayed transfusion.

Aims: We used a novel intervention; Haemovigil, an end-to-end software and electronics driven system to prevent

i) WBIT

ii) Issue of incorrect components

iii) Incorrect/no patient identification at bedside

Methods: Haemovigil comprises of: 1. Haemovigil Wristbands for recipients - consist of a unique 6-digit number and 6 peel-off labels with encrypted alphabetic codes (to be affixed on specimen tubes during phlebotomy), 2. Haemovigil Software in the Blood Bank – that decrypts the alphabetic code on the label on specimen tube and generates the same 6-digit number on Haemovigil Wristband, 3. Digital Transporter – An insulated box with a digital lock; lockable by entering the 6-digit number generated by the software and opened by the same number present (only) on recipient's Haemovigil Wristband. We analysed data of one year to assess number of transfusion errors prevented/detected by Haemovigil.

Results: 5300 patients were provided Wristbands and 9753 components were transfused to these patients and four errors were detected/prevented by Haemovigil. 1. One case of WBIT: The sample was collected from patient who wasn't the intended recipient. At the time of transfusion, the Digital Transporter did not open and the Haemovigil system confirmed that sample was drawn from the wrong patient. 2. One case of wrong requisition/ordering form: Sample was collected from correct patient, but the requisition form was of another patient. This error was noted at sample receiving window of the blood bank, but even if this was overlooked, the Haemovigil system would have prevented the access of the blood component at bedside since the unit would have gone to recipient whose form was sent, but the 6 digit lock would have been from the patient whose sample was sent. 3. One instance of Haemovigil Wristband being removed so final bedside identification couldn't be done and component not accessed. 4. One case of wrong component requisition: A patient's reserving requisition was for plasma, while issue form was that for platelets. Since Haemovigil software stores reserved components data; it didn't allow issue of blood component.

Summary/Conclusions: SHOT has identified nine critical steps in transfusion process, of which sample collection and patient identification are most crucial. Haemovigil covers both steps and any deviation leads to inability to access blood component. In line with flow of transfusion process, Haemovigil ensures necessary labeling of patient specimens at the bedside, while at the blood bank correct components are issued. Finally, at the bedside, Haemovigil reinforces final patient identification for accessing blood components. Haemovigil is a cost effective, simple intervention to prevent WBIT, incorrect blood component issues and patient mis-identification prior to transfusion.

P-771

NATURE AND CAUSES OF ERRORS IN THE PROCESS OF BLOOD TRANSFUSION

G Kaur, G Kaur and P Kaur

Transfusion Medicine, Government Medical College & Hospital, Chandigarh, India

Background: The transfusion services aim to provide a high-quality facility with no to minimum risk to the recipients. However, a wide range of errors ranging from near-miss events to errors that lead to patient injury and even mortality may occur at various steps of the transfusion process.

Aims: To identify the nature and causes of errors in the process of blood transfusion.

Methods: A prospective analytical study was conducted in the department of Transfusion Medicine at a tertiary care hospital in North India over a period of 18 months. All the errors occurring during blood transfusion process, from donor phlebotomy till the transfusion of blood component to the patient (i.e. vein to vein) were reported and analyzed. All the events and their causes were calculated as percentages, frequencies and proportions. Risk Assessment Index (RAI) was calculated for each error as multiple of quantified estimate of severity of the actual or potential harm to the patient and quantified estimate of the probability of this event recurring. Root cause analysis was done for all errors having RAI ≥ 0.5.

Results: A total of 156 errors were reported during the study period. Incidence of error occurrence was found to be 0.3% of all the blood components issued. Maximum number of errors were found to be associated with PRBC components (60.9%). Majority of the errors were found to be near-miss errors (85.3%). No-harm and adverse events were 10.2% and 4.5%, respectively. Pre-analytical phase was associated with majority of the errors (71%). Laboratories (48.1%) were found to the most error-prone area. Among transfusion services, maximum errors occurred in the serology laboratory (65.3). Among wards, majority of errors occurred in emergency ward (41.7%). Maximum errors were reported to occur in evening shift (49.4%). Out of all personnel involved in the blood transfusion chain, doctors were involved in majority of the errors (46.8%). Incorrect unit was issued in 25.6% of the cases. Administration of incorrect unit, surpassing all the checks implemented in the blood transfusion process to ensure patient safety, was detected in 13.5% cases. Whereas planned or unplanned recovery occurred at some point in rest 83.3% of the cases. 30.1% of the total errors were high and medium-risk errors with RAI≥0.5 and 69.9% were low risk errors with RAI<0.5. Maximum errors were discovered in the laboratory (85.3%). Majority of the errors were discovered during morning shift (48.7%). Doctors (42.9%) were involved in the discovery of utmost number of errors. Blood bag labelling error was found to be the overall most common error as categorized by MERS-TM classification, as well as the most common type amongst errors due to transfusion services. Patient request and patient sample collection were found to be the second and third most common errors and collectively they formed the most common type amongst bedside errors. Blood bag labelling and incorrect unit issuance were the most commonly occurring errors in the pre-transfusion and post-transfusion phase, respectively.

Summary/Conclusions: Human errors are an indispensable part of any process and are found to occur whenever and by whomsoever there is a potential for their occurrence. A strict adherence to departmental Standard Operating Procedures (SOPs) should be mandatory. Clinical staff needs to undergo formal training in phlebotomy procedure. There should be a functional hospital transfusion committee to address error prone areas and suggest remedial measures to prevent further occurrence of adverse events.

P-772

TACO: HOW DO WE PROMOTE AWARENESS AND REPORTING?

C Akers[1], H Atkinson[1], G Bates[1], L Bielby[1], P Crispin[1], E Wood[1], B Glazebrook[1], C Hennessy[1], C Hogan[1], E Maxwell[1], T Noutsos[1], R Rogers[1], M Cole-Sinclair[1], G Kelsey[1], A Yttrup[1], A Wynne[1], C Flores[1], L Saravanan[1], A Keegan[1], M Comande[1], A Davis[1] and J Daly[2]

[1]Blood Matters STIR Expert Group, Department of Health & Human Services, Australian Red Cross Blood Service, Melbourne [2]Clinical Services and Research, Australian Red Cross Blood Service, Queensland, Australia

Background: The Serious Transfusion Incident Reporting (STIR) program (Victoria, Australia) has collected information on transfusion associated circulatory overload (TACO) since its inception in 2007. Currently STIR receives reports from four states and territories with 93 health services registered. Initially TACO was reported on the acute transfusion reaction (ATR) investigation form; in 2011, with the implementation of electronic reporting, TACO and transfusion-related acute lung injury (TRALI) were separated onto a new form. STIR has identified 3 areas for practice improvement regarding TACO: staff awareness, use of risk assessment tools and use of single unit transfusion policies.

Aims: To describe STIR work to increase the awareness of TACO among clinical staff.

Methods: Due to concern of under recognition of those at risk and underreporting of TACO, STIR developed an education campaign regarding TACO risk factors, preventative measures and treatment for health services to implement during September 2017. Campaign resources included posters for clinical areas, swing tags to attach to blood bags and information sheets for blood fridges. The information was based on the TACO pre-transfusion checklist from the UK Serious Hazards of Transfusion Annual report 2016. 7000 tags were sent to 79 health services, along with posters

and information on use. The tags were sent directly to pathology providers, with the Transfusion Nurse (TN) or equivalent informed to support campaign.

Results: TACO notifications to STIR have always been low (average 8 per year, range 1–14); however, their severity is rated high (28% have had a severity rating 2 - events that result in a temporary loss of function, unrelated to the natural course of the patient's illness and differs from the expected outcome of care), although no deaths have been described. Increase in reporting TACO correlates with the increasing numbers of health services registered rather than the move from reporting on a general ATR form to a specific TRALI/TACO form, or regular recommendations in annual reports. In the 6-month period (Jan-Aug) prior to the campaign there were 7 notifications; in the 4-month period (Sept-Dec) following the campaign there were 9 notifications (with no change in registered health services). Feedback for the education campaign was positive with several health services requesting additional tags. A survey of TN demonstrated that the majority participated and would do so again, and the campaign had been useful in raising awareness of TACO. Health services outside the campaign area requested tags for use. Supporting materials have been made available on the Blood Matters website.

Summary/Conclusions: Time has not allowed for full evaluation of the campaigns impact. There has been a slight increase in reporting, however, it is difficult to determine if this is due to the campaign or normal fluctuations. In addition, any change in reporting may reflect increased recognition of TACO (increased reports) or improved clinical care for those at risk (decreased reports). Awareness campaigns, such as that described, help to educate clinical staff and will assist in improving the care of those who require transfusion but are at risk of volume overload.

P-773

UTILIZATION OF DIFFERENT CODING SYSTEMS TO IDENTIFY CHARACTERISTICS OF BLOOD COMPONENTS TRANSFUSION IN ELECTRONIC HEALTH DATABASES

K Chada[1], J Obidi[1], J Gruber[1], G Dores[1], E Storch[1], A Williams[1], J Banda[2], S Gombar[2], D Balraj[2], R Hayden[3], P Biondich[3], S Grannis[3], G Hripcsak[4], T Falconer[4], K Natarajan[4], E Allakhverdiiev[5], S Dempster[6], C Reich[6], N Selvam[6], N Williams[6], S Anderson[1] and A Shoaibi[1]

[1]Center for Biologics Evaluation and Research, Food and Drug Administration, Silver Spring [2]Stanford University, Stanford [3]Regenstrief Institute, Indianapolis [4]Columbia University and also with Observational Health Data Sciences and Informatics (OHDSI), New York [5]Odysseus Data Services Inc., Cambridge [6]IQVIA, Durham, United States of America

Background: Blood transfusion is associated with immunologic (e.g., alloimmunization) and non-immunologic (e.g., bacterial sepsis or transfusion-associated circulatory overload) complications. Health insurance claims, administrative billing, and electronic health record (EHR) data may provide rich data sources to support safety monitoring of blood transfusions. In the United States (U.S.), multiple coding systems are utilized mainly for medical billing and reimbursement, including the International Classification of Diseases (ICD9, ICD10), Current Procedural Terminology (CPT), Healthcare Common Procedure Coding System (HCPCS), and revenue codes. These coding systems often lack specificity with respect to blood components and timing of administration. However, a relatively new coding system used by Blood Banks, the Information Standard for Blood and Transplant (ISBT)-128, contains comprehensive and granular blood and blood components data which have the potential to be used for blood transfusion hemovigilance.

Aims: To describe the ability of various coding systems in healthcare data sources to capture blood transfusion events, and the completeness and specificity (component type, processing, storage) of data associated with transfused components.

Methods: Data providers from the Observational Health Data Sciences and Informatics (OHDSI) network were enlisted to participate in this study. The frequency of ICD9/ICD10, CPT, HCPCS, and ISBT-128 codes for blood transfusions and specific information related to transfused components was assessed in distinct OHDSI databases comprised of claims (160 million), hospital billing (83 million), ambulatory care (44 million), EHR (7.8 million), and claims with EHR (17 million) patient records. An identical query was distributed to participating sites to identify code-specific frequencies associated with all transfusion events during 2010–2017. Where available, information was collected about the type of blood component (e.g., red blood cells, platelets, plasma), collection method (whole blood donation, apheresis), processing (leukocyte reduced, irradiated, washed, deglycerolized), storage (thawed, fresh, additives, temperature), specialized testing (HLA typing, cytomegalovirus), and other features (unit, pooled, autologous).

Results: Transfusion events and details of transfused blood components varied significantly across coding systems. Hospital billing data sources predominantly

captured blood transfusion using the ICD9/ICD10 coding systems and identified the blood component (99.0X, 302XX: whole blood, red blood cells, plasma, platelets), non-autologous attribute of donation (302XX) and storage (302XX- fresh or frozen) for red blood cells as well as plasma. Claims data captured blood transfusion using mainly HCPCS (P90XX series) codes and included information related to the blood component, collection, processing, thawed or fresh attribute for storage, and some specialized testing. CPT coding was the least utilized system for recording transfusion events and lacked granularity for transfused blood products. EHR data sources utilized ISBT-128 coding system along with ICD9/10 and HCPCS codes while claims and hospital billing data sources did not contain ISBT-128 codes.

Summary/Conclusions: Various coding systems currently utilized in U.S. healthcare data sources identify detailed transfusion events to different degrees. Coding systems with better specificity and sensitivity, such as that used in the ISBT-128, would improve the ability to conduct hemovigilance activities using Real World Data.

P-774

DO TRANSFUSIONS OF LONG–STORED RED BLOOD CELLS (RBCS) POSE HIGHER RISK OF POST–TRANSFUSION REACTIONS?

E Klausa, K Piniarska-Laszczyk and A Smolarczyk

Laboratory Department, Regional Centre of Transfusion Medicine and Blood Bank, Wroclaw, Poland

Background: Red blood cell concentrates (RBCCs) stored in standardized conditions (temperature 2 to 6°C, 42 days from blood collection) are subject to progressive metabolic, biochemical, structural and functional changes which may negatively impact on RBC viability and functions after transfusion. Numerous research papers published in the course of the last several years suggest that adverse reactions during or in a short period after transfusion occur statistically more often in case of RBCCs which have been stored for a long period of time, or have not undergone leucodepletion. Researchers' views differ as regards the length of period from blood collection within which RBCs should be considered "fresh" (some argue for 5 days, others for 8, 10, 14 days), or after which RBCs should be considered "old" (15, 20, 21, 40–42 days).

Aims: 1. To analyze numbers and types of registered adverse reactions in patients after transfusions of non-leucodepleted RBCCs and leucodepleted RBCCs. 2. To answer a question: does the RBC storage period impact on occurrence of adverse post-transfusion reactions?

Methods: Between 2009 and 2017, 440 post-transfusion reactions were registered. This amounts to circa 0.08% of all RBCC transfusions. An analysis of numbers and reaction types depending on the RBCC storage period was undertaken in four groups: 1–10, 11–20, 21–30, 31–42 (storage) days. Numbers of adverse reactions after transfusions of non-leucodepleted RBCCs vs. leucodepleted RBCCs were compared.

Results: After transfusions of RBCs stored for: 1. 1–10 days, reactions such as: allergies/anaphylaxes (17 persons), FNHTR (34), TACO (8), TAD (13) and other unclassified (pain, nausea, vomiting, hypertension - 14) occurred in 86 persons, including in 40 after non-leucodepleted RBCC transfusions. 2. 11–20 days, reactions such as: allergies/anaphylaxes (26), FNHTR (68), TACO (11), TAD (20), TRALI (4) and other unclassified (16) occurred in 145 persons, including in 111 after non-leucodepleted RBCC transfusions. 3. 21–30 days, reactions such as: allergies (21), FNHTR (66), TACO (10), TAD (22), TRALI (1) and other unclassified (15) occurred in 135 persons, including in 105 after non-leucodepleted RBCC transfusions. 4. 31–42 days, reactions such as: allergies (10), FNHTR (42), TACO (4), TAD (8), and other unclassified (10) occurred in total 74 persons, including in 61 after non-leucodepleted RBCC transfusions.

Summary/Conclusions: The analysis of clinical data showed that a number of post-transfusion reactions was twice higher in the case of non-leucodepleted RBCCs than leucodepleted RBCCs, and there was no correlation between the occurrence of adverse post-transfusion reactions and the RBC storage period. Based on analyzed data, it is not possible to conclude that transfusion of RBCs stored longer than two weeks (and described as "old") creates more risk of morbidity and mortality in patients. Haemovigilance system's quality control examination has confirmed a 42-day RBCC storage period as safe. The extension of a storage period makes it possible to secure blood for a larger number of patients.

P-775

COMPARISON OF HEMOVIGILANCE DATA OF THE GERMAN RED CROSS BLOOD DONOR SERVICE WITH DATA FROM THE GERMAN AUTHORITY PAUL-EHRLICH-INSTITUTE

M Schmidt[1], B Bruns[2], G Capalbo[1], S Findhammer[1], K Gubbe[3], B Jahrsdörfer[4], M Müller-Steinhardt[5], U Pawlowski[6], S Seyboth[7] and E Seifried[8]

[1]Quality Management, German Red Cross, Frankfurt [2]QM, German Red Cross, Lütjensee [3]Quality Management, German Red Cross, Plauen [4]Quality Management, German Red Cross, Ulm [5]Quality Management, German Red Cross, Mannheim [6]Quality Management, German Red Cross, Berlin [7]Quality Management, German Red Cross, Baden-Baden [8]Management, German Red Cross, Frankfurt, Germany

Background: The German Red Cross Blood Transfusion Services are responsible for about 75% of all blood products in Germany. In addition, blood products are produced by government institutions (universities) and private companies. All transfusion-related reactions are reported in haemovigilance reports and transmitted annually to the Paul Ehrlich Institute. The Paul Ehrlich Institute publishes the overall data for Germany in a haemovigilance report. The categorization is based on the guidelines of the International Hemovigilance Network (INH). All transfusion reactions are divided into 13 categories.

Aims: In the present study, the hemovigilance data from the blood transfusion service Baden-Württemberg - Hesse and the blood transfusion service North-East are systematically analyzed for the year 2017 and compared with the hemovigilance data of whole of Germany reported by the Paul Ehrlich Institute.

Methods: All data of the electronic hemovigilance system from 2017 of the German Red Cross Baden-Wuerttemberg - Hesse as well as of the German Red Cross North-East were analyzed. Transfusion reactions were normalized to reaction per million blood transfusions. The data were compared with the hemovigilance data published by the Paul-Ehrlich Institute for whole Germany.

Results: In 2017, a total of 1,271,666 blood transfusions were performed (BaWüHe 759,605 and Northeast 512,061). The observed transfusion reactions were each normalized to 1 per million transfusions. There are fewer acute transfusion reactions in our blood transfusion service than in whole Germany (3.15 per million versus 18.73 per million). In contrast we observed, more delayed haemolytic transfusion reactions than in whole Germany (4.72 per million versus 0.4 per million). Transfusion-related bacterial or viral transmissions are only occasionally observed in our blood transfusion service as well as in whole Germany. The number of severe transfusion reactions in our blood transfusion service is comparable to the number in Germany (71.56 per million versus 70.15 per million). The transfusion of the wrong blood components is not observed in our haemovigilance system.

Summary/Conclusions: The 2017 hemovigilance data focuses on acute transfusion reactions, transfusion-associated circulatory overloads (TACO), and severe transfusion reactions. In essence, the results of our blood transfusion service are comparable to the German haemovigilance data reported by the PEI. Thus, the data of our blood transfusion service can be interpreted as representative values for Germany. Basically, there might be a bias that serious transfusion reactions are reported more frequently as minor transfusion reactions, so that they might outweigh in the haemovigilance report. The low proportion of transfusion-related bacterial and viral transmissions represents the high safety standard in our blood transfusion service. A cause that transfusions of wrong blood components were not reported can also be explained by the fact that a bed-side test is mandated in Germany. In addition, electronic patient identification systems for patients and blood products are currently undergoing in clinical trials.

P-776

LOOK BACK PROCEDURES WHICH HAVE BEEN CARRIED OUT BY REGIONAL CENTER OF BLOOD DONATION IN CRACOW IN THE YEARS 2012–2017 RESULTS OF DIAGNOSTIC TESTS CONDUCTED AT RECIPIENTS OF BLOOD COMPONENTS

M Szeląg[1], M Suliga[1], J Kusmierczyk[2] and J Ras[3]

[1]Quality Assurance [2]Laboratories of Viral Markers [3]Medical director, RCKiK w Krakowie, Kraków, Poland

Background: As required there should be a system to ensure effective communication between the Center of Blood Donation and Treatment, hospitals and plasma fractionators. A look back is a procedure to be followed if it is found retrospectively that a donation should have been excluded from transfusion use or from processing because that unit was collected from donor who was subsequently rejected due to a reactive viral marker, risk behavior, exposure to other risks related to infectious

diseases. A look back procedure of reactive viral marker consists of tracing previous donations within a time period of at least 6 months prior to the last donation with negative tests results.

Aims: In this study, we perform the evaluation of traceability of all relevant supplied blood components in look back procedures in the years 2012–2017.

Methods: Blood donors have been tested at each donation for antibodies HIV-1/HIV-2, for antibodies anti HCV, for HBs antigen and NAT (nucleic acid amplification technology) tests for HIV, HCV, HBV. The tests have been conducted with TMA and CMIA methods in Department of Viral Markers Transmitted by Blood of Regional Center of Blood Donation and Treatment in Cracow. The confirmatory tests were made in reference laboratory of Institute of Hematology and Blood Transfusion in Warsaw. The look back procedures of all components of blood taken within 6 months back from the last donation with negative result have been conducted. The notifications to clinical recipients of blood components have been sent in order to confirm or rule out infection in recipients. The factories to which plasma has been supplied have been notified.

Results: The number of detected infections in repeat and regular donors in the years 2012–2017: HBV-10, HCV-14, HIV-13. The type and number of blood components under the procedure: red blood cells concentrate- 58, fresh frozen plasma-50, platelets concentrate- 12. The use of blood components: transfused- 71, designed for fractionation- 16, destroyed- 33. 24 patients (34%) have been screened for infectious disease: HBV or HCV or HIV respectively. All results were negative. 39 patients (55%) haven' t been screened because of death. There was no answer with results from hospital about 8 patients (11%) because for example there was no possibility to contact with patient.

Summary/Conclusions: There was no transmission of viral infection to the recipient during the diagnostic window in the studied cases.

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THE SURVEILLANCE AND EVALUATION OF ADVERSE TRANSFUSION REACTIONS DURING HEMOVIGILANCE ESTABLISHMENT

L Kasraian[1], L tahmasbi[1], M karimi[1] and N naderi[2]

[1]Blood Transfusion Research Centre, High Institute for Research and Education in Transfusion Medicine [2]Shiraz University of Medical Science, Anesthesiology Department of Shiraz Medical University, Shiraz, Iran

Background: The life-saving role of blood transfusion is fully recognized, however it may be associated with some adverse reactions. The hemovigilance program is a systematic surveillance of adverse transfusion reactions for improving the quality and the safety of blood transfusion. Evaluation of the frequency of acute adverse transfusion reactions (ATRS) in blood recipients will help us to understand the magnitude of ATRS, evaluate of current reporting systems, and prevent the recurrence of ATRs by recognizing their causes

Aims: This study aims to estimate the adverse transfusion reactions (ATRS) in blood recipients to plan effective hemovigilance programs to reduce the incidence and. recurrence rate of ATRs., and make blood transfusion process as safe as possible.

Methods: This cross –sectional study was conducted at all hospitals, Shiraz, Iran from March 2010 to Sep 2017. The hemovigilance system was launched gradually from 2010. Every transfusion reaction must be reported even mild ones via a standard form that had to be completed and delivered to the blood transfusion services. According to Iran hemovigilance guideline all adverse transfusion reactions must be reported mandatory even mild ones via a standard form that had to be completed and delivered to the blood transfusion services. The demographic characteristics, clinical signs and symptoms, types of ATRs were surveyed. The frequency of ATRs in thalassemia and non-thalassemia patients also were compared.-'. Thereafter, the incidence of ATRs was calculated.

Results: The incidence of ATRs during study period were 0.009%, 0.26%, 0.036%, 0.103%, 0.030%, 0.067%, 0.235% and 1.43% respectively. The incidence rate of ATRs was seen to increase after the establishment of the hemovigilance system. The most frequent ATRs were allergic then febrile non hemolytic reactions (FNHTR)s. The most frequent symptoms were chills (28.7%), fever (19.6%), itch (18.7%) rash (15.6%) and urticaria (14.7%).The types of blood products which resulted in transfusion reaction were 82.3% packed Red blood cell, 13.1% platelet, and 4.5% fresh frozen plasma The incidence rate of ATRs were more in thalassemia patients. The most frequent ATRs among non-thalassemia patients were FNHTRs (42.1%) and allergic reaction (41.58%) whereas in thalassemia patients were allergic reactions (68.5%), and FNTHRs (21.56%).

Summary/Conclusions: The incidence of ATRs increased gradually after the establishment of the hemovigilance system. So, hemovigilance establishment could be

enable blood transfusion service to introduce measures that would lead to improvements in the diagnosis and reporting of ATRs, identifying and correcting the causes of ATRs, preventing future recurrence of ATRs, and ultimately improving blood safety.

P-778

Abstract has been withdrawn

P-779

CLINICAL IMPACT OF IMPLEMENTING UNIVERSAL LEUKOREDUCTION ON BLOOD SAFETY IN LEBANON

A Haddad[1,2], T Bou Assi[3,4], F Jaffal[5], P Salameh[2,6] and O Garraud[7]

[1]Clinical Pathology and Blood Banking, Sacré-Coeur Hospital, Lebanese University, Beirut, Lebanon [2]EA3064, Faculty of Medicine of Saint-Etienne, University of Lyon, Saint-Etienne, France [3]Laboratory Medicine, Psychiatric Hospital of The Cross, Jaledib [4]Laboratory Medicine and Blood Bank, Saint Joseph Hospital, Dora [5]Faculty of Medicine [6]Faculty of Medical sciences, Lebanese University, Beirut, Lebanon [7]Institut National de la Transfusion Sanguine, Paris, France

Background: Universal leukoreduction (ULR) was nationally implemented in 2013 following the recommendations of the Lebanese National Committee of Blood Transfusion in order to improve safety in transfusion medicine. It is widely known that removal of leukocytes minimizes among others febrile non-hemolytic transfusion reactions, HLA alloimmunization, platelet refractoriness in multitransfused patients and prevention of transmission of leukotropic viruses such as EBV and CMV etc... Despite the fact that this strategy is currently an international standard recommended by several western international scientific societies and institutions, there is occasionally some debate regarding its cost-benefits especially for low and middle income countries.

Aims: To describe the clinical impact of implementing ULR on the incidence of acute transfusion reactions (ATR) in a major tertiary healthcare facility in Lebanon where the hemovigilance reporting system is well organized since two decades.

Methods: Acute transfusion reactions (immunologic and non-immunologic) reported to the department of clinical pathology and blood banking at Sacré-Coeur hospital, between 2003 and 2012 (before the implementation of ULR), following transfusion of blood products were compiled and compared with those that occurred between 2013 and 2017.

Results: A total of 22,341 blood products (Packed Red blood cells and Fresh frozen plasma) were transfused in the first study period compared to 6,741 in the second one. The overall incidence of ATR slightly decreased following the implementation of ULR from 4.38 to 3.26 per 1,000 blood products; however, this difference was not statistically significant (P=0.207). Immunologic ATR were the most frequent reactions in both study periods (around 90%) with around 55% febrile non-hemolytic transfusion reactions, followed by allergy and transfusion associated circulatory overload (30% and 9% respectively).

Summary/Conclusions: This experience in a single major tertiary healthcare facility in Lebanon contradicts the widely recognized notion that implementing ULR significantly decreases the incidence of ATR. Hence, the need to compile such data at a national level is urgently needed in order to confirm or refute our findings. Reporting delayed transfusion reaction should be also included. Finally, such findings question the cost effectiveness and thus the relevance of applying ULR versus a selective reduction strategy.

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Abstract has been withdrawn

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HAEMOVIGILANCE REPORTING AT A TERTIARY CARE HOSPITAL BETWEEN 2009 AND 2017

C Vaz, C Monteiro, F Vasconcelos, M Lopes, T Ventura, J Baldaque, A Leite and M Koch

Imunohemoterapia, Centro Hospitalar de São João, Porto, Portugal

Background: In Portugal, institutions that transfuse patients report serious adverse events of blood components to Instituto Português do Sangue e Transplantação, which is responsible for ensuring the National Haemovigilance System (NHS) and cooperates with the European Haemovigilance Network. The Portuguese adverse reaction notification rate in blood components in 2016 was 13.0 per 10.000 units transfused. Our centre created in 2012 a transfusion committee, that is responsible for managing the hospital haemovigilance system, reporting the incidents related to transfusions to NHS, training professionals annually, and providing a transfusion medicine manual online.

Aims: Describe the incidence and types of adverse events in blood products at our centre between 2009 and 2017.

Methods: Centro Hospitalar de São João is an university hospital and tertiary care centre with 1142 beds, where close to 6600 patients and 31.000 blood components are annually transfused. We performed a retrospective analysis of errors, near miss errors and transfusion reactions (TR) of blood components reported by our centre to NHS. Data was collected online (www.hemovigilancia.net). Institutions that perform transfusions of blood components are registered, in this platform, and report their data annually.

Results: 190 TR, 10 errors, and 19 near miss errors were reported between 2009 and 2017. 90.5% of TR occurred associated with transfusion of erythrocyte components. 53.7% occurred in women. The mean age of patients was 63.8 years. 50.0% of TR were reported in oncologic patients, 14.5% surgical patients and 9.6% gastrointestinal bleeding. 78.4% of the patients had a past transfusion. The most reported TR were Late Serologic Transfusion Reaction (62.1%), Allergic/Urticarial Reactions (17.4%), Non-Haemolytic Febrile Reactions (14.2%), Dyspnea associated with transfusion (2.6%), and Anaphylaxis (1.1%). 91.6% of TR were considered non-serious. 8 (4.2%) serious reactions were notified. TR occurred 26.3% in medical services, 22.6% in surgical services, 21.6% in intensive care units, and 11.1% in oncology day hospital. 63.7% were considered late events, 60.5% of patients did not present clinical manifestations, and 55.3% did not receive treatment for TR. 73.4% of the events were considered predictable and probable. 70% of errors occurred at the head of the patient and 20% in the laboratory. 60% of the errors led to administration of a wrong blood component. 94.7% of the near miss errors occurred in clinical setting, and 84.2% were caused by wrong identification of the patient. We reported per year 1.1 Errors, 2.1 Near Miss Errors and 21.1 TR during the study period.

Summary/Conclusions: Reporting patterns were irregular, requiring a greater participation of professionals. The majority of TR occurred in patients with a past transfusion, and recurrent transfusion needs. The most reported TR are in accordance with the literature. The near miss errors occurred at the request of the blood product resulting from the incorrect identification of the patient. Incidents are mostly late, not serious, without clinical risk for the patient. Reported errors occurred mostly at the head of the patient, by administering blood products to incorrectly identified patients.

P-782

Abstract has been withdrawn

P-783

SEVERE ADVERSE EVENTS IN SLOVENIAN HAEMOVIGILANCE NETWORK FROM 2013 UP TO 2016

I Maric[1], B Zivkovic[2], L Lokar[2], I Bricl[1] and K Zeleznik[1]

[1]Immunohaematology, Blood Transfusion Centre of Slovenia, Ljubljana [2]Centre for Transfusion Medicine, Maribor, Slovenia

Background: Severe adverse events of transfusion are defined by Slovenian legislation (based on EU legislation) as all the events that could cause death of a patient, have long term complication of illness or prolong hospitalisation. By this legislation it is mandatory to analyse every severe adverse event after which it is necessary to implement corrective measures. We have to report then to Slovenian competent authority which reports to European commission. Hemovigilance law was written in 2007 and it is a bit outdated. Since then there were many changes which are not taken in

consideration so the classification of adverse events in it is outdated too. Since 2016 we started to use new classification but we still didn't change the law, so for the purpose of reporting to the competition authority we have to use classification from 2007 and for the other purposes such as publications or informal reporting we use 2016. Adverse events by the 2007 classification are divided into eight categories of where did the event happen (collection of whole blood, apheresis, testing the donors, whole blood processing, storage, distribution, materials and others events) and into four categories of whose fault is it (error in product, error in equipment, human error and other). A 2016 classification is divided into four categories of type of the event (transfusion of the wrong blood component, transfusion of the blood component that doesn't meet the standards or requirements, wrong handling with blood component outside the transfusion department and near miss) with subcategories by how did it happen.

Aims: By implementing 2016 classification in our law we would update reporting system in our country and at the same time would reduce amount of unnecessary work for National hemovigilance office.

Methods: We reviewed and analysed all severe adverse events from 2013 up to 2016 using both classifications.

Results: Since 2013 up to 2016 there were 4306 adverse events of transfusion of which 107 were classified as severe once, making it less than 3%. 2007 classification: there were 94 other events of which 87 were human error and 7 other error, 8 were distribution events, 2 "collection of whole blood" events, 1 whole blood processing event, 1 storage event and 1 material event. 2016 classification: there were 5 events of transfusion of the wrong blood component, 3 events of not meeting the standards and 99 near misses. None event was classified as other.

Summary/Conclusions: 2007 classification doesn't tell us how did the event happen or what was the event about. Majority of events were classified as other events which doesn't help us with analysing the source of the event and implementing corrective measures consequently making safer transfusion practice which is sole purpose of our work. By using the new classification we simplified reporting making it more transparent and easier to compare us with other countries so we could evaluate work of National hemovigilance office.

P-784

POST–TRANSFUSION REACTIONS IN PATIENTS WITH REFRACTORINESS TO TRANSFUSIONS OF DONOR PLATELETS

A Rakhmani[1], E Mikhaylova[2], I Dubinkin[3], O Kalmikova[3] and T Gaponova[1]

[1]*Clinical Research Department of Processing and Cryopreservation of Blood Cells* [2]*Department of Chemotherapy for Hematological Diseases and Hematopoiesis Depressions* [3]*Laboratory of Quality Control and Safety of Transfusion, National Medical Research Center for Hematology of the Russian Federation in Moscow, Moscow, Russian Federation*

Background: Platelet concentrate (PC) transfusions are the major treatment of thrombocytopenia in hematological patients with bone marrow aplasia against immunosuppressive therapy, as well as in the period of agranulocytosis during cytostatic therapy. However, multiple transfusions (more than 20 during treatment) may be a risk factor for allosensitization of the recipient by donor blood cells Human Leukocyte Antigen (HLA) and Human Platelet Antigen (HPA), which subsequently leads to immunological refractoriness, the development of post-transfusion reactions and the lack of clinical effectiveness of PC transfusions. Individual HLA/HPA matching of donor and recipient may mitigate that risk.

Aims: Comparison of post-transfusion reactions in refractory patients with individual matching and without individual matching receiving PC transfusion support.

Methods: From August 2015 till December 2017, we observed 1112 patients, who received 16720 PC transfusions. Patients developing refractoriness to PC transfusions received PCs selected by individual cross-matching with the Galileo-Neo (Immucor) analyzer. Statistical processing was performed using the chi-squared test with Yates' correction.

Results: In total, 91 patients (8% of the total number of recipients of donor platelets) developed refractoriness to PC transfusion. Subsequently they received transfusions with individually selected units by cross-matching – 4094 individually selected units have been transfused (24% of the total number of transfusions). Post-transfusion reactions (PTR) before the individual selection was recorded 27 episodes in patients with refractory of 4094 PC transfusions. Among them: aplastic anemia (AA) -6: non-hemolytic febrile reactions (NHFR)-1, bronchospasm-2, urticaria-3; myelodysplastic syndrome (MDS) -3: (NHFR-2, bronchospasm-1); acute myeloid leukemia (AML) - 16: NHFR-11, bronchospasm-1, urticaria-1, combined-3); acute lymphoblastic leukemia (ALL) - 2: NHFR-2. Against the background of the individual selection of refractory patients recorded 5 episodes of PTR. Of these: AA-1 NHFR; MDS-1 bronchospasm; AML-3 (NHFR -1, bronchospasm-1, combined reaction-1).

Thus, refractory patients without selection were performed 2515 PC transfusions, of which 27 episodes of post-transfusion reactions were recorded, which was 1.07% of the total number of PCs transfusions. Refractory patients with selection performed 1579 PC transfusions, of which 5 episodes of post-transfusion reactions were recorded, which were 0.31% of the total number of PC transfusions.

Summary/Conclusions: Conducting an individual selection allowed to reduce the frequency of post-transfusion reactions by 80%, which allowed to increase the immunological safety of transfusions. The difference in the groups of refractory patients without selection and with the selection in the PTR frequency is statistically significant at a significance level of P <0.01. The highest risk of allosensitization and development of immunological post-transfusion reactions were observed in patients with acute myeloid leukemia (16 pts – 16 episodes). To reduce the risk of post-transfusion reactions and adequate complex therapy, refractory patients require PC transfusions with an individual selection of a donor-recipient pair.

P-785

DESIGN, DEVELOPMENT AND IMPLEMENTATION OF A HAEMOVIGILANCE SYSTEM IN COLOMBIA (SIHEVI)

MI Bermudez Forero[1], P Gardeazabal Acuña[1], J Soto Viafara[1] and M Garcia Otalora[2]

[1]*Blood Banks and Transfusion Services Network, National Institute of Health* [2]*Unit of Physiology, Medicine School, Universidad del Rosario, Bogotá, D.C, Colombia*

Background: Colombia is a country with a mixed financing health system, with public and private participation and a population over 48 million inhabitants. The Blood Banks and Transfusion Services network has public and private participation and although efforts have been made to move towards centralization, currently there are 81 blood banks registered, distributed in 35 cities which supply more than 580 clinics and hospitals

Aims: Improve the process of donor selection through verification of donation history. Strengthen blood transfusion safety by integrating the information of each blood bank, and hospital institution allowing to trace origin, processing and final destination of each blood component obtained in the country. Identify adverse events related to donor and transfusion in each event the associated blood component

Methods: SIHEVI software was designed by National Institute of Health of Colombia and information is supplied by each blood bank and hospital institution, with nominal data of the donors attended, results of serological and immunohematological tests, fractionation, and final destination of each blood component. A donor selection module was created in which each blood bank can consult the history of donations made by a person in any blood bank of the country. Additionally, modules were created that allowed to consult hemocomponents and transfused patients, as well as adverse transfusion events per patient and to generate individual reports, which can be consulted from any hospital institution in the country

Results: During the implementation phase of SIHEVI, seven donors were identified who were positive for infectious markers, but who persisted donating in blood banks different from the one who confirmed them, being the most dramatic case a positive donor for HIV with three attempts of donations after the first detection. Likewise, two donors were identified who being non-reactive, approached to donate whole blood in more than one bank at intervals less than 15 days between each donation, so they were deferred temporarily in order to mitigate the risk of transfusion-transmitted infections (TTI). A national list of permanent deferred donors (n = 16,225 people) was constructed, based on information prior to the implementation of SIHEVI, which will be interoperable with sources of epidemiological information of the country (SIVIGILA). In one month, 168 hospital institutions reported the transfusion of 45,143 blood components in 5,716 patients; a demand satisfaction of 84.7% was estimated for the red blood cells. 71 adverse transfusion events (ATE) were notified in 35 hospital institutions, located in 16 different areas of the country, 3 severe and 14 attributable to the transfusion

Summary/Conclusions: Implementation of SIHEVI allows improvement of transfusion safety, while identifying potential donors whose motivation is to have laboratory test results for infectious markers such as HIV, thereby reducing the risk of TTI. Having this type of information in real time reduces risks associated with both donation and transfusion, while allowing ATE to be identified more quickly, and the availability of blood components throughout the country. Being interoperable with other sources of information, the impact on public health is generated by improving the access of infected patients to follow-up and control programs.

Alternatives to Blood Transfusion

P-786

POSTOPERATIVE VENOUS THROMBOEMBOLISM PROPHYLAXIS IN PERIOPERATIVE TRIALS OF TRANEXAMIC ACID: A SYSTEMATIC REVIEW AND META–ANALYSIS

J Taylor[1], I Perelman[1], J Yates[2], S Khair[1], J Lampron[2], A Tinmouth[2], A Davis[2] and E Saidenberg[2]

[1]Ottawa Hospital Research Institute [2]The Ottawa Hospital, Ottawa, Canada

Background: The efficacy of Tranexamic acid (TXA) in the reduction of perioperative bleeding has been proven in numerous studies. Previous studies have indicated that there is no increased rate of VTE in patients treated with perioperative TXA as compared to placebo or other therapies.

Aims: We aimed to assess whether the use of postoperative VTE prophylaxis and the type of therapy selected are factors in determining the risk of postoperative VTE in patients treated with perioperative TXA.

Methods: We searched electronic databases (MEDLINE, Embase, CENTRAL, clinicaltrials.gov) from inception through September 2017. Randomized control trials of perioperative TXA involving a comparator group and reporting on postoperative VTE events were included. Study characteristics, results of VTE-related outcomes, and VTE prophylactic regimens were abstracted and meta-analyzed using a Der Simonian and Laird random effects model.

Results: 198 trials were identified, of which 86 used postoperative VTE prophylaxis measures. Meta-analysis showed that TXA was not associated with an increased risk of postoperative VTE for all surgery types and for orthopedic surgeries specifically (P>0.05), regardless of whether VTE prophylaxis was provided to patients. In studies using VTE prophylaxis, the risk of VTE in patients treated with perioperative TXA was not significantly (P>0.05) different for the various pharmaceutical and physical VTE prophylaxis methods employed.

Summary/Conclusions: VTE is uncommon in patients treated with TXA perioperatively, especially when proper postoperative prophylactic methods are employed. Additionally, the type of VTE prophylaxis does not seem to impact the already low risk of VTE in this patient population. Future studies are required to assess the use of VTE prophylaxis in patients with a prior history of VTE who are treated with perioperative TXA. However, for other patients, risk of VTE should not be considered a barrier to the use of TXA to minimize blood loss and transfusion need.

P-787

EXCLUSION CRITERIA AND ADVERSE EVENTS IN PERI-OPERATIVE CARDIAC SURGERY TRANEXAMIC ACID TRIALS: A SYSTEMATIC REVIEW AND META–ANALYSIS

J Yates[1], I Perelman[2,3], S Khair[2], J Taylor[2], J Lampron[1], A Tinmouth[1,3] and E Saidenberg[1,3]

[1]The Ottawa Hospital [2]University of Ottawa [3]Ottawa Hospital Research Institute, Ottawa, Canada

Background: Cardiac surgeries are often associated with substantial blood loss, putting patients at increased risk for blood transfusions. The use of tranexamic acid (TXA), an anti-fibrinolytic agent, as a blood conservation strategy has gained popularity in many surgical specialties, and it has been shown to be both an effective and safe therapy. However, TXA remains underutilized, largely due to fear of potential thromboembolic events, which are of concern in cardiac surgery. Another possible contributing factor to the under-use of TXA is the lack of evidence-based guidelines outlining which patient groups should not receive TXA due to risks outweighing the benefits.

Aims: We conducted a systematic review to determine which patients were excluded from clinical trials of TXA in cardiac surgery to help determine if there are patient groups in whom the risk of TXA therapy cannot be estimated. As a secondary objective, we assessed the safety of systemic TXA. We hope the findings of this review will enable the development of evidence-informed exclusion criteria for TXA use in patients undergoing cardiac surgeries.

Methods: The databases Medline, EMBASE, and the Cochrane Central Register of Controlled Trials were searched from inception until September 2017. Eligible studies were randomized controlled trials (RCTs) administering systemic TXA perioperatively to patients undergoing any cardiac surgery. Comparator groups of placebo, no intervention, or an active comparator were accepted. Our primary outcome was a description of the exclusion criteria for each RCT, and as a secondary endpoint we assessed the rate of adverse events associated with TXA use. A descriptive synthesis was performed to synthesize study characteristics and analyze the exclusion criteria. TXA safety was assessed with meta-analysis using a random effects model.

Results: 70 eligible RCTs were included in this systematic review. A variety of cardiac surgeries were included, the most common one being coronary artery bypass graft surgery (45.7% of studies). The two most common reasons for excluding patients from TXA trials in cardiac surgery were major hepatic, renal, or cardiac comorbidities (75.7% of studies), and the use of medications affecting coagulation (55.7% of studies). Other patient groups frequently excluded from these trials were those with coagulopathy (41.4% of studies), known allergy to TXA (35.7%), an abnormal coagulation profile (32.9% of studies), a previous history of arterial or venous thromboembolic events (27.1% of studies), and anemia (20.0% of studies). Meta-analysis showed that systemic TXA did not increase the risk of adverse events compared to placebo or no intervention (RR = 0.97, 95% CI: 0.88, 1.07).

Summary/Conclusions: Systemic TXA is safe to use peri-operatively in cardiac surgery, and evidence-based guidelines for its use in surgery can be developed for many patient populations. Regarding the patient groups commonly excluded from TXA trials in cardiac surgery, some of the exclusions may not be warranted based on current evidence. However, due to frequent exclusion from RCTs, there may be limited efficacy and safety data on TXA in these populations, and further research on TXA in these patient groups may be warranted.

P-788

RETICULOCYTE HEMOGLOBIN EQUIVALENT AS A SURROGATE MARKER FOR THE IDENTIFICATION OF IRON DEFICIENCY

P Morin[1], S Ning[1], R Barty[1,2], N Li[1,2], Y Liu[1,2], D Arnold[1,2,3] and M Zeller[1,2,3]

[1]Department of Medicine [2]McMaster Centre for Transfusion Research, McMaster University, Hamilton, Ontario [3]Canadian Blood Services, Ancaster, Ontario, Canada

Background: Red blood cells (RBCs) are often transfused inappropriately to iron deficient, anemic patients. The most common methods for identifying iron deficiency (ID) are biochemical and hematologic indices. Serum ferritin is an accessible and popular biochemical test with high specificity but low sensitivity that increases in settings of inflammation, making it an imperfect test for iron status. Additional biochemical indices are used and each has limitations. Measurement of reticulocyte hemoglobin content has emerged as a potential surrogate test for identifying patients with ID, as it reflects iron availability for the formation of new red blood cells. Accessibility to this measure was expanded with reticulocyte hemoglobin equivalent (RET-He) using Sysmex analyzers. A RET-He is performed on the same tube collected for a complete blood count with a short turnaround time. This could allow for rapid identification of ID as a cause for anemia and optimize management with iron repletion instead of RBC transfusion where possible. The RET-He test is already incorporated into iron repletion algorithms for patients with chronic renal disease, but has not been widely validated in other populations.

Aims: This study evaluates the diagnostic accuracy of RET-He as a surrogate marker for the identification of ID when compared to ferritin and transferrin saturation in an outpatient population.

Methods: We conducted a retrospective study on all outpatients at three hospitals with both a RET-He and a ferritin measurement on the same day. Patients with severe chronic renal disease are treated at a different hospital and were excluded from this study. Data was obtained via a large comprehensive database containing demographic and laboratory information on all patients in Hamilton hospitals. Diagnostic accuracy of RET-He was evaluated with ROC curve analysis, under two definitions of ID: 1. Absolute ID (ferritin <30 ng/ml and transferrin saturation <20%), and 2. Functional and absolute ID (ferritin <30 ng/ml or transferrin saturation <20% and ferritin <200). Associations between RET-He and other markers of ID were assessed using Pearson's correlation test.

Results: Data extracted from July 2016 to December 2017 identified 1980 outpatients who had both a RET-He and ferritin result. Absolute ID was identified in 616 patients; 844 patients were identified when including functional ID. For absolute ID, area under the curve (AUC) for RET-He was 79.8%; the optimal cut-off was 33 pg, with a sensitivity of 80.7% and specificity of 65.3%. When including subjects with functional ID, AUC was 75.1%, and the optimal cut-off was 34 pg, with a sensitivity of 79.9% and specificity of 60.2%. In absolute ID, RET-He correlated positively with ferritin (cor=0.508, 95% CI 0.447–0.564), transferrin saturation (cor=0.775, 95% CI 0.726–0.817), hemoglobin (cor=0.755, 95% CI 0.719–0.787) and MCV (cor=0.794,

95% CI 0.763–0.822), all with P<0.0001; similar results were obtained when including functional ID.

Summary/Conclusions: RET-He had good accuracy for the identification of ID in the outpatient population; accuracy, though decreased, was fair when including patients with functional ID. At a cut-off of 33 pg, sensitivity is better than specificity, suggesting a higher rate of false positives. RET-He correlated moderately with ferritin, and strongly with transferrin saturation. RET-He was less performant in our cohort than in published studies, where AUC approximates 90%; further analysis is required to identify in which populations RET-He can be used as an accurate measure of ID.

P-789

RETROSPECTIVE ANALYSIS OF OBSTETRICS AND SURGICAL REFERRALS IN JEHOVAH'S WITNESSES: THE EXPERIENCES IN ROYAL INFIRMARY OF EDINBURGH 2015–2016

C Manchanayake[1], F Clayton[2] and K Majodob[3]

[1]Transfusion Medicine, Scottish National Blood Transfusion Service [2]Urology
[3]Haematology, NHS Lothian, Edinburgh, United Kingdom

Background: Jehovah's Witnesses (JW) represent a minor but significant and challenging cohort of patients seeking obstetric and surgical procedures within the Royal Infirmary Edinburgh. Scottish Blood Transfusion (SNBTS) consults each patient about the acceptance or refusal of blood products including autologous procedures and takes necessary steps to minimise bleeding risk.

Aims: To undertake retrospective review of JW patients referred by obstetric, surgery and anaesthetic within a single NHS Lothian hospital, regarding their characteristics and management. To describe an evolving service co-ordinated by transfusion medicine doctors in SNBTS with the purpose of evaluating the benefits of the service to patients and clinical colleagues.

Methods: A retrospective audit of the referral letters and blood results of all JWs referred by RIE clinical teams from 2015–2016 was carried out. Patient notes supplied information on demographics, diagnosis, surgical procedures, pre- and postoperative bloods and complications. Exclusions: paediatric patients; patients with non-religious refusals. Only descriptive statistics (through systematic questionnaires) were used as the study's target population was fully represented. No statistical comparisons to other health boards were made. Information was analysed according to compliance with local and national guidelines where available.

Results: A total of 36 patients (2 male–34 female, 9 surgical, 27 obstetric) were included. Ethnicity: White Scottish 36.11%, Polish 13.8%, African 19.44%, White English 8.33%, Indian 2.7%, Eastern European 2.7%, Caribbean 2.7%, Black Scottish 2.7%, non-disclosed ethnicity 11.11%. 100% refused primary blood components; 9% additionally rejected secondary blood components; 9.9% refused recombinant factor VIIa. 97% refused fibrin sealant, 100% accepted tranexamic acid. Erythropoietin refusal was 2.7% (contains animal plasma) 100% accepted continuous intra-operative cell salvage. Only 5.5% agreed to transfusion of any blood component as an alternative to certain death from non-transfusion- due to family commitments.100% accepted all forms of medical treatment except blood transfusion. *Surgical patients*: 9 surgical patients (two male, seven female)- mean age of 58 years (range 34–90)- underwent a total of 8 procedures. All patients were consented, and continuous cell salvage arranged. However only two patients required transfusions. One cardiothoracic patient developed anaemia. There were no deaths. *Obstetric patients*: 84% of patients were referred at second trimester. 27 patients' baseline FBC showed 13.5% were anaemic according to gestation-specific ranges. Post referral bloods included serum ferritin (96%), B12 and folate (96%), coagulation screen (92%), and reticulocyte count (16%). Anaemia was due to iron deficiency in all patients. 29% had iron supplements throughout pregnancy. 6% received iron infusion, 0% received erythropoietin. The majority underwent normal vaginal delivery; only 5.4% had Caesarean section. Cell salvage was available for all sections but utilised only once.

Summary/Conclusions: Since 2015, all JW patients are seen by a transfusion expert to discuss blood products, transfusion alternatives and optimisation of haematological parameters. This practice has improved anaemia monitoring. SNBTS liaises with clinicians and co-ordinates pre-planning with the JW Hospital Liaison Committee. This study identified the need for improvement in documentation and staff education in guideline adherence. Separate policies for obstetrics and other surgical patients should be created.

P-790

PREOPERATIVE AUTOLOGOUS BLOOD DONATION FOR ORTHOGNATHIC SURGERY

H Chung[1], Y Kim[1], J Kim[2], S Kim[2] and M Lee[1]

[1]Department of Laboratory Medicine, Ewha Womans University College of Medicine
[2]Department of Oral and Maxillofacial Surgery, Ewha Womans University Medical Center, Seoul, Korea

Background: Preoperative autologous blood donation (PABD) is the process of collecting and storing the patient's blood before a planned operation, with the purpose of having a personal store in the case the patient develops postoperative anemia. PABD has been used in patients undergoing elective, and the main indications for PABD are patients with rare blood groups, patients with multiple alloantibodies, and patients who refuse consent to allogeneic blood transfusion for personal reasons. Orthognathic surgery is widely performed to correct dentofacial deformities and improve function and physical appearance. It is associated with a significant risk of blood loss and blood transfusion. PABD has been commonly used for orthognathic surgery but not much is known on the current state of PABD and blood transfusion practice and the number of studies on this issue is limited.

Aims: Our study designed to investigate the current state of PABD for orthognathic surgery in a tertiary university hospital, which is important not only for safe and appropriate transfusion in the patients but also for rational management and proper service of hospital blood center.

Methods: The records of patients requested for PABD undergoing orthognathic surgery in the period between January 2013 and December 2017 were retrospectively reviewed. One or two units of autologous blood were collected, one unit at a time, with about a 1-week interval between collections; the last unit was collected >72 h preoperatively. The blood volume collected was 320 ml.

Results: A total of 152 units from 90 patients were collected; 1 unit from 28 patients (1-unit PABD) and 2 units from 62 patients (2-unit PABD patients). For 1-unit PABD patients mean Hb before PABD was 14.2±1.7 g/dl, for 2-unit PABD patients mean Hb before 1st PABD and 2nd PABD were 14.5±1.5 g/dl and 13.5±1.6 g/dl, respectively. No serious side effects have been observed after blood collection. A total of 139 of 152 units (91.4%) of PABD were transfused to 82 patients (91.1%). Among 82 patients received blood transfusion, 72 patients (87.8%) could avoid allogeneic blood transfusion. The incidence of additional allogeneic blood transfusion was 11.1% (10/90); 10.7% (3/28) of 1-unit PABD patients and 11.3% (7/62) of 2-unit PABD patients. The mean postoperative Hb of patients received transfusion 9.8 g/dl, which means that they were not over-transfused. The wastage rate of PABD was 8.6% (13/152), which was significantly higher than that of allogeneic blood in the same period (less than 1%); 21.4% (6/28) of 1-unit PABD and 5.6% (7/124) of 2-unit PABD.

Summary/Conclusions: PABD reduced the incidence of allogeneic blood transfusion in patients undergoing orthognathic surgery and the risk associated with allogeneic blood transfusion. However, the high wastage rate of PABD indicated inappropriateness of the indication of PABD. PABD plays important role in patient blood management (PBM), but to achieve PBM, it is necessary to indicate PABD appropriately and use it adequately without discarding.

Transfusion Practitioner Related Clinical Practice Improvement

P-791

Abstract has been withdrawn

P-792

CONSUMPTION OF POLYVALENT IMMUNOGLOBULINS ACCORDING TO INDICATIONS

M Lukic, M Raos, F Plenkovic and B Golubic Cepulic

Transfusion Medicine and Transplantation Biology, Clinical Hospital Center Zagreb, Zagreb, Croatia

Background: Polyvalent immunoglobulins (IGs), both intravenous (IVIG) and subcutaneous (SCIG), are used in the replacement therapy for primary immunodeficiency and in immunomodulating treatment of autoimmune diseases and neuroimmunological disorders. In the last decades, indications have been extended to secondary immunodeficiency, especially to haematological diseases such, as lymphoproliferative diseases (LPDs) and multiple myeloma (MM). Furthermore, IG are used for iatrogenic hypogammaglobulinemia due to immunotherapy (e.g. Rituximab), in immunosuppressive therapies (steroids, sulfasalazine, mycophenolate mofetil) and bone marrow (BMT) or solid organ transplantation. In clinical usage, when there is a lack of scientifically proven benefit, IG therapy is applied off-label.

Aims: The aim of this study is to retrospectively analyze the usage of IG according to the indications.

Methods: We retrospectively analyzed data on the type and quantity of IG issued for 541 patients during 2016. The data were collected from the transfusion and hospital information system. Out of 541 examined patients, 538 (99.4%) were treated and 3 (0.6%) were not. Indications for IG application were determined according to "Clinical Guidelines for Immunoglobulin Use", NHS Scotland, 2012 Modified 2017.

Results: From 538 patients treated with IG, 273 (50.7%) were male and 265 (49.3%) female, of which 105 (19.5%) children and 433 (80.5%) adults (median age 48, range 0–90). A total of were treated according to medical indications: 75 (71.4%) children and 377 (87.1%) adults. Off-label treatment was received by 30 (28, 6%) children and 56 (12.9%) adult patients. A total of 525 (97.6%) patients received only IVIG, 7 (1.3%) patients received only SCIG, and 6 (1.1%) patients received IVIG and SCIG. A total of 82,788 g of IG was used and patients were treated on average with 153 g (range 2.5 - 1640 g), of which 78,846 g (95.2%) IVIG and 3,942 g (4.8%) SCIG. The analysis of consumption of IG in adults and children can be divided into three categories. Firstly, there are haematology-oncology patients with a total of 41,201 g (49.7%) – mostly BMT patients (allogeneic, autologous or stem cells) with 18,387 g (44.6%). Secondly, patients with autoimmune diseases and a consumption of 20,624 g (24.9%) – the highest number of patients with primary immunodeficiency (PID) with 11,864 g (57.5%). The third category comprises neurological patients with a consumption of 7,025 g (8.5%) – mostly adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) with 2,365 g (33.7%) and children with Guillain-Barre syndrome with 360 g (5.1%).

Summary/Conclusions: A total of 538 patients, 28.6% of children and 12.9% of adults were treated with polyvalent immunoglobulin off-label. Due to a constant increase of IG consumption and expansion of clinical indications, it is a necessity to compose national guidelines for treatment, which would help rationalize the consumption of precious resources (e.g. human plasma).

P-793

Abstract has been withdrawn

P-794

AN EVIDENCE BASED AUDIT OF FRESH FROZEN PLASMA (FFP) USE AT SEALS PATHOLOGY OVER WINTER 2016 AND NEW LOCAL GUIDELINES FOR APPROPRIATE USE OF FFP

MM Menzies Wojtowicz, S MacCallum and D Stern

Haematology, SEALS Pathology, Prince of Wales Hospital, Sydney, Australia

Background: Fresh frozen plasma is a precious resource often used inappropriately, despite evidence available to guide its use; and it is well established to definitely cause harm. Frequently, there is too much emphasis placed on abnormal coagulation studies, rather than considering the entirety of the clinical context. Particular settings where FFP is used inappropriately include to correct mildly deranged coagulation studies prior to an invasive procedure (Veera et al, Blood, 2012), liver dysfunction and in the absence of bleeding or with normal coagulation studies (NICE, NHS Blood and Transplant, 2014). A more conservative approach to plasma transfusion is therefore warranted, particularly in the non-bleeding patient.

Aims: To examine primarily how many adult FFP transfusions were "appropriate" or "inappropriate," according to current evidence, in particular the National Blood Authority (NBA) Patient Blood Management (PBM) Guidelines 2012. Qualitative and quantitative data was analysed to reach a conclusion.

Methods: A retrospective local audit from June-August 2016 was conducted. Data was collated with an audit template, to record the demographic details, PBM category, whether the patient was bleeding, FFP dose and whether this was therapeutic (12–15 mL/kg) (NBA PBM Guidelines 2012), proposed indication, ROTEM involvement, pre and post FFP transfusion coagulation studies, prescribed anticoagulants, use of Prothrombinex for warfarinised patients, vitamin K use and adverse events attributed to FFP use; and translate this information into appropriateness for transfusion. Abnormal coagulation studies were defined as greater than the upper limit of our reportable ranges. Data was used to derive recommendations to improve transfusion practice (AABB Technical Manual, 2011) and decrease future inappropriate transfusions (Tinmouth, Transfusion, 2007).

Results: 60% of FFP transfusions were found to be "appropriate" and 40% "inappropriate." Unsurprisingly, most FFP was administered in acute areas of the hospitals, most commonly for surgical (upper gastrointestinal and cardiothoracic) and obstetric patients. Coagulation studies did not tend to normalise with administration of FFP and many patients did not receive a therapeutic dose. Bleeding patients were more likely to receive an "appropriate" transfusion but only a third of them received a therapeutic dose and bleeding reduction was poorly documented. 34% of episodes involved a patient on an anticoagulant, but FFP was not necessarily given to reverse effect. 7/10 episodes for warfarinised patients were inappropriate and prothrombinex was underutilised. The ROTEM was used in 19% bleeding episodes, all within cardiothoracic surgery. Vitamin K was used in 28% of bleeding patients. None of the FFP transfusions from the audit period were documented to lead to harm. Several interesting case vignettes illustrate some interesting scenarios of FFP use at our institution, including the contexts of renal transplant, massive bleeding associated with warfarin therapy and catastrophic surgical bleeding.

Summary/Conclusions: This audit was used to educate clinicians and supplement new restrictive local guidelines for appropriate and inappropriate FFP use, to improve future transfusion practice and ultimately reduce inappropriate FFP transfusions.

P-795

A PROSPECTIVE STUDY OF THE EFFICACY OF PLATELET TRANSFUSIONS IN PATIENTS RECEIVING A BONE MARROW TRANSPLANT

RB Sawant[1], R Ahmed[1], M Gupta[1], V Vadera[1], S Tulpule[2] and S Sen[2]

[1]Transfusion Medicine [2]Bone Marrow Transplant Unit, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India

Background: Patients receiving a BMT are more likely to receive platelet transfusions prophylactically as well as therapeutically. BMT has been reported to be a major factor independently associated with poor response to platelet transfusions.

Aims: To study the efficacy of platelet transfusions in patients receiving a BMT in our hospital setting.

Methods: A prospective study was done to determine the effectiveness of platelet transfusions in BMT patients by determining the 24 h corrected count increment. 180 platelet transfusion events in 36 BMT patients (9 autologous BMT and 27 allogeneic BMT) were studied. 24 h CCI of <4500/UL was considered as indicative of refractoriness to platelet transfusion. All patients received either ABO identical, pooled and leucodepleted random donor platelets or ABO compatible apheresis platelet transfusions only. Any association of reduced CCI with clinical factors in these patients was recorded.

Results: The mean threshold for platelet transfusion in BMT patients was at platelet count of 10644+1800/UL. Platelets were transfused on mean Day −2 of storage and mean platelet dose per unit transfused was 2.6×10^{11}. The overall mean CCI was 5618 +2120/UL, whereas it was 9473+2260/UL in the autologous BMT patients and 5064+1328/UL in the allogeneic BMT patients. The CCI was < 4500/UL for 102/180 (56.6%) platelet transfusion episodes. Nine patients (7 allogeneic BMT and 2 autologous BMT) were found to be refractory to platelet transfusion based on the CCI values. Severe mucositis, increased bilirubin and increased cyclosporine-A levels were found to be associated with reduced CCI in these patients. The mean CCI in adult patients (n=9) who received 41 platelet transfusions was 4005+1960/UL and in pediatric patients (n=27) who received transfusion of 139 platelet units, the mean CCI was 6094+1416/UL. No adverse reaction or clinical bleeding were reported during the study period. None of our patients were investigated for anti-platelet and anti-HLA antibodies.

Summary/Conclusions: The 24 h CCI was found to be a reliable indicator for evaluating clinical effectiveness of platelet transfusions. Efficacy of platelet transfusions in BMT patients was found to be better in paediatric patients and in patients undergoing autologous BMT. Clinical factors also affect efficacy of platelet transfusions significantly.

P-796

Abstract has been withdrawn

P-797

BLOOD UTILIZATION AND IMPACT OF CHRONIC TRANSFUSION THERAPY (CTT) IN A LARGE COHORT OF BRAZILIAN SICKLE CELL DISEASE (SCD) PATIENTS

S Kelly[1], D Rodrigues[2], M Flor-Park[3], A Carneiro-Proietti[4], P Loureiro[5], C Maximo[6], R Mota[7], D Brambilla[8], L Preiss[8], E Sabino[9] and B Custer[1]

[1]*Blood Systems Research Institute, San Francisco, United States of America* [2]*Fundação Hemominas, Juiz de Fora* [3]*Instituto da Criança-Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Sao Paulo* [4]*Fundação Hemominas, Belo Horizonte* [5]*Universidade de Pernambuco/Fundação Hemope, Recife* [6]*Fundação Hemorio, Rio de Janeiro* [7]*Fundação Hemominas, Montes Claros, Brazil* [8]*RTI, Rockville, United States of America* [9]*Faculdade de Medicina & Instituto de Medicina Tropical da Universidade de São Paulo, Sao Paulo, Brazil*

Background: Red blood cell transfusions are used in SCD patients to treat acute complications or as CTT to prevent severe disease manifestations.
Aims: 1. Describe utilization, indications for and adverse events (AEs) associated with transfusions in SCD. 2. Compare outcomes between patients treated or not with CTT.
Methods: A Brazilian SCD cohort was established to investigate transfusion and other outcomes. Patients with 1+ encounter in the prior 3 years were randomly selected as eligible from 6 Brazilian centers (Sao Paulo, Rio de Janeiro, Belo Horizonte, Juiz de Fora, Montes Claros and Recife). Medical and blood bank records were abstracted for clinical history and detailed information on transfusions in the year prior to enrollment. CTT was defined as scheduled transfusions (10+ in a year-long period) to prevent SCD complications. Two controls not treated with CTT were selected for each CTT case matched on center, SCD genotype, gender and age. Clinical outcomes were compared between the two groups using standard statistical methods.
Results: Of 2,795 patients enrolled in the cohort from 2013–2015, 55.9% were children <18 years. Hemoglobin (Hb) SS was the most common SCD genotype (70.7%), followed by HbSC (23%), Sβ0 (3.0%) and Sβ+ (2.9%). Most of the cohort (75.0% of children and 89.2% of adults) had been transfused at least once with 29.2% of children and adults transfused in the prior year. The most common indication for transfusion was CTT (77.2% of 2585 transfusions in children and 66.4% of 1916 transfusions in adults). The next three most common indications in children were acute chest syndrome (ACS 6.8%), acute symptomatic anemia (5%) and vaso-occlusive pain episodes (VOE 4.9%), while acute symptomatic anemia (13%) was followed by VOE (9.9%) and ACS (3.9%) in adults. AEs were reported in 30 of 4501 transfusion episodes (allergic=14, febrile non-hemolytic=13, bacterial contamination=1, acute hemolytic=2). AEs were reported with 11 of 1234 acute transfusions (0.89/100 transfusions) and 19 of 3267 CTT (0.58/100 transfusions). There were 166 (10.6%) children and 113 (9.2%) adults treated with CTT, most commonly for history of clinical stroke (56.6% of children and 68.1% of adults) followed by abnormal transcranial doppler (38%) in children and frequent VOE (21.2%) in adults. A majority (75.6%) of transfusions for CTT were administered as manual exchange compared to simple transfusion. Children not treated with CTT were more likely to have a VOE and ACS hospitalization in the prior year than treated (25.6% vs 11.6% P=0.0002 and 21.3% vs 9.1%, P=0.0006, respectively) while adults treated or not did not differ in these acute events. Approximately half of both children and adults treated with CTT were iron overloaded (defined as ferritin>1000 ng/dl) and alloimmunization was more common in CTT cases compared to controls (26.2% vs. 12.2%, P<0.0001 in children and 38.5% vs. 19.3, P=0.0003 in adults, respectively).
Summary/Conclusions: Transfusion is common in this SCD cohort, with the majority administered as part of CTT. Transfusion reactions were not common but alloimmunization and iron overload were, highlighting the need for novel clinical strategies to mitigate these risks of CTT in SCD.

P-798

HOW PERIOPERATIVE ANTICOAGULATION AFFECTS TRANSFUSION IN CARDIAC SURGERY

M Najafi[1,2], F Yousef Shahi[3], P Farrahi[4] and J Zebardast[5]

[1]*Anesthesiology, Tehran Heart Center, Tehran University of Medical Sciences* [2]*Cardiac Outcome Research and Education (CORE), Universal Scientific Education and Research Network (USERN)* [3]*Anesthesiology* [4]*Surgery* [5]*Research, Tehran University of Medical Sciences, Tehran, Iran*

Background: The practice of transfusion medicine in cardiac setting has encountered significant changes recently due to substantial prescription of anticoagulants with different mechanisms of action. With regard to overwhelming costs of transfusion, it is mandatory to know the effects of anticoagulants on the need for transfusion in cardiac surgery, even though it is unavoidable to continue some forms of anticoagulation until operation.
Aims: This study was aimed at determining how administration of anticoagulants affects the need for transfusion in cardiac surgery candidates in a tertiary hospital.
Methods: We recruited 462 patients to a correlational study and followed them up from their admission until discharge from the hospital. All candidates for cardiac surgery in Tehran Heart Center were enrolled in this cross-sectional study. In addition to demography and anthropometric measures, lab data and details of perioperative consumption of blood and blood products as well as complete history of anticoagulants including type, dosage, and timing of usage were assessed in this study. Operation room and postoperative events including bleeding volume were recorded too.
Results: Out of 314 men (67.2%) and 153 women (32.8%) who were studied, 355 patients received blood and blood products including 3 warm whole blood units, 939 units packed RBCs, 236 units FFP, 133 units Platelet, and 14 units cryoprecipitate. With regard to anticoagulant consumption Aspirin ranked first by 55.2% followed by Heparin 43.2%, Clopidogrel 15.2%, Warfarin 2.4%, and Enoxaparin 0.9%. Multivariate analysis of predictors of packed RBC consumption showed that gender, age more than 75 years, body surface area (BSA), and preoperative hemoglobin were the most important predictors of transfusion in coronary patients with 4.43, 7.67, 0.07, and 0.41 odds ratios (OR) respectively. Aspirin usage before surgery was among predictors of massive postoperative transfusion (more than four units) in coronary patients (P=0.040, OR and 95% confidence interval (CI) were 1.82 and 1.07–13.67 respectively). Heparin was associated with fresh frozen plasma usage in valvular patients (P=0.024, OR 15.09, 95% CI 1.44–155.01. Moreover, patients who had stopped Clopidogrel at least three days before surgery had significantly less bleeding compared to the others (P=0.013).
Summary/Conclusions: The most important predictors of perioperative transfusion of packed RBC in coronary artery surgery are gender, age, BSA, and preoperative hemoglobin. Though the anticoagulants are not ranked among the most important predictors of transfusion, their dosage and timing of discontinuation should be carefully monitored due to the risk of massive bleeding in patients on this group of medications.

P-799

ANALYSIS OF BLOOD USAGE IN ELECTIVE SURGICAL PROCEDURES IN A DISTRICT GENERAL HOSPITAL, SRI LANKA: STEP TOWARDS MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE (MSBOS)

TI Withanawasam

National Blood Transfusion Service, Colombo, Sri Lanka

Background: Sri Lankan National Blood Transfusion Service 100% depends on voluntary non-remunerated blood donors. Blood prescribing clinicians are not aware of the blood stock management and over ordering of blood is a common practice. In the absence of an explicit Maximum Surgical Blood Ordering schedule, requesting is on clinicians' assessment.
Aims: This study was done with the objective of evaluating the current practice of blood ordering and utilization in elective surgical procedures. It aims the formulation of MSBOS to streamline the blood usage and stock management and reduce the unnecessary blood wastage.
Methods: This is a retrospective, hospital based study conducted for the duration of six months. All cross match requests related to elective general, orthopedic, genitourinary, otorhinolaryngology and facio-maxillary surgeries and renal biopsies were analyzed for number of blood units requested and transfusions during first six months of 2017. The cross match: transfusion (C: T) ratio (Number of units cross matched divided by the number of units transfused), transfusion index (TI)(Number of units transfused divided by the number of patients cross matched)and transfusion

probability (%T)(Number of patients transfused divided by the number of patients cross matched X 100)were calculated for each procedure.

Results: Total number of procedures those requested blood transfusion were 35 in 2348 patients. The highest number of requests (23%) were for the elective lower segment Caesarian section, 13% were for the laparotomy and 9% for the dynamic hip screw and total abdominal hysterectomy surgeries. 9% of the total blood transfusions (n =2073) during the study period is for the elective surgical procedures. Only 192 (8%) of procedures have utilized cross matched blood during or immediate postoperative period and 92% were uncomplicated and have not required blood transfusion. Cross match: Transfusion (C: T) ratio is higher than the standard for all the surgeries except for open reduction internal fixation surgery (2.5:1). The highest ratio is for the saphenofemoral ligation (53:1). The only procedure which has Transfusion Index (TI) > 0.5 is the total knee or hip replacement surgery (0.7). Only three orthopedic surgeries have %T of > 30%; closed reduction internal fixation (36%), open reduction internal fixation (66%) and total knee or hip replacement (75%).

Summary/Conclusions: The analyzed data was presented at the Hospital Transfusion Committee meeting. The indices used to determine the efficiency of blood ordering and utilization are C: T ratio, TI and %T. C: T ratio <2.5 and/or TI of 0.5 or more indicates efficient blood usage. %T of 30% and above consider indicative of significant blood usage. According to this study majority of surgeries could be managed by Group and Save method without cross matching blood for each procedure. The requirement of a MSBOS was agreed unanimously by the clinicians and the blood bank. MSBOS is a guide to optimize blood usage in surgeries which can decrease over ordering of blood thereby reducing blood wastage and laboratory workload without compromising standard patient care.

P-800

TRANSFUSION PRACTICES IN REPEATEDLY TRANSFUSED PATIENTS IN LADY RIDGEWAY HOSPITAL FOR CHILDREN SRI LANKA

C Seneviratne

Blood bank, National Hospital of Sri Lanka, Colombo, Sri Lanka

Background: Appropriate goals of transfusion therapy and optimal safety of transfused blood are the key concepts in the protocol for routine administration of red blood cells to patients who are on repeated transfusions to sustain their lives. Families of these patients have to compromise prioritizing the need of the patients bringing a negative social impact to the families. In order to find out the practice it is necessary to carry out a situational analysis.

Aims: To describe the transfusion practices in repeatedly transfused patients in Lady Ridgeway Hospital for Children, Sri Lanka.

Methods: This prospective descriptive cross sectional study was carried out in Lady Ridgeway Hospital for Children, Sri Lanka during three months period. Presenting complaints of repeatedly transfused patients in all medical wards at admission, the pre and post transfusion Haemoglobin levels, current transfusion practices in relation to types of blood used, the volumes and the frequency of transfusion, adverse events, their outcome and the social impact of transfusions were analyzed.

Results: A total of 358 episodes were analyzed in 127 patients, of whom 55.9% were males. 88.2% were Thalassaemic patients. 61.4% did not have their extended phenotype done prior to initial transfusion. 96.9% of admissions were for routine transfusion. 47% were transfused for an Hb level of lower than 9 g/dl. Only 28.2% had their post transfusion Hb done and 72.3% achieved Hb levels between 12–14.5 g/dl. Buffy coat removed RBCs as special blood products were given to all patients. Approximately 30% of patients were getting Rh and Kell matched products prior to alloantibody formation. 42% used two units of blood per episode. 45% were transfused in a frequency of 15–21 days. Only 11% had adverse reactions to transfusion out of which 5.5% were urticarial and allergic reactions, 3.9% were febrile reactions and only 0.8% were haemolytic reactions. Clinically significant alloantibodies were positive in 5.5%. All patients with significant alloantibodies were Thalassaemic patients who were above 8 years of age. Study population did not have anti D antibodies. 55% of patients had one day admissions per episode which kept them away from home with a parent/guardian. 14% missed one school day per episode.

Summary/Conclusions: Patients in the study population predominantly comprised of males. Relatively older children have developed alloantibodies. Repeatedly transfused patients always received ABO and Rh D matched, Buffy coat removed RCCs. Social problems in families of these patients varied according to the distance from home to transfusion centre. A significant amount of money was spent for the episode by the families which emphasizes on developing a plan to provide the same facility and service in other peripheral hospitals so that the distance of travel can be minimized thereby minimizing the expenditure and loss of school days. There should

also be a plan to build up faith on the services given by the peripheral hospitals in these children's parents which will improve the outcome.

P-801

BLOOD TRANSFUSION IN SURGICAL PATIENTS – TIMING AND PRODUCT SELECTION

T Kunori[1,2], S Fujita[3] and K Suzuki[3]

[1]Surgery, Iwaki Kyoritsu Medical Center [2]Blood Service, Iwaki Blood Center [3]Blood Service, Iwaki Kyoritsu Medical Center, Iwaki, Japan

Background: Surgical procedures have been much improved this decade, which contributed to save blood at operations. Total amount of blood products, however, seems not significantly reduced.

Aims: To clarify the relation with surgery, full year data of blood transfusion (BTF) in each patient were collected.

Methods: Patients and operative procedures: Four surgical clinics, consuming 49% of all, surgery (SG), orthopedics (ORT), cardiovascular surgery (CAVS) and gynecology (GNE), were selected for analysis. Total gastrectomy (n=85; mean age, 68 years), colectomy (331; 70), rectal resection (151, 66), hepatectomy (90; 66) and pancreas resection (74; 67) in SG. Replacement of hip joints (544, 70) and of non hip joints (652; 80) in ORT. Open repair of aortic aneurysms (200; 66), repair of valves (311; 69) and aortic stenting (418; 72) in CAVS. Total hysterectomy (746; 54) and elective caesarian section (772; 33) in GNE. Timing of blood transfusion: BTF patients (%) were counted in 5 pre-/postoperative periods; TMB, A%/B%/C%/D%/E% indicating; A%,over a month before, B%, within 30 days; C%, operation day, D%, within 30 days; E%, over a month. Number of products per a BTF patient was expressed as RFPAA (RBC/ FFP/ PC/ 5%ALB/ 25%ALB).

Results: 1. Timing of BTF (TMB) in pre-/postoperative periods. a) BTF in SG: 34% of patients with total gastrectomy received BTF: TMB; 4.7%, 14%, *13% (at operation), 10%, 5.8%: RFPAA 6.9/ 1.7/ 0.3/ 2.2/ 2.5. Colectomy 37%:TMB; 4.2%, 8.8%, *15%, 11%, 6.3%: RFPAA 8.1/ 2.6/ 1.9/ 2.3/ 2. Rectal resection 31%: TMB; 1.3%, 6%, *15%, 15%, 4.6%: RFPAA 5.7/ 2.9/ 3.1/ 2/ 0.1). Hepatectomy 42%: TMB; 3.3%, 6.6%, *25%, 20%, 3.3%: RFPAA 4.4/ 4.3/ 2/ 2.1/ 1.5. Pancreas resection 50%; TMB; 4%, 4%, *27%, 25%, 13%: RFPAA 4.6/ 5.4/ 1.2/ 2.1/ 3.7. b) BTF in ORT: Replacement with artificial hip 40%: TMB; 3.0%, 11%, *7.6%, 7.6%, 2.6%: RFPAA 2.1/ 0.5/ 0.6/ 0.02/ 0.1/auto blood 2.4. Non hip 56%: TMB; 1.3%, 40%, *7.5%, 11%, 4.1%: RFPAA 1/ 0.3/ 0.3/ 0.04/ 0/auto blood 3.3. c) BTF in CAVS: Open repair of aneurysm 89%: TMB; 2.5%, 4.5%, *84%, 61%, 13%: RFPAA 49/ 43/ 41/ 5.3/ 6.9. Aneurysm stenting 39%: TMB; 3.3%, 2.4%, *21%, 18%, 7.4%: RFPAA 14/ 7.4/ 5.6/ 1.4/ 17. Valve 87%: TMB; 4.5%, 7.1%, *79%, 43%, 8%: RFPAA 13/ 9.2/ 9.1/ 1.9/ 2. d) BTF in GNE: Total hysterectomy 12%: TMB; 2.1%, 2.2%. *5%, 2.5%, 2.8%: RFPAA 6.7/ 1.5/ 1.5/ 0.7/ 0.7. Elective caesarean section 2.7%: TMB; 0.1%, 0.5%. *1.8%, 0.3%, 0%: RFPAA 2.9/ 1.3/ 0.7/ 0.1/ 0.3.

Summary/Conclusions: TMB (timing of BTF) and RFPAA (type of products) showed distinctive features of operative procedures: long-term pre-/postoperative use of RBC in SG or GNE and excess use of postoperative ALB in SG. Autologous RBC was limited to ORT. Postoperative use was comparative to intraoperative use in most procedures. 3 products, RBC, FFP and PC, were equally used in CAVS. Thus TMB and RFPAA analyses may contribute to forecasts of demand and rational use of blood products.

P-802

DESCRIPTIVE STUDY ON THE APPROPRIATE USE OF FRESH FROZEN PLASMA AMONG PATIENTS IN NATIONAL HOSPITAL OF SRI LANKA (FROM 25TH JUNE 2016 TO 25TH DECEMBER 2016)

L Wijesekara

National Blood Transfusion Service, Sri Lanka, National Hospital of Sri Lanka, Colombo, Sri Lanka

Background: Despite the presence of guidelines on the appropriate use of the product, the literature reports a high percentage of inappropriate transfusions of FFP, at the stake of overall patient wellbeing. This article presents the results of a descriptive study on the use of FFP in medical and general surgical wards of National Hospital of Sri Lanka.

Aims: To study and analyse practices and effectiveness of FFP transfusions, in the major tertiary care hospital in Sri Lanka. To study and analyse practices and effectiveness of FFP transfusions, in the major tertiary care hospital in Sri Lanka.

Methods: The study was carried out for a period of 22 week, examining the requests forms for FFP from medical and general surgical wards of National Hospital of Sri Lanka and clinical data obtained from the bed head ticket of transfused patients, manually. The indicators identified and evaluated were: demographic data of the patients, completeness of the request forms, appropriateness of the indication and dose in each transfusion episodes, availability of pre and post transfusion tests of coagulation, adverse events, efficacy of the treatment (evaluated by improvement in PT and APTT ratios by Wilcoxon signed-rank test). Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant, by British Committee for Standards in Haematology, in 2004 was taken as the benchmark.

Results: Six hundred forty five transfusion episodes utilizing 2576 units of FFP for 382 inward patients and 77.5% of the related clinical records were scrutinized. Only 14.73% of requests had satisfactory completeness of the requests forms. The indication for transfusions was appropriate according to the Guidelines in 39.08% of the transfusion episodes evaluated. High INR of undocumented aetiology, with active bleeding or high risk for bleeding, was found to be the commonest indication (30.56%) for which FFP was transfused appropriately. The commonest inappropriate indication was Liver disease with prolonged PT and/or APTT, in the absence of bleeding or a risk of bleeding (27.74%). The dose was appropriate in 47.25% of the requests. A comparison of pre- and post-transfusion PT and APTT ratios showed a significant correction with FFP transfusions (P <0.001).

Summary/Conclusions: Despite the clinical justification that may warrant the use of FFP by the clinicians in a resource poor setting, large proportion of the FFP transfusions were carried out for indications deemed inappropriate by the guidelines. The utilization of coagulation test guided component therapy is still not a routine practice. Attention should be drawn to the completeness of the request forms, from clinical staff as well as the blood bank staff.

P-803

WHAT DO THE ANTENATAL MOTHERS KNOW AND THINK ABOUT BLOOD TRANSFUSION AND SHOULD WE INCLUDE EDUCATION ON BLOOD TRANSFUSION DURING THE ROUTING ANTENATAL CARE? A DESCRIPTIVE ANALYSIS

M Krishnapillai[1] and S Sivachandran[2]

[1]National Blood Centre' [2]Obstetrics and Gynecology, De Soysa Maternity Hospital, Colombo, Sri Lanka

Background: Obstetric hemorrhage is one of the common indications for blood transfusion. It is recommended to obtain consent before blood transfusion but it may not be possible in critical emergencies. Most of the antenatal management guidelines have not recommended the routine education on blood transfusion.

Aims: Aim was to analyze the knowledge and attitudes regarding blood transfusion among antenatal mothers and the need of routine education regarding blood transfusion among the antenatal population.

Methods: A descriptive study was conducted among transfusion naive 320 antenatal women in their 3rd trimester attending antenatal clinic at De Soysa Maternity Hospital, Colombo, Sri Lanka. Data was collected with a self-administered questionnaire and analyzed with SPSS and Microsoft excel.

Results: Study population included 37.5% (120) primi and 62.5% (200) of multi gravida. Analyzing to the religions, 49.7% (159), 28.1% (90), 16% (51), 9.3% (30) of them were Buddhists, Hindus, Christians and Muslims respectively. None of them were Jehovah's witnesses. None of the mothers were counselled about blood transfusion during their antenatal visits by health care workers. Out of the total population, 31.9% (102) were aware of at least one indication for the blood transfusion. Bleeding and anemia were the indications known by 20.3% (65) and 14.7% (47) of mothers respectively. Only 45.3% (145) of mothers knew at least one side effect of the blood transfusion. Transfusion transmitted infections and allergic reactions were the complications known by 31.2% (100) and 21.6% (69) of mothers respectively. Among study population 94% (301) agreed that they would agree for blood transfusion irrespective of the indication if it was suggested by health staff whereas 6%(19) participants mentioned that they would agree for blood transfusion only in an acute life threatening situation. None of them mentioned that that they would refuse the transfusion even during a life threatening situation. Among the mothers who'd agree only in a life-threatening situation, 2.8% (9) of them decided so since they considered blood transfusion to be dangerous, whereas 2.5% (8) due to needle fear and 0.6% (2) mothers were scared to see the blood. Religious reasons were not mentioned by any of them as a restricting factor for transfusion. Among study population

97.1% (311) of the mothers suggested that all pregnant mothers should be routinely counselled about blood transfusion in the antenatal care.

Summary/Conclusions: Although the knowledge on blood transfusion was inadequate, most of the mothers accepted blood transfusion as an important clinical management. Majority of the study population favored the inclusion of education and counselling on blood transfusion during the antenatal period.

P-804

Abstract has been withdrawn

P-805

VARIABILITY OF HEMATOLOGICAL PARAMETERS IN CARDIAC SURGERY

S Mahjoub[1], A Chamakh[2], F Ghedira[3], T Denguir[4] and N Ben Romdhane[5]

[1]Hematology, La RABTA [2]Surgery Departement [3]Surgery Departement, Hopital La rabta [4]Surgery Departement, La rabta [5]Hematology, Hopital La rabta, Tunis, Tunisia

Background: Cardiac surgery is currently one of the most consumptive specialties of blood products with a great heterogeneity between services. The identification of preoperative bleeding risk factors and early diagnosis of hemostatic disorders are essential to rationalize the consumption of blood products.

Aims: Our study aimed to study hematological variations induced by extracorporeal circulation in cardiac surgery and to evaluate the transfusional practices during this surgery.

Methods: Data on consecutive adult patients who underwent first –time cardiac surgery between January and April 2017 were collected. Variables included standardized bleeding history, prothrombin time (PT), activated partial thromboplastin time, fibrinogen level, hemoglobin (Hb) and platelet count. For each patient, blood samples were taken pre-bypass before heparinisation (T1), per surgery (T2), 5 min after protamine administration (T3) and 24 h post operation (T4). Blood loss was measured and the amount of transfusion products was recorded.

Results: Thirty patients were enrolled; the average age was 54 years. Hemodilution of the extracorporeal circuit induced a hemoglobin drop of 28%, a platelet count of 31% and fibrinogen level of 24%. The mean rate of fall of hemoglobin between T1 and T4 was 2.5 +/- 1.6 g/dl. The evaluation of transfusion practices had shown that 76% of patients were transfuses with a least (01) labile blood product (LBP), whereas 14% of patients were excessively transfused.

Summary/Conclusions: Our study shows significant variations in hemostatic parameters during cardiac surgery with a transfusion rate around 76%. The implementation of a transfusion savings strategy is necessary to reduce the number of transfused patients.

P-806

PATIENT AND PUBLIC ENGAGEMENT IN BLOOD TRANSFUSION AT ROYAL COLLEGE OF PATHOLOGISTS' NATIONAL PATHOLOGY WEEK INITIATIVES

S Allard[1,2], C Denison[2], J McCullagh[1], C Booth[1], N Sharma[1] and F Sear[3]

[1]Barts Health NHS Trust [2]NHS Blood and Transplant, London [3]NHS Blood and Transplant, Cambridge, United Kingdom

Background: The Royal College of Pathologists in the UK organises an annual National Pathology Week highlighting the important contribution pathologists make to healthcare with many events for a range of people of all ages.

Aims: To improve awareness and engagement with schools, political figures, health care professionals and the public.

Methods: During National Pathology Week in November 2017, under the key theme of 'Pathology in the Community', the RCPath hosted a free Science Fair entitled 'Adventures in Health: Secrets of the Lab' inviting school students and families to the Mile End Ecology Pavilion. Attendees joined a team of doctors and scientists to go behind the scenes of a hospital laboratory with a variety of fun hands-on activities, demonstrations and displays. Over 250 school students of all ages and over 320 members of the public attended this Science Fair.

Results: Hospital Transfusion Practitioners and Haematologists at Barts Health NHS Trust in collaboration with the Patient Blood Management and Donor Marketing teams at NHS Blood and Transplant (NHSBT), the national blood service in England, organised a highly successful display on Blood Transfusion. We had several interactive tables showing the journey of safe blood transfusion including; patient information, sample taking, blood components, blood grouping and antibody testing and safety checks needed prior to administration. A further display highlighted special requirements for patient groups such as those with Sickle Cell Disease and the need to recruit more donors from Black, Asian and Minority Ethnic (BAME) groups. We discussed indications also for organ donations, engaging many visitors who also took away information on how to join the national organ donor register. A 'make and take' stand allowed participants to make a model of a red cell with add on ABO and D type with further models of antibodies to demonstrate fundamentals of blood group serology and consequences of ABO mismatch. This stand was highly popular and very well attended with students both young and old leaving as proud owners of their very own ABO, D typed model red cell! During preceding National Pathology Week initiatives, the team at Barts Health NHS Trust & NHSBT organised specifically patient-focused events entitled 'The Patient's Voice'. We asked patients with sickle cell disease (SCD) and thalassaemia to share their perspectives and the impact of transfusion on their lives with healthcare professionals working 'behind the scene' within hospital laboratories and the blood service who in turn spoke about the 'safe journey of blood' and steps to improve the blood supply. This was followed by an active joint discussion on how better to reach different ethnic minorities to encourage the donation of rare blood units essential for these patients who develop red cell antibodies.

Summary/Conclusions: We were able to reach-out to many members of the public and in particular school children of all ages and their families raising awareness around safe blood transfusion and also raising interest in blood and organ donation. Our Patient's Voice events helped share experiences between patients and hospital laboratory and blood service teams.

P-807

LOW TRANSFUSION REQUIREMENT AND INCIDENCE OF VENOUS THROMBOEMBOLISM IN GASTRIC CANCER PATIENTS IN TAIWAN

J Lin and Y Chen

Division of Transfusion Medicine, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, China

Background: Packed red blood cell (PRBC) transfusion may be associated with the development of venous thromboembolic phenomena. The amount of PRBC transfusion and incidence of venous thromboembolism (VTE) in Taiwan patients with gastric cancer have not been determined.

Aims: We queried the Taiwan health insurance database to study the transfusion requirement and the incidence of VTE in gastric cancer patients.

Methods: We conducted a nationwide population-based study using data retrieved from the Taiwan Longitudinal Health Insurance Database 2005 which contained claims data of one-million beneficiaries randomly selected from the Registry of Beneficiaries of NHIRD in 2005. We analyzed the data from 2005 to 2011 for patients with gastric cancer (ICD-9-CM code 151.0–151.9) which was diagnosed during the period 2005 - 2010. VTE includes deep vein thrombosis (DVT) (ICD-9-CM code 453.8) and pulmonary embolism (PE) (ICD-9-CM code 415.1; not including iatrogenic PE [ICD-9-CM code 415.11]).

Results: Of the1,036 patients with gastric cancers randomly selected, the median age was 71 years (range: 22 to 100 years) and 61.1% were male. PRBC transfusion was prescribed in 662 patients (662/1036 = 63.9%). The amounts of PRBC transfused were the following: 0 unit in 374 patients, 1 unit in 7 patients, 2 units in 234 patients, 3 units in 15 patients, 4 units in 175 patients, and higher than 4 units in 231 patients. The number of transfusions was: no transfusion: 374 patients (36.1%), transfusion once: 478 patients (46.1%), transfusion twice: 113 patients (10.9%), transfusion 3 times: 38 patients (3.7%), transfusion more than 4 times: 33 patients (3.2%). Seventeen patients (1.64%) developed VTE; DVT alone: 15 patients, PE alone: 1 patients, and both DVT and PE: 1 patient. Seven out of 17 patients with VTE received PRBC transfusions after VTE occurrence, but none of them received PRBC transfusion before VTE episodes.

Summary/Conclusions: Both requirement of PRBC transfusion and incidence of VTE are low in gastric cancer patients in Taiwan. PRBC transfusion was not identified as a risk factor for VTE in these patients.

P-808

CHRONIC TRANSFUSION DATABASE ASSISTS WORKLOAD AND INVENTORY MANAGEMENT

H Gerges[1], G Clarke[1], H Blain[1], C Mah[2], K Lew[2] and SN Nahirniak[1]

[1]Laboratory Medicine and Pathology, Alberta Health Services/University of Alberta
[2]Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

Background: Although transfusions are considerably safer than in the past, transfusion-related risks persist. Since the risks are typically per unit, they are of high concern in chronically transfused patients in addition to the inventory challenges and costs associated with supporting these patients. To manage these patients and their workload impact, a database of the chronically transfused patients in the Edmonton Zone (EZ) has been complied containing transfusion frequency, phenotyping, adverse events, transfusion indications and underlying diagnosis information. In our system, chronically transfused patients are defined as those who have been transfused at least once every two months for six months or longer.

Aims: To highlight how a database can assist in managing inventory and workload for chronic transfusion recipients.

Methods: Since 2013 the Blood Bank Lab Information System (Sunquest) and relevant clinical information was used annually to populate the database. Data is stored on secure institutional shared drive to allow retrospective analysis of the database.

Results: Between 2013–2016, a total of 1249 patients were entered in the database but ranged between 163–223 per year. The frequency of the gender and blood group have remained consistent during the study period (average: male 55.5%, female 44.5%, A- 5.8%, B+ 12%, B- 1.5%, O+ 39%, O- 6.8%, AB+ 3.3%, AB–0%). Hematologic diseases accounted for 64% of the patients. The proportion of hemoglobinopathy patients have increased over time from 7% to 13%. A decreasing trend for chronic transfusion renal failure, chronic GI bleeding, and anemia (iron deficiency anemia, anemia of chronic disease) patients is noted. Alloimmunization was highest in 2013 (41%) but dropped to a stable 30% in 2014. The data showed an increase in any phenotype matching from 30% to 37% of patients with those receiving full phenotypes increasing from 24% to 36%. In 2013, only 6% of all patients were phenotyped for Rh and Kell and 24% had full phenotypes matches. In 2016 only 1% were restricted to Rh and Kell matches but 36% had full phenotype matches. Overall alloimmunization rates have decreased with the increased use of phenotype matching with189 antibodies in 89 patients in 2013 versus 106 antibodies in 52 patients in 2016. Non-phenomatched transfusions occurred in 58% of the 52 patients in 2016 with 10% of those patients developing an antibody as a result of that.

Summary/Conclusions: A significant drop in the number of chronically transfused patients was noted in 2016 compared to previous years. This may be due to altered treatment plans for several disorders, changes in transfusion guidelines, use of IV iron therapy, erythropoietin stimulating agents or bone marrow sparing therapies. Due to the proportion of Hematologic disorders, ongoing discussion with clinical hematology allows increased awareness of these factors. The initial drop in the alloimmunization rate from 40% in 2013 to 30% in 2014 is likely due to increased phenotyping which had increased steadily during the study period, with more prevalence of full phenotypes. This database has allowed us to predict phenotype requirements for inventory by blood group impacting the workload of the blood bank.

P-809

RISK SCORE TO PREDICT TRANFUSION IN ELECTIVE CARDIAC SURGERY

A Pajares[1], L Larrea[2], I Zarragoikoetxea[1], A Lopez Gomez[1], R Vicente[1], P Carmona[1], M López-Cantero[1] and P Argente[3]

[1]Anesthesiology and Cardiac Critical Care, La Fe Hospital [2]Centro Transfusion de la Comunidad Valenciana [3]Anesthesiology and Critical Care, La Fe Hospital, Valencia, Spain

Background: Blood transfusion acquires a special relevance in the cardiac surgery setting, since it is one of the surgical specialties of greater haemorrhagic risk. These surgical procedures are characterized by high requirements of packed red blood cells (RBC). A large number of adult cardiac surgery patients receive a perioperative transfusion; however, the inter-centre range is very broad with RBC transfusion rates ranging between 7.8% and 92.8%. This variability may be due in part to different preoperative assessment and management, different bleeding risk, and the absence of an internationally accepted standard in perioperative transfusion management of this type of patients. To reduce this variability, various strategies have been tried, including the study, development and description of several transfusion risk scores that may identify a target population with the highest probability of being transfused.

Aims: Definition of preoperative variables that, independently, affect RBC transfusion rate in cardiac surgery in order to develop a transfusion risk score in our setting.

Methods: Data on consecutive patients older than 15 years from the same hospital who underwent elective cardiac surgery (n=604) were taken in two periods between December 2012 to July 2013 (no blood saving protocol, prep group; n=293) and October 2015 to May 2016 (protocol was already implemented, postp group; n=311). Clinical and demographic characteristics, haematological parameters, biochemical and haemostatic analytical data, and transfusion information were evaluated. Primary outcome was the exposure to RBC transfusion in the operative and first postoperative days. Multivariable logistic regression techniques were used to determine the relationship between each independent variable and exposure to RBC transfusion.

Results: The overall transfusion rate of the entire group was 78.1% (69.4% for RBC, 28.4% for FFP and 36.8% for platelets). Protocol implementation decreased the overall transfusion rate from 89.5% to 67.6%, RBC from 83.6% to 56.4%, FFP from 36.2% to 21.2% and platelets from 40.8% to 32.7%. All these differences were significant. The hemoglobin level at hospital discharge was similar in both groups (10.47 grdL) The multivariate analysis showed that the variables that positively influenced in the reduction of the RBC transfusion rate were: protocol implementation, higher preoperative Hb value and preoperative congenital cardiac condition and interatrial communication. On the contrary, previous cardiac surgery, mixed cardiac conditions and chronic renal failure were unfavourable.

Summary/Conclusions: Implementation of a blood saving protocol managed to decrease the transfusion rate without lowering the haemoglobin level at discharge. In our setting, the preoperative variables that constitute transfusion risk factors were: absence of a blood saving protocol, lower preoperative Hb, lower minimum Hb in CPB, interatrial communication, previous cardiac surgery, mixed cardiac conditions and chronic renal failure.

P-810

Abstract has been withdrawn

P-811

Abstract has been withdrawn

P-812

A COMPARISON OF TRANSFUSION PERFORMANCES OF PRT-TREATED AND NON-TREATED PLATELET CONCENTRATES IN THROMBOCYTOPENIC PATIENTS

P Szykuła[1], A Gronowska[1], D Marciniak-Bielak[2], M Nowicki[1], R Małachowski[2] and J Staniewicz[3]

[1]Regionalne Centrum Krwiodawstwa i Krwiolecznictwa w Łodzi [2]Department of Hematology, Copernicus Memorial Hospital in Łódź, Łódź [3]Terumo BCT Polska Sp z o.o., Katowice, Poland

Background: Platelet concentrates (PC) are used worldwide to prevent or treat bleeding due to thrombocytopenia. Oncology and haematology patients are the most frequent receivers of PC. In our Institution patients who received bone marrow stem cell transplants, or those undergoing immunosuppressive treatment preferentially receive PC collected by apheresis from single donors. To reduce the risk of pathogen transmission through PC transfusion, Pathogen Reduction Technologies (PRT) have been implemented. The Mirasol PRT System (Terumo BCT), using riboflavin and UV light, has been used at the Regional Centre for Blood Donation and Haemotherapy (RCKiK) in Łódź since 2010. In 2017 778 PC were collected by apheresis. The platelets were suspended both in platelet additive solution (T-PAS) or plasma. 78 (10%) units of PC apheresis-derived PC were treated with the Mirasol technology (84% in plasma and 16% in T-PAS).

Aims: The aim of this study is to compare transfusion performance of apheresis-derived platelet concentrates (PC), treated with the Mirasol PRT system with untreated PC.

Methods: Clinical result of 64 single PC transfusion administered to haemato-oncological patients with thrombocytopenia was analysed retrospectively. Transfusion of

PC treated with Mirasol PRT (n=34) is called "treated" group and transfusion of PC non-treated with PRT (n=30) is called "control" group. Number of patients who did not present increase in platelet count 24 hr post transfusion is determined for both groups. For patients who presented increase of platelet count increment of platelet count 24 h post transfusion ($CI_{24\ h}$), corrected count increment ($CCI_{24\ h}$), was calculated:

$$CI_{24\ h} = (24\text{-h post-transfusion platelet count}) - (\text{pre-transfusion platelet count})$$
$$CCI_{24\ h} = [CI_{24\ h}/\text{transfused platelet dose}] \times BSA$$
$$BSA = 0.0202457 \times Height^{0.725} \times Weight^{0.425}$$

Results: The average $CI_{24\ h}$ was 10.9×10^9 ($\pm$ 7.36) n=19 and 10.3×10^9 ($\pm$ 9.73) n=22 in the treated and control group respectively (P>0.05). $CCI_{24\ h}$ for treated and control group was 6.9×10^9 ($\pm$ 5.0) n=15 and 6.1×10^9 ($\pm$ 5.91) n=17 respectively (P>0.05). There were patients refractory to platelet transfusion ($CI_{24\ h}$<0) in both groups: 15 (44%) in treated group and 8 (27%) in control (P=0.056). Reasons might be related to administered medication, fever or anti-HLA and anti-HPA antibodies.

Summary/Conclusions: The preliminary data presented in this abstract suggest that platelets treated with the Mirasol-PRT System showed similar performance when to untreated platelet concentrates collected by apheresis. Successful transfusion rates of 56% and 73% of patients in treated and control group are in concordance with previous reported experiences. Prospective and randomised analysis would be needed to exclude possible bias.

P-813

BLOOD TRANSFUSION PRACTICES OF HEALTHCARE PROVIDERS AT A UNIVERSITY HOSPITAL IN HAITI

DC Gervais[1] and M Cauvin[2]

[1]Notre Dame University of Hati [2]National Society of Haitian Red Cross, Port au Prince, Haiti

Background: In Haiti, Separation of blood components improved in 2013 when fresh frozen plasma, platelet concentrates, and cryoprecipitates were introduced by the National Service of blood transfusion of the Haitian Red Cross. Unfortunately, the majority of Haitian healthcare providers were not accustomed to the use of these blood products and Transfusion education was not included in their medical curriculum. Appropriate use of blood is fundamental for blood transfusion safety and Healthcare providers need to be continuously trained and updated to improve the system.

Aims: To describe transfusion practices of healthcare providers and identify constraints encountered in the integration of fractionated blood components in their patients' management at a University Hospital in Haiti.

Methods: We conducted a survey from September 1st 2014 to January 31st 2015 with a questionnaire intended for nurses and doctors in residency assigned in Internal medicine, pediatrics, anesthesiology, surgery, orthopedics, Obstetrics and gynecology departments of a University Hospital in Haiti. The questionnaire included: Information and Consent of blood recipients, Blood products' prescription and utilization; Blood products' Infusion practices and adverse reactions monitoring; and Post transfusion follow-up. Comments of participants were also listed.

Results: 117 questionnaires were delivered to residents and nurses of the hospital. We had a low response rate of 38.5% with 45 healthcare professionals who agreed to complete and return the questionnaire. Good transfusion practices were notified regarding Information and Consent of patients before Transfusion. Nevertheless, more efforts are needed for appropriate utilization of blood components. Platelet concentrates were reported for "severe thrombocytopenia". Only 56% of caregivers declared the use of Fresh frozen plasma mostly for "Disseminated Intravascular Coagulation" and "hypoproteinemia". Cryoprecipitates were unknown to 95.5% of them. Although the Haitian Red Cross is promoting prescription of fractionated blood components, 71% of caregivers stated that they've used whole blood, with "massive bleeding" as indication for 24 of them. Furthermore, good blood products' infusion and monitoring practices were reported. But, many constraints were disclosed for post Transfusion follow-up. Caregivers stated that they have to face "low financial resources of patients", "recurring unavailability of laboratory tests" and "delay between blood products ordering and issuance to blood receivers". They also emphasized the "need for additional education in transfusion medicine".

Summary/Conclusions: Despite of the low response rate to questionnaires, we noticed insufficient knowledge in utilization and limitations in post transfusion follow-up of blood products. We strongly recommend more researches over clinical transfusion, Transfusion medical educational programs for healthcare providers and Protocols for post-transfusion patients' follow-up with reinforcement of the hospital's blood bank.

P-814
RED BLOOD CELL TRANSFUSION ADEQUACY INDEX AS TOOL FOR IMPROVING PATIENT BLOOD MANAGEMENT PROGRAM

J Marques Jr[1,2], A Vigoritto[1,2], F Aranha[1,2], M Rodrigues[1,2] and G Duarte[1,2]

[1]Hematology, Vera Cruz Hospital [2]Hemotherapy, Cellular Hemotherapy Center in Medicine, Campinas, Brazil

Background: Transfusion is a vital and life-saving therapy. To achieve improved patient outcomes by avoiding unnecessary exposure to blood products through effective conservation and management of a patient's own blood, Patient Blood Management (PBM) program have been created. This program aims to promote medical education associated with blood transfusion alternatives in patient care and rationale blood utilization.

Aims: To optimize this task we have been studying the "Red Blood Cell Adequacy Index" since 2008, and this report demonstrate its value in providing a useful tool for PBM program.

Methods: In our Institution, all transfusion requests are audited and classified as "proper" or "non-proper" based on internationally-adopted guidelines. "Non-proper" requests are then adapted to suit these protocols. From April to October 2008, requests for red blood cells (RBC), were identified that pre-transfusion hemoglobin higher than 9.0 g/dl, and absence of information on hemoglobin levels were associated with a higher likelihood of "non-proper" indication. These two characteristics were then used to calculate the so-called "RBC transfusion adequacy index" (RAI), which represents the proportion of RBC transfused in which any of these two characteristics was present. RAI was monitored prospectively is six different health care institutions of Campinas, Brazil, as a tool from the PBM program, providing information to promote interventions in the institution practices.

Results: During the first part of the study, 1495 transfusions requests were analyzed, of which 12.9% were classified as "non-proper". In the second part of the study, from January 2008 until December 2017, 101.879 blood units were transfused and the RAI was monitored. The data can show that the overall global RAI, assessing the whole six units, have a positive correlation regression value, but when each unit individually is evaluated, different realities are shown, with different patterns and tendencies. For example, the Unit E shows an improvement in annual RAI and in the SD, unlike Unit A that has worse results in the last two years in both. The acceptable RAI can vary significantly from service to service according to institutional focus and to local patterns of RBC transfusion. But the real value of the tool is to enable to follow the progress of each institution during time and measure the efficacy of the PBM program. Another contribution of this tool, is that it makes possible to measure this index in any hierarchic level, e.g., all the hospitals supplied by the blood bank, each hospital unit, a surgery specialty or even a specific physician. Therefore continuous monitoring of the RAI allows one to identify deviations from the established standards, identifying the focus of the deviation and providing information to more accurate interventions, ultimately improving transfusion safety.

Summary/Conclusions: The optimal management of blood transfusion and patient related risks are an on course task. The RAI as part of a PBM programs can be a helpful tool in this process.

P-815

Abstract has been withdrawn

P-816
THE CLINICAL APPLICATION INVESTIGATION OF PATIENT BLOOD MANAGEMENT IN SHANGHAI, CHINA

J Sun[1], C Wang[2], Y Liu[3], R Zhou[4], D Xie[5], Y Meng[5], R Ma[5] and Y Shen[5]

[1]Donor and Hospital Service, Shanghai Blood Center, [2]Shanghai Dongfang Hospital [3]Shanghai Huadong Hospital [4]Shanghai Zhongshan Hospital [5]Shanghai Blood Center, Shanghai, China

Background: Patient blood management (PBM) is an evidence-based, multidisciplinary approach to optimizing the care of patients who might need transfusion. It encompasses all aspects of patient evaluation and clinical management surrounding the transfusion decision-making process. After the patient blood management proposed by World Health Organization in 2010, the concept of blood transfusion had a comprehensive change and clinical practice of patient blood management were made in the developed countries. However, PBM is still in the study stage and there are few clinical studies and practices in China now.

Aims: We want to investigate the clinical application of PBM in Shanghai, China now.

Methods: 232 patients with blood transfusion in Shanghai are investigated from 2016 to 2017. We collect clinical case of PBM, and the interventions including preoperative use of iron and erythropoietin before surgery and preoperative use of hemostatic agents and controlled hypotension technology during surgery.

Results: Two of the 11 departments (18.18%) were given iron supplementation to correct anemia. Nine of them (72.73%) used hemostatic drugs, such as tranexamic acid. Ten (90.91%) departments used at least one intervention before or during surgery, and were the most widely used in cardiac surgery and general surgery. No department took more than 2 interventions, and none of the departments had preoperative EPO to boost hemoglobin.

Summary/Conclusions: Our study demonstrated that PBM is still in the early stage and not attracted enough attention in Shanghai, China.

P-817
LABORATORY EVALUATION OF FACTORS AFFECTING THE EFFICIENCY OF ASPIRIN THERAPY

A Antic[1], Z Stanojkovic[1] and M Lazarevic[2]

[1]Blood Transfusion Institute Niš [2]Department of Cardiac Surgery, Clinical center Nis, Nis, Serbia

Background: Although it is established an unambiguous role of aspirin in the primary and secondary prevention of cardiovascular and cerebrovascular adverse events, there are cases of suboptimal response to the ASA, called the resistance, which are associated with adverse outcome of therapy.

Aims: The aim of this study was to identify the factors that influence the variable response of aspirin on platelet function, measuring platelet aggregation by method of impedance aggregometry.

Methods: The examination included 180 patients, treated with one of three different aspirin preparations after acute myocardial infarction, as a single therapy or with clopidogrel.. Platelet function was measured using impedance aggregometer Multiplate (Multiplate Platelet Function Analyzer, Roche) in blood samples with heparin for ASPI and TRAP tests. We investigated the impact of the following factors on the value of the TRAP and ASPI: gender, age, type of ASA preparation, the presence of diabetes mellitus, smoking and the use of drugs (anti-coagulant agents, proton pump inhibitors, beta-blockers).

Results: Age and the use of anticoagulants reduce the basic platelet function, while the proton pump inhibitors increase it. Diabetes is a risk factor that reduces the efficiency of ASA (Beta=0.553; P<0.001), as well as smoking (Beta=0.543; P<0.001) and the use of proton pump inhibitors (Beta=0.536; P<0.001). On the other hand, the use of anticoagulants enhances the effect of ASA (Beta=−0.529; P<0.001), as also the use of Aspirin protect (Beta=−0.435; P<0.001).

Summary/Conclusions: Smoking, diabetes, the use of proton pump inhibitors and anticoagulants, as well as the type of the applied aspirin preparation stand out as the most important factors that affect the efficiency of aspirin on platelet function as measured by the method of impedance aggregometry.

Cellular Therapies – Stem Cell and Tissue Banking, incl. Cord Blood

P-818
EVALUATION OF POST-THAW CORD BLOOD QUALITY BETWEEN THE BAG AND THE SEGMENTS

N Pineault[1], R Pasha[1], M Halpenny[2] and H Elmoazzen[2]

[1]Center of Innovation, [2]Cord Blood Bank and Stem Cell Manufacturing, Canadian Blood Services, Ottawa, Canada

Background: Cord Blood (CB) banks must understand the relationship of quality and potency between attached segments and main cord blood unit (CBU) bag. This relationship may vary between banks due to differences in bags, equipments, processing, thawing and testing procedures. Moreover, low post-thaw CD45+ cell viability is a frequent issue experienced by CB banks, which can results from osmotic

shock during thawing and dilution, and during red blood cell (RBC) lysis treatment with ammonium chloride solutions. Altogether these also contribute to the high variability in testing results between banks.

Aims: To establish the relationship between the viability of CB cells in segments and bag for CBUs processed at the Canadian Blood Services (CBS) and, to optimize the post-thaw cytometry staining protocol to minimize toxicity to CB cells.

Methods: CBUs are stored in a 20 ml buffy coat final product with 4 attached segments. All CBU were obtained with informed consent. Red cell and plasma reduction was carried out with Hespan and a Sepax2 cell separator, and CBUs frozen in a BioArchive. CBUs were thawed in a 37°C water bath and diluted 5-fold in a two-step (15 mins/step) equilibrium phase dilution protocol with a PlasmaLyte-A/4% human albumin solution. CD45+ and CD34+ cell viabilities and cell counts were measured using the Stem Kit (Beckman Coulter) which include a 10 min. RBC lysis step. Viability and cell counts were monitored in the bag and in the outermost segment 1 (S1) for all CBUs. For 6 CBUs, segment 4 (S4) closest to the bag was also analyzed. Potency was monitored using the colony forming unit (CFU) assay.

Results: Analyses of 16 CBUs revealed that viability of CB cells post-thaw was generally lower in the outermost segment S1, with a mean viability for CD45+ cells of 45 ±8% compared to 55 ±10% in the bag (P<0.0001). Viability of CD34+ was slightly lower in S1 (94 ±6%) as well but this difference vs the bag (96 ±4%) was not significant (P=0.09). Six CBUs were analyzed in more detail; for those, viabilities of CD45+ cells in the segment closest to the bag (S4) was found similar to that of the bag, both of which were higher (P<0.05) than in S1. The recovery of viable CD34+ cells was also lowest in S1 than the bag (69 ±21 vs. 98 ±15%, P<0.05). Similarly, recovery of CFU was also lowest in S1 (15 ±7%, P<0.001), whereas CFU recovery in S4 (43 ±20%) was similar to the bag (49 ±16%). Post-thaw CD45+ cell viability fell below the standard threshold of 40% in 4 of 22 measurements from 3 of 16 CBU tested. Hence, we optimized the staining protocol to minimize cell loss likely due to osmotic-induced necrosis. RBC lysis was found to be the most important cause of toxicity (P<0.001), and reducing the length of RBC lysis treatment from 10 to 5 min partially restored high CD45+ cell viability. Furthermore, reducing the time between post-thaw sample dilution and start of cell staining from 30 to 20 min also improved CD45+ viability (P<0.05). Hence, no RBC lysis staining provided the highest CD45+ cell viability (69 ±5%, n=3) followed by samples stained at 20 min post-thaw with a 5 min RBC lysis step (65 ±6%), whereas control samples had the lowest viability (55 ±9%).

Summary/Conclusions: CB cell viability and potency are significantly underestimated in the outermost segment, as such it is safe to assume that the quality of the CBU will be superior in the main bag. Low post-thaw CB CD45+ cell viability is the results of the high sensitivity of mature myeloid cells to osmotic and physical stress that lead up to necrosis. This can be partially overcome by minimizing the RBC lysis treatment.

P-819
CORD BLOOD CELLS: A RAPID ALTERNATIVE METHOD FOR ANTIBODY SCREENING IN PATIENTS UNDER THERAPEUTIC CD38–TARGETING ANTIBODY (DARATUMUMAB)

M Schleck, O De Mos and M Monfort
Immuno-Hematology, CHU of Liège, Liège, Belgium

Background: Daratumumab (DARA), an anti-CD38 IgG1 human monoclonal antibody that binds CD38 on myeloma cells, is used as a promising new therapy in multiple myeloma. Nevertheless, as CD38 is also weakly expressed on red blood cells (RBC), this drug interferes with routine pre-transfusion laboratory tests, causing false positivity in antibody screening test. Therefore it significantly delays the distribution of compatible RBC units. In order to eliminate this interference, dithiothreitol (DTT)-treated screening cells are used to deplete CD38 expression on RBC. However, this method is cumbersome, poorly reproducible and time-consuming. Moreover, DTT is known to destroy some erythrocyte antigens (among which KEL1), hampering the detection of the corresponding antibodies.

Aims: As cord blood cells (CBC) have low-to-no CD38 antigen, we developed a protocol using a panel of phenotyped group O CBC as an alternative rapid antibody screening method in patients under DARA treatment.

Methods: We prepared a panel of extensively phenotyped (RH, KEL, FY, JK and MNS systems) group O CBC (twenty different cord blood samples) in order to detect most clinically significant alloantibodies. To validate this method, as no patient under DARA treatment was previously immunized (no antibody development after transfusion or pregnancy), we added in equal volume plasma of patients under DARA treatment to several plasma samples containing a clinically significant low titer alloantibody (anti-RH1, -RH2, -RH3, -RH4, -RH5, -RH8, -KEL1, -FY1, -JK1, -

JK2, -MNS1, -MNS3, -MNS4). Then, each "spiked" plasma was tested against corresponding antigen positive and antigen negative CBC.

Results: In total 9 patients under DARA treatment were screened for antibodies with CBC and the results were all negative. Whereas alloantibodies (n=13) that were used in mixture with plasma from DARA patients were detected. CBC preserved in stabilization solution (ID-CellStab®) remained stable for 6 weeks.

Summary/Conclusions: In order to avoid interferences in antibody screening test in patients under DARA treatment, we developed a protocol using a panel of phenotyped group O CBC as an alternative method to DTT-treated cells. All clinically significant alloantibodies tested were detected, among which KEL1 normally destroyed by DTT. Although achieving an extended phenotype takes time (CBC are not commercially available) and requires to test many cord blood samples before selecting suitable cells (e.g. homozygous cells), this screening method is rapid and reproducible as CBC remain more stable over time compared to DTT-treated cells (6 weeks versus 24 to 72 h respectively). This technique can easily be implemented in blood banks to provide safe RBC units in emergency cases for patients under DARA treatment.

P-820
TRANSPLANTATION OF HYPOXIA PRECONDITIONED HUMAN UMBILICAL CORD BLOOD MESENCHYMAL STEM CELLS IMPROVE PROTECTIVE EFFECTS IN MOUSE MODEL OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

Z Asadpoor Dezaki and M Kheirandish
Immunology, Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: Multiple Sclerosis (MS) is a demyelinating disease that is associated with progressive disability. Hypoxia preconditioning of mesenchymal stem cells (MSCs) prior to their use in therapy is an adaptive way that prepares them to survive in the threatening environment and to enhance their regulatory function of the local immune responses in EAE model.

Aims: In the present investigation, we hypothesize whether hypoxic preconditioned umbilical cord blood mesenchymal stem cells (HPC-UCB-MSCs) could promote remyelination and recovery in the experimental autoimmune encephalomyelitis (EAE) mouse model of MS more effectively in comparison with UCB-MSCs.

Methods: In the present study, MSCs from human umbilical cord blood (UCB-MSCs) were exposed to hypoxia (15 min, 2.5% O_2) and reoxygenation (30 min, 21% O_2). Subsequently, hypoxia preconditioned hUCB -MSCs were exposed to hypoxia (48 h, 2.5% O_2 and 5% CO_2) in cell culture (HPC-UCB-MSCs). We hypothesize that HPC-UCB-MSCs could promote remyelination and recovery in the experimental autoimmune encephalomyelitis (EAE) mouse model of MS more effectively in comparison with UCB-MSCs cultured in normoxia (Norm-UCB-MSCs) condition (48 h, 21% O_2 and 5% CO_2 at 37°C).

Results: After hypoxia preconditioning, cell viability and expansion rate of umbilical cord blood mesenchymal stem cells significantly increased without any alter on cell surface marker expression. Our results show that transplantation of HPC-UCB-MSCs leads to considerable functional improvement and pathological tests outcomes in EAE models.

Summary/Conclusions: Hypoxia preconditioning provides a powerful culture condition to promote efficiency of transplanted umbilical cord blood mesenchymal stem cells in EAE model. It is hoped that the translation of knowledge gained in murine models may ultimately help to find the way to increase the therapeutic efficacy of HPC-UCB-MSCs in MS patients.

P-821
QUALITY CONTROL EVALUATION OF CORD BLOOD UNITS CRYOPRESERVED AT THE NATIONAL CENTER OF BLOOD TRANSFUSION, MEXICO

L Salazar[1], J Rojo Medina[2], J Dimas-Gonzalez[3] and A De León-Becerra[3]
[1]Blood Bank, Centro Nacional de la Transfusión Sanguínea, [2]Head Director, Centro Nacional de la Transfusión Sanguínea, [3]Cord Blood Bank, Centro Nacional de la Transfusión Sanguínea, Mexico, Mexico

Background: Umbilical cord blood (UCB) has been widely used as a rich source of hematopoietic progenitor/stem cells (HPC/HSC) for the treatment of malignant and non-malignant diseases. UCB cells have lower probability of immune rejection, with

more tolerance to differences in human leukocyte antigen (HLA). HPC/HSC are characterized by being able to self-renewal, to have a higher proliferation and expansion potential for supporting blood cell formation in vivo and after transplantation. UCBs are collected, processed and cryopreserved in biobanks for future transplantation. Steps of processing, freezing, and thawing can damage HPC/HSC, therefore care should be taken in every process. CD34+ cell count, cell viability, and Colony-Forming-Units (CFU) content are commonly analyzed for quality control to asses and maintain high viability and pluripotency of UCB for transplantation. In vitro or in vivo studies suggest that duration of storage does not affect HPC/HSC of UCB however cryopreservation is practiced in cord blood biobanks and the impact on HPC/HSC function has been only partially studied.

Aims: To evaluate quality control of cryopreserved UCB with different thawing methods.

Methods: We selected 27 cryopreserved UCBs during the period of 2003–2015 in National Center of Blood Transfusion biobank in Mexico. Inclusion criteria were: UCBs with range $1.0–2.3 \times 10^6$ CD34 cells prior to its cryopreservation, UCBs with 3 fragments available, and CBUs with quality control achieved (>80 ml volume, $>8 \times 10^8$ leukocytes, negative microbiological cultures, and HIV, HBV, HCV, Treponema pallidum, Trypanosoma cruzi no reactive). We used 3 thawing methods: 1) CBUs fragment is rapidly thawed in hands, 2) CBUs fragment is fast thaw in a 37°C water bath, and 3) CBUs fragment is diluted 1:2 with solution (v/v Rheomacrodex glucose solution and human albumin 20% solution). Immediately after thawing each UCBs fragment was analyzed for CD34 hematopoietic stem cells and viable CD45 marker by flow cytometry; moreover, for each UCBs fragment of Human Colony-Forming Unit (CFU) assays were performed in a methyl-cellulose culture medium by duplicate for determining pluripotency of HPC/HSC.

Results: Method 1 has an average of 1.0×10^6 viable CD34+ cells, 0.33×10^6 CFU, 38.8% E-clone, and 92.2% of cell viability. Method 2 with 1.0×10^6 viable CD34+ cells, 0.41×10^6 CFU, 34.8% E-clone, and of 92.2% cell viability. Method 3 with 0.95×10^6 viable CD34+ cells, 0.37×10^6 CFU, 42.34% E-clone, and 89.4% cell viability.

Summary/Conclusions: These results suggests that all three thawing methods of UBCs analyzed in do not affect the CD34+ number of cells, CFU and cell viability, furthermore, the cryopreservation time of UCBs in the biobank neither affects the variables of quality control.

P-822

USING SUSPENSION CULTURING METHOD AS A SIMPLE STRATEGY TO IMPROVEMENT OF PARACRINE POTENTIALITIES OF MESENCHYMAL STEM CELLS USING SIMPLE

F Amiri and M Movahed

Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: Mesenchymal stem cells (MSCs) are isolated from different tissues including (WJ). They have shown to have paracrine ability to support hematopoietic stem cells (HSCs) expansion in vitro. However, the WJ-derived MSCs are very heterogeneous and have limited capacity to secret cytokines that involve in hematopoiesis. Hence, improvement of their culture condition might promote the secretion capacity of WJ-MSCs.

Aims: Herein, we set up a simple culturing method for WJ-MSCs which promote their cytokines secretion.

Methods: WJ-MSCs were separated from Wharton's jelly. The isolated cells were added to Methocult medium diluted in α-MEM and seeded in poly-HEMA-coated plates. WJ-MSCs conditioned medium was harvested and concentrated from serum free media. The expression of some cytokines including IL-6, IL-11, granulocyte-macrophage colony-stimulating factor (GM-CSF) was evaluated by RT-PCR and western blot techniques.

Results: WJ-MSCs that cultivated under suspension condition expressed more GM-CSF and IL-11 in comparison to those of that cultured in adherent conditions (P< 0.05 and P< 0.001). There is no significant difference between the secreted amount of IL-6 from suspended and adherent WJ-MSCs.

Summary/Conclusions: Suspension cultivation of WJ-MSCs enhances their ability to produce some important hematopoietic cytokines. These suspended WJ-MSCs could be used for more effective low cost in vitro expansion of HSCs.

P-823

THE ROLE OF CANADIAN BLOOD SERVICES IN FACILITATING STEM CELL RESEARCH IN CANADA

M Golder[1], M Halpenny[2], S Chargé[1], K Mostert[2], N Dibdin[2] and H Elmoazzen[2]

[1]Centre for Innovation [2]Cord Blood Bank, Canadian Blood Services, Ottawa, Canada

Background: Biomedical research on cord blood increases our knowledge about current blood stem cell transplantation practices, as well as the current processes for collecting, manufacturing and storing cord blood. In addition, stem cells obtained from cord blood are being investigated in the development of new treatments for many diseases. Such stem cell research provides hope for more safe and effective medical therapies in the future.

Aims: Canadian Blood Services' Cord Blood Bank (CBB) supports research with cord blood through two mechanisms: 1- The Cord Blood for Research Program (CBRP) and 2- A process for returning non-qualifying cord blood units to the collection hospitals and their research communities.

Methods: In August 2014, Canadian Blood Services CBB in partnership with The Ottawa Hospital launched the CBRP by implementing processes to distribute de-identified cord blood units not suitable for storage and transplantation to the Canadian scientific community. Fresh, unprocessed cord blood units and frozen processed cord blood units are made available by the CBRP for research distribution to approved biomedical research projects. With the CBRP, consent for research is obtained by Canadian Blood Services CBB as part of its collection process. Starting in 2015, the CBB developed a process to return non-qualifying cord blood units to designated collection hospitals. With this process, hospitals manage maternal consent requirements and distribution of the units to the research community according to local processes.

Results: A retrospective data analysis for the CBRP from go live Aug 5, 2014 to Jan 5, 2018 was performed. A total of 11 projects have been approved for research distribution. A total of 7127 CBU were collected at The Ottawa Hospital with a total of 5217 mothers consenting to donate their CBU for the CBRP (73.2% consent rate). A total of 4227 CBUs were available for research distribution (990 CBUs qualified for CBB banking). 736 CBUs have been distributed for research projects (17.4% of available research inventory). Distributed CBUs had an average volume of 71.8 ml (38.2–167.9 ml) and average TNC 80.7×10^7 ($30.2–200.9 \times 10^7$). In addition, 132 cryopreserved CBUs have been added to inventory for research distribution. Cryopreserved CBUs have an average TNC 138.0×10^7 ($58.4–282.9 \times 10^7$), total CD34 5.87×10^6 ($0.72–15.12 \times 10^6$), total CFU-GM 23.0×10^5 ($3.4–74.4 \times 10^5$), and viability of 95.8% (73–99%). From May 10, 2015 to Jan 5, 2018, a total of 6136 cord blood units collected by the CBB have been returned to the collection hospitals (other than The Ottawa Hospital) to be made available for research.

Summary/Conclusions: Through the implementation of formal processes developed in partnership with hospitals, Canadian Blood Services' CBB is facilitating stem cell research in Canada to ultimately benefit Canadian patients.

P-824

CD34 POSITIVE CELLS NEEDED. CAN THE BLOOD VOLUME TO PROCESS BE CALCULATED?

H Vrielink[1] and M Neyrinck[2]

[1]Transfusion Medicine, Sanquin Blood Supply, Amsterdam, Netherlands
[2]Hematology, AZ Delta, Roeselare, Belgium

Background: In FACT/JACIE standards C2.9, C4.10 and C4.14 (6th ed) is given that procedures and policies must be designed amongst others to reduce risks for the HPC donor. Too long or too many collection procedures including mobilization of HPCs to the peripheral circulation can increase risks for the donor of the HPCs. In the mathematics section of the 6th edition of ASFAs Principles of Apheresis Technologies, we give a formula to calculate the donors' blood volume to be processed to collect a requested number of HPCs: BVprocessed = CD34 needed/(CD34 donor x collection efficiency).

Aims: Validation of the formula BVprocessed = CD34 needed/(CD34 donor x collection efficiency).

Methods: In 1114 HPC collection procedures in 720 autologous patients (2015–2017), we calculated the collection efficiency and the blood volume to process to collect the requested number of CD34 positive cells. Based on the CD34 count on the day, independent from this formula, CD34 collections were performed. Processed volume, outcome, and collection efficiency were registered.

Results: In 1114 HPC apheresis collection procedures (all Spectra Optia (Terumo BCT)), the requested number of CD34 positive cells was collected in one or more procedures. On average 12.2 liters of the patients' blood volume (=2.6× TBV) was

processed to collect on average 5.4 CD34-positive cells per kilogram of the recipients' bodyweight. The collection efficiency with Spectra Optia was 60% with a standard deviation of 0.33. A regression model of the calculated versus the real processed blood volume showed that with 80% accuracy can be predicted what number of CD34 positive cells will collected with this formula.

Summary/Conclusions: With this formula, with 80% accuracy can be predicted what number of CD34 positive cells will be collected in processing a calculated blood volume of this autologous donor. Known is that collection efficiencies can vary with the disease background. Probably data per disease and/or per gender are needed to have better prediction models. On the other hand, with a reasonable certainty can be known during the procedure that prolonging the procedure with an additional processing of 1000 or 2000 ml of blood could avoid an additional collection procedure on a subsequent day with avoiding additional mobilization therapy in the donor and shortening the central venous catheter insertion. With this formula therefore risks for the donor can be reduced.

P-825

KNOWLEDGE AND PERCEPTIONS OF PREGNANT WOMEN WITH REGARD TO COLLECTION AND BANKING OF UMBILICAL CORD BLOOD STEM CELLS IN NIGERIA

SO John-Olabode[1], K Okunade[2], O Ajie[3] and O Oyedeji[1]

[1]Department of Haematology and Blood Transfusion, College of Medicine University of Lagos [2]Department of Obstetrics and Gynaecology, College of Medicine University of Lagos [3]Department of Clinical Pathology, College of Medicine University of Lagos, LAGOS, Nigeria

Background: Approximately 50% of patients who need an unrelated blood stem cell transplant are unable to find a timely suitable match due to the diversity of Human Leucocyte Antigen (HLA) alleles and antigens. This is particularly true for Nigerian patients who have unique stem cell matching needs reflecting Nigeria's extensive ethnic diversity. To address this problem, the Bone Marrow Registry in Nigeria was launched on February 24, 2012 with 300 donors with the future plan of constructing a cord blood bank (CBB). Unfortunately; awareness levels remain a substantial limitation to harnessing the benefits of umbilical cord blood (UCB) especially among pregnant women whose support is crucial to the success of cord blood transplant program.

Aims: To examine the knowledge and perception of pregnant women with regard to collection and banking of umbilical cord blood stem cells.

Methods: On-going study with questionnaires administered to pregnant women attending antenatal clinics in Lagos University Teaching Hospital. Part 1 assessed issues of awareness and knowledge of UCB. Part 2 assessed perception and attitude towards UCB donation. Data was analysed using SPSS version 22.0 statistical package for windows manufactured by IBM Corp., Armonk, NY, United States.

Results: One hundred surveys have so far been analysed in this on-going study; the mean age was 31.6 years±4.8, 73.7% of the respondents were aware that UCB can be used to treat some diseases. Though the level of awareness of UCB was high more than two-thirds (70%) of the respondents were not confident of their knowledge of UCB and would like their healthcare provider to provide more information on purpose and uses of umbilical cord blood. 50% of the respondents agree to cord blood donation if a CBB were available in the country. 66.6% of the respondents that agreed to cord blood donation said religion will not influence their decision and 62.2% of these respondents said they would prefer a public CBB to a private one. 49% of respondents disagree that donated cord blood should only be for the use of family members.

Summary/Conclusions: Nigeria with its large population is uniquely placed to set up the largest cord blood bank to cater for Nigerians and ultimately the whole of Africa. However, as is well understood there can be no blood donation without prioritizing donor education. The findings of this on-going study exemplifies this fact as half of the study population expressed willingness to donate cord blood if a cord blood bank was available in the country. Not only do majority of the respondents agree to cord blood donation (CBD), they also choose to donate cord blood to a public blood bank. Ironically, this positive attitude towards CBD is despite being poorly informed, uneducated and lacking knowledge regarding UCB. Also, surprisingly in a deeply religious country, two-third of the women open to CBD admitted that religion has no influence on their decision to UCB donation. Our results so far provide insights that infer that at the conclusion of this study the data gathered can be meaningfully incorporated into government cord blood banking policy.

P-826

AGARICUS BLAZEI MURILL–BASED MUSHROOM EXTRACT INDUCES S–G2/M CELL CYCLE ARREST IN HUMAN MULTIPLE MYELOMA CELL LINES

M Mirlashari[1], J Tangen[2] and G Hetland[3]

[1]Immunology and Transfusion Medicine, Oslo University Hospital [2]Acute Medicine [3]Immunology and Transfusion Medicine, Clinical Medicine, University of Oslo, Oslo, Norway

Background: AndoSan™ is a water extract prepared from medicinal Basidiomycetes mushrooms, mainly Agaricus blazei Murill (82%), but it also contains Hericeum erinaceus (15%) and Grifola frondosa (3%). In recent years, many studies have reported that different extracts of Agaricus blazei Murill have various anticancer effects, ranging from the improvement of immunomodulatory activity to the inhibition of tumor growth via direct inhibition of tumor-induced angiogenesis in mice.

Aims: The present study was carried out to investigate the effect of AndoSan™ on myeloma cell lines RPMI-8226, U226 and INA-6 in vitro.

Methods: Myeloma cells lines or peripheral blood mononuclear cells (PBMC) were exposed to various concentrations of AndoSan™ (0.5- 10%) and maintained in a humidified atmosphere with 5% CO_2 at 37°C for 96 h in 24-well plates. The total number and percent viable cells were counted by NucleoCounter using the NucleoCassette kit (Chemometec, Allerød, Denmark) according to the manufacture's manual. For cell cycle analysis by flow cytometry, 1×10^6 cells (controls and treated myeloma cells) were washed with PBS and fixed by slow addition of 2 ml 100% ice cold methanol on mixer and stored at −20°C until analysis. Cell cycle analysis was performed according to Vindelov et al. "Vindelov, Cytometry, 1983 "and analysed on a FACS Aria cell sorter (Becton Dickenson, San Jose, CA).

Results: AndoSan™ induced a dose-related inhibitory effect on the myeloma cell lines RPMI-8226, U226 and INA-6, but not on PBMC. Furthermore, in a cell cycle study the percentage of cells was higher in S phase and G2-M phase in cells cultured with Andosan™ 10% vs. controls, suggesting cell cycle arrest at S and G2-M phase.

Summary/Conclusions: Our data suggest that AndoSan™ can reduce myeloma cell line viability via induction of S/G2-M arrest, without harming normal peripheral blood mononuclear cells

P-827

PREPARATION OF HEMATOPOIETIC STEM CELL BY HARVEST APHERESIS

K Mousavi Hosseini and M Navidroian

Biotechnology, Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: In general, apheresis involves removal of whole blood from a patient or donor. This medical procedure separates the blood into individual components in a way that one particular component can be removed, and the rest of remaining blood components then are returned back into the blood stream of the donor or patient.

Aims: The aim is the collection of a patient own stem cells prior to high dose chemotherapy.

Methods: The patient may receive injections of growth factors in order to increase the number of peripheral stem cells in the blood. On the day that the blood cell count has reached a sufficient level, blood is removed through a needle or catheter and circulated into a blood cell separator machine. The blood is separated and mononuclear white blood cells and peripheral blood stem cells are transferred to a collection bag. They are saved and frozen. The other blood components (plasma, red blood cells, and platelets) circulate back to the patient through a return needle.

Results: Hematopoietic stem cell harvest apheresis is found as the primary method for obtaining the cells that are transplanted in the procedure called bone marrow transplantation. This is used in the treatment of various types of leukemia, lymphoma and other cancers, and occasionally for certain genetic diseases that lead to anemia or immune deficiency.

Summary/Conclusions: Originally, bone marrow transplant, requires placing a needle into the interior of a bone to obtain these cells. Nowadays, in most of the cases, equivalent cells can be collected from the bloodstream by hematopoietic stem cell harvest apheresis, avoiding the painful and more complex procedure of bone marrow aspiration.

Collection, Processing, Storage and Release

P-828

IMPLEMENTATION OF AN AUTOMATED CLOSED VOLUME REDUCTION SYSTEM IN PROCESSING OF HEMATOPOIETIC PROGENITOR CELLS FOR AUTOLOGOUS TRANSPLANT

JL Holovati[1,2], B Letcher[1], K Murphy[1], S Langevin[1], M Halpenny[3] and H Elmoazzen[3]

[1]Cord Blood and Stem Cell Manufacturing, Canadian Blood Services [2]Laboratory Medicine and Pathology, University of Alberta, Edmonton [3]Cord Blood and Stem Cell Manufacturing, Canadian Blood Services, Ottawa, Canada

Background: Autologous hematopoietic progenitor cell (HPC) transplantation following myeloablative therapy remains a standard intervention in the treatment of many hematological malignancies. HPCs are typically collected from peripheral blood by apheresis and cryopreserved through the addition of a cryoprotective agent, dimethyl sulfoxide (DMSO), followed by storage in liquid nitrogen, prior to the patient undergoing high-dose chemotherapy. When infused with the thawed cell suspension, DMSO may induce side effects, and many HPC manufacturing centres employ a manual volume reduction before freezing HPC units to reduce the volume of DMSO infused. An automated volume reduction process that provided HPC component centrifugation, separation and transfer was evaluated at Canadian Blood Services' Edmonton Stem Cell Manufacturing facility.

Aims: This study describes the effectiveness outcomes of the first Canadian experience in implementation of an automated closed volume reduction system (BioSafe Sepax 2 PeriCell) in processing of HPCs for autologous transplant.

Methods: Leukapheresis for all autologous stem cell transplant patients was performed using a Spectra Optia apheresis system collection procedure for mononuclear harvesting. 34 HPC units from 30 patients were volume reduced using the automated system prior to freezing. Effectiveness monitoring included unit volume reduction, % recovery of nucleated cells (Sysmex automated cell counter), CD34+ cell recovery and total cell viability (flow cytometry), overall clonogenic capacity (colony forming unit assay), and sterility (bacterial and fungal cultures). Hematological (platelet and ANC) engraftment was monitored for the patients receiving the autologous volume reduced HPC unit transplant.

Results: The initial volume of the 34 HPC units was 303 ± 29 ml, which was reduced by 19% after the automated centrifugation processing (247 ± 9 ml), resulting in estimated reduction of DMSO by 9 ml per HPC unit. Recoveries of nucleated and CD34+ cells was $93.2 \pm 4.3\%$ and $91.4 \pm 8.0\%$, respectively. White blood cell viability remained high, at $99.2 \pm 0.4\%$. All microbiologic cultures on HPC units were negative. Twenty eight patients underwent stem cell autologous transplant. The mean doses of CD34+ and CFU infused/kg recipient body weight were $4.0 \pm 1.1 \times 10^6$/kg and $4.4 \pm 1.7 \times 10^5$/kg, resulting in no adverse reactions and the median time to neutrophil and platelet engraftment of 13 and 20 days.

Summary/Conclusions: The effectiveness outcomes of the first Canadian experience in implementation of BioSafe Sepax 2 volume reduction system in processing of HPCs for autologous transplant have met the predetermined acceptance criteria, supporting the use of this automated closed system in a stem cell manufacturing laboratory compliant with good manufacturing practice regulations.

P-829

THE EFFECT OF CD34-PRE-COUNT, GENDER, AGE AND TYPE OF COLLECTION PROCEDURE ON COLLECTION EFFICIENCY IN STEM CELL COLLECTION FOR MULTIPLE MYELOMA

FH Swaneveld, A Mäkelburg, J Drent, A Smienk and H Vrielink

Sanquin Blood Supply, Amsterdam, Netherlands

Background: High-dose chemotherapy with autologous hematopoietic cell transplantation is the preferred first-line therapy for patients with multiple myeloma (MM). These stem cells are collected by apheresis. As the yield of CD34+ stem cells can vary considerably amongst patients, we wondered if the collection efficiency (CE) varies with CD34-pre-count, gender, age or type of procedure: mononuclear cell collection (MNC) vs continuous mononuclear cell collection (cMNC).

Aims: To evaluate the influence of CD34-pre-count, gender, age and type of procedure on CE in MM patients.

Methods: We retrospectively studied the data of all MM patients who underwent stem cell collection in our facility between 2015 and 2017. We compared the mean CE between groups using the independent samples t-test. We used the Independent Samples Median Test to compare median CE in patients stratified by CD34-pre-count and to compare median CD34-pre-count in patients stratified by age group.

Results: Between 2015 and 2017, 338 patients underwent 555 apheresis procedures. For 508 procedures (91.5%) in 307 patients CE-data were available. Of these 307 patients 67.4% were male. Median age was 61 years (range 35–72 years); 61 years in men (range 35–71 years) and 64 years in women (range 37–72 years). Mean CE was 58.7% (range 8.9% - 185.8%, SD 18.9%); 60.3% (SD 19.7%) for males and 55.5% (SD 16.7%) for females. This difference was significant (P=0.007, 95%CI −1.35–8.35%). However, when stratified for CD34-pre-count, no significant difference between males and females was observed. When stratified by age-group there was no significant difference in mean CE for patients with a distribution above or below 55 years of age (58.4% and 59.9% respectively; P=0.479, 95%CI −5.46–2.56%); 60 years of age (58.4% and 59.4% respectively; P=0.570, 95%CI −4.41–2.43%); 65 years of age (57.2% and 59.7%; P=0.155, 95%CI −5.86–0.93%) or 70 years of age (59.8% and 58.7%; P=0.728, 95%CI −5.28–7.56%). We also compared patients younger than 45 years (n=22) with patients older than 70 years (n=20) and patients aged 45–55 years (n=110) with patients aged 65–70 years (n=139). There were no significant differences in mean CE (P=0.861 and P=0.790). Stratified by gender we also didn't find significant differences in mean CE in different age groups. Median CD34-pre-count didn't differ significantly between age groups (P=0.831). There was a significant difference in median CE when patients were stratified by CD34-pre-count (P=0.044): CD34-pre-count <25×10⁶/L: 61.4%; CD34-pre-count 25–50×10⁶/L: 59.1%; CD34-pre-count 50–75×10⁶/L: 59.3%; CD34-pre-count 75–100×10⁶/L: 55.8% and CD34-pre-count >100×10⁶/L: 53.0%. This explained the difference seen in mean CE between men and women, as women had a significantly higher CD34-pre-count than men ($87.8×10^6$/l vs $64.0×10^6$/L, P=0.007), 95%CI −40.9 to −6.6). Finally we compared mean CE between types of procedure: 59.6% in MNC and 55.9% in cMNC (P=0.038). Yet, significance disappeared after stratification for CD34-pre-count, indicating confounding. Mean CD-34-pre-count was significantly lower in MNC than CMNC: $65.4×10^6$/L vs $94.8×10^6$/L; P=0.005, 95%CI −49.9 to −9.0.

Summary/Conclusions: In our population of 307 MM-patients, CD34-pre-count influenced CE. A lower CD34-pre-count seemed to be related to a higher CE, whereas gender, age and type of collection procedure were not related to CE.

P-830

SELECTIVE PURGING OF HUMAN MULTIPLE MYELOMA CELLS FROM PERIPHERAL BLOOD STEM CELL TRANSPLANTATION GRAFT

A Lee and S Kim

Department of Laboratory Medicine, Daegu Catholic University School of Medicine, Daegu, Korea

Background: Multiple myeloma (MM) is a neoplastic plasma cell disorder characterized by a clonal proliferation of malignant, monoclonal plasma cells in the bone marrow and/or extramedullary sites. High-dose chemotherapy followed by autologous peripheral blood stem-cell transplantation (PBSCT) are standard of therapy for selected patients diagnosed with MM. Relapse may be due to the insufficient eradication of malignant plasma cells by high-dose chemotherapy and the reinfusion of residual malignant plasma cells with the PBSCT. Ex vivo manipulation of the autograft prior to infusion to remove contaminating residual myeloma cells, a process called purging, could improve patient outcomes.

Aims: In this study, a purging method of human multiple myeloma cells from peripheral blood mononuclear cells was developed using chemotherapeutic drug treatment and the efficacy of myeloma cell removal was evaluated.

Methods: The human myeloma cell line RPMI-8226 (Seoul, Korea) was treated with bortezomib (Selleck Chemicals, USA) or lenalidomide (Sigma Aldrich, USA). Cell viability assay was performed using the cell counting kit-8 assay to determine the proper concentration of drugs. The mixture of the human peripheral blood mononuclear cell line PCS-800-011 and RPMI-8226 were treated with bortezomib or lenalidomide for 24 h. The efficacy of purging myeloma cells was evaluated by 8-color flow cytometric analysis.

Results: The cytotoxicity of bortezomib (10–160 nmol/L) and lenalidomide (200–3200 nmol/L) was investigated on RPMI-8226 myeloma cell line. A 24-h incubation with bortezomib at 10, 20, 40, 80, 160 nmol/L induced $5.45 \pm 0.07\%$, $47.15 \pm 1.20\%$, $57.15 \pm 0.21\%$, $72.35 \pm 0.07\%$, and $84.75 \pm 0.49\%$ growth inhibition in RPMI-8226 cells, respectively. A 24-h incubation with lenalidomide at 200, 400, 800, 1600, 3200 nmol/L induced $5.45 \pm 0.07\%$, $7.55 \pm 0.07\%$, $9.75 \pm 0.35\%$, $18.25 \pm 0.21\%$, and $39.75 \pm 0.78\%$ growth inhibition in RPMI-8226 cells, respectively.

Bortezomib (40 nmol/L, 24 h) and lenalidomide (3200 nmol/l, 24 h) effectively removed CD38+CD138+ cells from peripheral mononuclear cells. RPMI-8226 cells showed aberrant phenotype CD56+/CD45–.

Summary/Conclusions: The results of the present study demonstrated that the bortezomib and lenalidomide treatment in RPMI-8226 multiple myeloma cells effectively removed the contaminated plasma cells.

P-831

EFFICIENCY OF HEMATOPOIETIC STEM CELL MOBILIZATION WITH PLERIXAFOR IS GREATER IN PATIENTS WITH MULTIPLE MYELOMA THAN MALIGNANT LYMPHOMA

M Okubo[1], Y Nakamura[2], T Sawada[1], N Nakamura[1], N Tada[1], K Kina[3], A Morimoto[1], E Hasegawa[1], Y Sekiguchi[4], M Wakabayashi[4], K Sugimoto[4], H Takizawa[4], H Iizuka[4], S Sakajiri[4], T Ohsawa[2], Y Furuta[2], K Miyake[3], M Noguchi[4] and A Ohsaka[5]

[1]Department of Transfusion Service, Juntendo University Urayasu Hospital, Urayasu
[2]Department of Transfusion Service, Juntendo University Hospital, Tokyo
[3]Department of Laboratory Medicine [4]Department of Hematology, Juntendo University Urayasu Hospital, Urayasu [5]Department of Transfusion Medicine and Stem Cell Regulation, Juntendo University School of Medicine, Tokyo, Japan

Background: Plerixafor (Mozobil) is used to mobilize hematopoietic stem cells (HSCs) combined with granulocyte colony-stimulating factor (G-CSF). Since 2017, plerixafor has been commercially available in Japan for mobilization of the HSCs in patients with multiple myeloma (MM) and malignant lymphoma (ML). However, the literature, based on which patients are advised plerixafor treatment, is limited. In our presentation, we have reported on the differences in mobilization efficiencies between patients treated with plerixafor and those previously treated without plerixafor.

Aims: This study aimed to evaluate the mobilization efficiencies of HSCs with G-CSF and plerixafor in Japanese patients with MM or ML. Additionally, we attempted to determine which patients showed better mobilization efficiency with plerixafor.

Methods: Retrospectively, we analyzed the clinical data of patients who underwent HSC harvesting with or without plerixafor, between January 2016 and January 2018, at Juntendo University Urayasu Hospital, Urayasu, Japan. The data consisted of the clinical diagnosis, number of harvests, and CD34+ cell counts. The target CD34+ cell counts in patients with MM and ML were 6×10^6/kg within two harvest days and 2×10^6/kg within four harvest days, respectively. This study was approved by the institutional review board or ethics committee.

Results: Totally, 26 patients, 12 with MM and 14 with ML, underwent 20 and 19 harvests, respectively. Among them, four patients with MM were treated with plerixafor [MM(+)], eight patients with MM were treated without plerixafor [MM(−)], seven patients with ML were treated with plerixafor [ML(+)], and seven patients with ML were treated without plerixafor [ML(−)]. The patients' mean CD34+ cell counts on the day before harvest were as follows: MM(+), 20.8 ± 33.22/μl; MM(−), 7.0 ± 7.39/μl; ML(+), 23.1 ± 39.42/μl; and ML(−), 48.9 ± 51.96/μl. The MM(+) and ML (+) patients' CD34+ cells increased to 3.9 ± 2.93 times and 4.1 ± 3.76 times, respectively. The mean CD34+ cell counts in the harvested bags were as follows: MM(+), $7.9\pm9.07\times10^6$/kg; MM(−), $2.0\pm1.86\times10^6$/kg; ML(+), $5.4\pm4.83\times10^6$/kg; and ML(−), $7.4\pm6.31\times10^6$/kg. Among the 26 patients, 3/4 MM(+), 1/8 MM(−), 6/7 ML(+), and 7/7 ML(−) achieved the target CD34+ cell counts. Plerixafor administration increased the success rate of stem cell collection in patients with MM from 12.5% to 75%. Sufficient stem cell harvest was not possible from one MM(+) and one ML(+) patient. Their CD34+ cell counts on the day before harvest were less than 5/μl. The mean numbers of harvest days were as follows: MM(+), 1.25 days; MM(−), 1.87 days; ML (+), 1.50 days; and ML(−), 1.43 days. In patients with MM, the number of harvest days was shortened by plerixafor administration.

Summary/Conclusions: The mobilization and collection efficiencies were greatly improved in patients with MM who were administered plerixafor. Though the CD34+ cell counts increased with plerixafor administration in patients with ML, the stem cell collection efficiency was less than in patients with MM. Although it is necessary to verify that a sufficient number (>5/μl) of CD34+ cells are mobilized into the peripheral blood with G-CSF alone, patients with MM should be advised plerixafor administration, along with G-CSF, for stem cell collection.

P-832

THE IMPACT OF THE CRYOPRESERVED PERIOD OF CB UNITS IN THE CHOICE FOR CB TRANSPLANTATION: THE CLINICIANS WOULD PREFER CB UNITS WITH SHORTER CRYOPRESERVED PERIODS THAN LONGER CB UNITS?

H Lee[1], E Roh[2,3,4], J Yoon[2,3,4] and S Shin[2,3,4]

[1]Department of Laboratory Medicine, National Medical Center [2]Department of Laboratory Medicine, Seoul National University College of Medicine [3]Department of Laboratory Medicine, Boramae Hospital [4]Seoul Metropolitan Government Public Cord Blood Bank (Allcord), Seoul, Korea

Background: The Seoul Metropolitan Government Public Cord Blood Bank (Allcord) was founded in May 2006, and the release of CB units for CB transplantation (CBT) started in July 2008. For CBT, the candidate CB units are selected based on the HLA matching with the patient's HLA type. Total nucleated cells (TNC) count, CD34+ cell count, and cell viability are analyzed from the CB of the segment for the evaluation of the quality of CB units. The clinicians choose the CB unit(s) for CBT according to the TNC and CD34+ cell counts. As the cryopreserved period of CB units exceeds 10 years, we have wondered whether clinicians would prefer CB units with shorter cryopreserved period than longer CB units.

Aims: We investigated the changes in quality of CB units over the cryopreserved period. And, we identified whether the cryopreserved period has an impact on clinicians' choice of CB units for CBT.

Methods: Until October 2017, 488 CB units are selected, and among them, 356 units were used for CBT. TNC count, CD34+ cell count, and cell viability were analyzed in 488 CB units. We conducted a comparative analysis to identify the presence of differences in the recovery rates of the TNC and CD34+ cell counts and the cell viability over the cryopreserved period. And, we investigated whether there were differences in the cryopreserved period, TNC and CD34+ cell counts of 356 CB units according to the CBT year (2008–2017).

Results: The mean cryopreserved period of the 488 CB units was 1,222 days (range, 16–3,801). The recovery rates of the TNC and CD34+ cell counts increased according to the increase of cryopreserved period (TNC, r=0.242, P<0.005; CD34+ cell, r=0.428, P<0.005). The difference between cell viability before freezing and cell viability after thawing increased according to the increase of cryopreserved period (r=0.105, P=0.021). For all the CB units, the mean cell viability percentages before freezing and after thawing were 89.0% and 86.4%, respectively. According to the CBT year, the number of CB units used for CBT is as follows; 4 (2008), 31 (2009), 40 (2010), 11 (2011), 18 (2012), 46 (2013), 54 (2014), 53 (2015), 59 (2016), and 40 (2017). The mean cryopreserved period was short in the CB units used during 2008 and 2009 (692 days, 585 days, respectively). The mean cryopreserved period showed the increasing tendency and was the longest (1,782 days) in the CB units used during 2017. There was no significant difference in TNC count according to the CBT year (P=0.101), and the mean of TNC count for all the CB units was 13.5×10^8/unit. For CD34+ cell count, there was no difference since 2010 CBT year (P=0.260), and the mean of CD34+ cell count for the CB units from 2010 to 2017 was 4.4×10^6/unit.

Summary/Conclusions: There were no significant decrease in TNC and CD34+ cell counts and no significant change in cell viability during cryopreservation up to 10 years. It is presumed that the cryopreserved period of CB unit does not have a significant effect on the clinicians' choice.

P-833

COLLECTION OF MOBILIZED PERIPHERAL BLOOD STEM CELLS IN HEALTHY DONORS – 17 YEARS OF EXPERIENCE

RM Grubovic Rastvorceva, S Useini, K Dimitrovski, E Petkovikj, G Andonov and M Grubovic

Institute for Transfusion Medicine of RM, Medical Faculty – Skopje, Skopje, Macedonia

Background: Allogeneic hematopoietic stem cell transplantation is an established therapy for many benign and malignant hematologic diseases. Since the discovery of the potential of peripheral blood stem cells (PBSC) in the hematopoietic reconstitution in mid 1980s and early 1990s PBSC gradually replaced bone marrow as the preferred source of stem cells. The introduction of hematopoietic cytokines that can mobilize large number of progenitors into circulation accelerated PBSC usage.

Aims: The aim of our study is to present our experience of 17 years with apheresis collecting of PBSC in healthy donors.

Methods: This is a retrospective study performed in the Institute for Transfusion Medicine of Republic of Macedonia and University Hematology Hospital for period from 2001 till 2018. All donors were HLA typed and matched; they were fully

informed on the donation procedure and signed an informed consent for donation. Minimum dose required to ensure successful and sustained engraftment was 2×10^6/kg CD34+ cells and 2×10^8/kg mononuclear cells (MNC). PBSC harvesting was performed with continuous flow cell separator Baxter C53000 and COBE Spectra using conventional-volume apheresis processing the 2–2.5 total blood volumes per apheresis. A femoral catheter was used for harvesting and Acid Citrate Dextrose formula A is used for anticoagulation. Recombinant human granulocyte colony-stimulating factor (G-CSF) is used to mobilize PBPC for collection. Harvesting of PBSC is usually performed after 4 to 5 days of G-CSF subcutaneous administration at a dose of 10 µg/kg body weight.

Results: There were 148 apheresis procedures performed in 95 healthy donors (1.56 apheresis per donor). Ninety four were sibling donors and one was unrelated donor recruited through Bone Marrow Donors Worldwide and our Registry, who donated PBSC for unknown donor in the USA. It was the first unrelated donation in our institution. There were 67 males and 28 females, aged 20–55. One to two apheresis procedures were required to collect adequate graft. The single procedure usually took 3–4 h and the volume of collected stem cells was 50–220 ml. The needed number of MNC and CD34+ cells was successfully collected by 1.56 apheresis. There were 27 ABO incompatible donors. Procedures for mobilization and collection of PBPC from healthy donors are generally well tolerated. The only adverse effects of the apheresis procedure were bone pain as reaction of G-CSF and numbness of the extremities as reaction of ACD-A (hypocalcemia), which occur rarely and were very mild. The collected PBSC were used in allogeneic stem cell transplantation in patients with: acute myeloid leukemia – 52 patients (55.3%), acute lymphoblastic leukemia – 14 patients (14.9%), chronic myeloid leukemia – 9 patients (9.6%), non-Hodgkin lymphoma – 3 patient (3.2%), myelofibrosis – 5 patients (5.3%), severe aplastic anemia – 5 patient (5.3%), myelodysplastic syndrome - 3 (3.2%), chronic lymphoblastic leukemia – 1 patients (1.1%), Hodgkin disease – 1 patient (1.1%) and multiple myeloma – 1 patient (1.1%).

Summary/Conclusions: The apheresis collection of mobilized PBSC in healthy donors is an effective and safe procedure. We are developing a National Stem Cell Donors Registry as a part of Bone Marrow Donors Worldwide. In that way we hope we will help widen the world network of stem cell donors and enlarge the possibility for each patient to find the right match.

P-834

EXTRACORPOREAL PHOTOPHERESIS IN THE MANAGEMENT OF GRAFT–VERSUS–HOST DISEASE IN CHILDREN

H Bilgen[1], S Anak[2], Y Yaman[2], K Ozdilli[2], A Kokrek[1], K Payalan[1], H Hızlı[1] and M Elli[2]

[1]Transfusion Center [2]Pediatric Hematology, Medipol University, Istanbul, Turkey

Background: Extracorporeal Photopheresis (ECP) continues to be a controversial treatment, probably due to the mechanism of action not being identified, the varying photopheresis procedures and treatment schedules,

Aims: In our study we investigated the outcomes of ECP in children who had stem cell transplantation and developed GvHD.

Methods: ECP was performed in our pediatric transplant center to 8 patients mean age of 12 years (4–18) diagnosed to have ALL (3 pts), Thalassemia (2 pts), Aplastic Anemia (1), Blackfan Diamond (1), Refractory Hodgkin Disease (1) following our internal protocol for 152 ECP sessions. Five of the patients had MUD, 3 had HLA id sibling transplants. Chronic GvHD was diagnosed in 2 of the patients 6 had acute GvHD. Skin was involved in all the patients, liver in 6 of the patients, lung in 3, gut in 6 and mucous membranes in 7 patients. The ECP treatment consisted essentially of three steps: 1) collection of MNCs from the patient, 2) processing of MNC buffy coat, and 3) return of MNCs to the patient. Collection was performed using a cell separator (Haemonetics MCS plus), processing two blood volumes. Our protocol provides for a maximum final MNC volume to be collected at 150 ml, with a hematocrit (Hct) value below 5%. The maximum procedure time was set at 180 min. The MNCs collected were adjusted to a constant volume of 300 ml by the addition of saline and 3 ml of 8-MOP in aqueous solution, to always obtain a final concentration of the drug of 200 ng/ml. The diluted buffy coat was transferred into a special UV-A–permeable bag (PIT-KIT medtech solutions), and UV-A radiation at 2 J/cm2 was performed (UVA-PIT irradiator). The photoactivated MNCs were returned to the patient within 30 min using a blood transfusion set. During ECP procedure, patients' vital signs were monitored. Anticoagulation consisted in acid citrate-dextrose Formula A set at a variable ratio (1:14- 1:20) according to the patient's characteristics (clinical conditions, body weight, coagulation values) and platelet (PLT) count. Prophylaxis of hypocalcemia consisted of the administration of calcium gluconate (5 ml diluted in 5–10 ml saline) every 30 to 45 min. All procedure related side effects were recorded. During the reinfusion and postreinfusion phases, the patients were monitored for fever, chills, headache, rash, erythema, urticaria, itching, and edema.

Results: All the patients had also steroids, 4 had concurrent mesenchymal stem cells. ECP was applied on 2 consecutive days every 2–4 weeks which is continued for approximately 6 months followed by a maintenance schedule tapered to an every 2- to 4-weeks. The mean session cycle was 19 (6- 51) between February 2015 to November 2016. The most commonly involved organ was the skin which demonstrated a response rate of 75%, followed by liver (66%), lung (25%), gut (18%) and mucous membranes (68%) The concurrent immunosuppression could be reduced during ECP therapy, and no increase in opportunistic infections was detected. 1/8 patient died after a relapse, 7/8 are alive with chronic mild GvHD. No serious complication was detected.

Summary/Conclusions: However, despite our good response rates, our understanding of ECP remains limited. Patients who suffer from acute and chronic GVHD have limited treatment options. ECP remains an important therapeutic option. Future basic, translational, and clinical research studies will provide a better understanding of its mechanism of action and optimize its therapeutic potential.

P-835

ASSESSMENT OF FACTORS ASSOCIATED WITH SUCCESSFUL MOBILIZATION AND COLLECTION OF PERIPHERAL BLOOD HEMATOPOIETIC STEM CELLS IN AUTOLOGOUS AND ALLOGENEIC DONORS

RM Grubovic Rastvorceva

Institute for Transfusion Medicine of RM, Medical Faculty – Skopje, Skopje, Macedonia

Background: Peripheral blood hematopoietic stem cells (PBSC) have largely replaced bone marrow derived stem cells in autologous transplantations, and have become the preferred source of stem cells in the majority of allogeneic transplantations. Sufficient number of mobilized and collected hematopoietic stem cells (HSC) is needed for successful hematopoietic stem cell transplantation.

Aims: The aim of our study was to analyze possible predictive factors that could influence hematopoietic stem cell yield.

Methods: This study was performed in the Institute for Transfusion Medicine of RM and the University Hematology Hospital from 2008 till 2016. There were 30 allogeneic and 90 autologous donors that underwent mobilization and collection of PBSC. The association between the number of collected PBSC and possible predictive factors, such as demographic characteristics, laboratory parameters and collection parameters in both groups, and mobilization strategy and clinical characteristics in autologous donors, was analyzed using Spearman Rank Order Correlation.

Results: There were 226 apheresis, 182 in autologous donors (mean 2, range 1–3) and 44 apheresis in 30 allogeneic donors (mean 1.5, range 1–2). The mean number of collected MNC in autologous donors was 3.09×10^8/kg and 2.85×10^6/kg CD34+ cells, and 3.23×10^8/kg MNC and 3.20×10^6/kg CD34+ cells in allogeneic donors. Significantly larger number of MNC and CD34+ cells was collected with the WBC set. There was a statistically significant correlation between the total number of collected MNC in autologous donors and platelet count before mobilization, the number of cycles in one apheresis procedure, quantity of collected graft and the number of collected MNC and CD34+ cells on the first day of apheresis. There was a statistically significant correlation between the total number of collected MNC in allogeneic donors and platelet count before mobilization, the number of cycles in one apheresis procedure, quantity of collected graft and number of MNC on the first day of apheresis. There was a strong correlation between the number of collected MNC and CD34+ cells on the first harvest and the total number of collected MNC and CD34+ cells in poor mobilizers, and inverse correlation with the number of apheresis procedures. Donors who donated MNC $\leq 0.7 \times 10^8$/kg and/or $\leq 0.7 \times 10^6$/kg CD34+ cells on the first harvest (84.6%) were strong predictors of poor mobilizers.

Summary/Conclusions: Determining the proper level of baseline and preapheresis laboratory parameters for initiating mobilization and apheresis procedure which is safe for donors and greatly efficient in collection of PBSC is needed for optimization of these procedures, as well as for early intervention in poor mobilizers.

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P-837

PROCEDURE MODIFICATION FOR BETTER QUALITY HEMATOPOIETIC STEM CELL PRODUCT: A STUDY ON COM.TEC APHERESIS SYSTEM

A Khetarpal, V Gupta and U Kotwal

Transfusion Medicine, Artemis Hospitals, Gurgaon, India

Background: The quality of the peripheral Hematopoietic Stem Cell (HSC) product is determined not only by the content of HSCs but also by the contaminating cells such as leucocytes, RBCs and platelets. The number and the viability of HSC is the most important factor in predicting success of engraftment. However the non-stem cells like granulocytes, RBCs and platelets along with cryoprotectant have been known to affect viability of the stem cells. Also many adverse events in the recipients have been reported (13.5–67.3%) in different studies which have been attributed to the infusion of damaged cellular products, complement activation, large volumes or DMSO. RBCs reduce viability, invasion and CFU capacity of the progenitor cells in a dose dependent manner. Hemolysis of RBCs results in high levels of free heme, causing cellular injuries leading to proximal renal tubules and endothelial cell damage. Similarly leucocytes and their breakdown debris have been implicated to play a direct causal role in the patho-physiology of infusion-related adverse events. As reported by many authors previously, we at our centre also noticed high RBC contamination with relatively high volume of stem cell product collected on COM.TEC apheresis system. The associations of adverse events with high hematocrit and volume prompted us to modify our existing program for a better product quality.

Aims: The aim of this study was to reduce RBC contamination and volume of stem cell product by modification of stem cell collection protocol on auto-MNC program of Fresenius COM.TEC Apheresis System (version 4.03)for collecting autologous HSC in adult patients and to analyze effects on other variables.

Methods: It is a retrospective study, comprising of 20 autologous stem cell collection procedures on mobilized patients with multiple sclerosis. These were divided in two groups – (A) with pre-modification program setting and (B) with modified program. Product quality and engraftment data was collected and analyzed.

Results: The mean volume of harvested product reduced from 379.3 ml(220–540) in group A to 287.6 (180–400) ml in group B. Cell product hematocrit in group A was 11.6% (6.1–19.1) and 5.68% (2.4–12.56) in group B. Thus mean dose of RBC decreased from 43.9 ml to 16.3 ml per infusion. MNC and platelets counts were 311.21 (103.9–473) /μl and 1892 (1704–3124)/μl in group A and 303 (211–351.5)/μl and 2409 (1742–3634)/μl in group B respectively. The harvested dose of CD34+ cells was 10.74 million/kg body weight (3.6–17.99) in group A and 8.54 million/kg body weight(5.2–13.41) in group B. The engraftment data showed neutrophil(NE) and platelet engraftment(PE) within normal range – group A mean NE was 8.7(7–10) and PE was 9.4 days(7–11) while group B mean NE was 9.2 (5–11) and PE was 9.2 days (7–11).

Summary/Conclusions: Our new protocol resulted in marked reduction of product hematocrit, volume and marginal decrease in leucocyte concentration without compromising the stem cell dose. Thus the product has become more economically efficient (volume reduction) for cryopreservation and of better quality.

P-838

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P-841

IMPACT OF *N*-ARYL-D-gluconamide Cryoprotectants on Engraftment of Cryopreserved Hematopoietic Stem and Progenitor Cells from Human Umbilical Cord Blood

MK Adam[1], S Jahan[2,3], T Charlton[1], J Manesia[3], N Pineault[2,3] and R Ben[1]

[1]Chemistry and Biomolecular Sciences [2]Biochemistry, Microbiology and Immunology, University of Ottawa [3]Centre for Innovation, Canadian Blood Services, Ottawa, Canada

Background: Isolation of hematopoietic stem and progenitor cells (HSPCs) from umbilical cord blood (UCB) offers a readily-available and non-invasive source of stem cells for life-saving therapies, such as hematopoietic stem cell transplantation (HSCT). HSPCs are clinically cryopreserved with 10% dimethyl sulfoxide (DMSO), a toxic cryoprotectant that fails to mitigate cellular injury resulting from ice recrystallization, and is unable to preserve the function of HSPCs post-thaw. Reducing HSCT complications associated with delayed or failed engraftment involves improving the post-thaw hematologic potency. Increased post-thaw function has been achieved in vitro when *N*-aryl-D-gluconamides, a class of ice recrystallization inhibitors, are used as cryoprotectants in conjunction with 10% DMSO during cryopreservation. Importantly, the use of these *N*-aryl-D-gluconamides as promising cryoprotectants for HSPCs has yet to be investigated in vivo.

Aims: The objective of this study was to examine how the use of *N*-aryl-D-gluconamides for cryopreservation affected the engraftment activities of cryopreserved HSPCs from human umbilical cord blood.

Methods: Human HSPCs from UCB were cryopreserved based on total nucleated cell (TNC) counts in the presence of 10% DMSO or *N*-aryl-D-gluconamides in conjunction with 10% DMSO using a 1 °C/min cooling rate. A two-step thaw and dilute method was implemented prior to transplantation of thawed HSPCs into immunocompromised NSG mice. Following a serial transplantation protocol allowed for the determination of platelet and leukocyte engraftment, HSPC differentiation activities, and HSPC self-renewal capabilities. Analysis at short-, mid-, and long-term time points as well as the bone marrow of primary and secondary recipients was achieved using fluorescence-activated cell sorting (FACS) and the clonogenic colony forming cell (CFC) assay.

Results: Post-thaw viabilities of HSPCs cryopreserved with *N*-aryl-D-gluconamides and DMSO are comparable to that of the 10% DMSO condition. Based on results from the clonogenic assay, HSPCs cryopreserved with 2-fluorophenyl-D-gluconamide differentiate and proliferate more than those cryopreserved with 10% DMSO alone. Increased platelet, progenitor, and B cell levels were observed in mice transplanted with HSPCs cryopreserved with the ice recrystallization inhibiting cryoprotectant in the first transplant experiment. Additionally, higher leukocyte levels were observed in secondary recipients in the *N*-aryl-D-gluconamide condition.

Summary/Conclusions: The use of ice recrystallization inhibitors, such as an *N*-aryl-D-gluconamide, for HSPC cryopreservation appears to increase engraftment activities of HSPCs.

Clinical Applications

P-842

A NOVEL MESENCHYMAL STEM CELL THERAPY IN STEROID REFRACTORY GRAFT-VERSUS-HOST DISEASE

E Molnar[1], A Barta[2], A Batai[2], Z Csukly[2], L Gopcsa[2], G Tatai[2], L Lengyel[2], G Kovács[2], T Masszi[3], G Mikala[2], M Paksi[2], M Réti[2], E Torbagyi[2], H Bönig[4], P Bader[4] and P Remenyi[2]

[1]Department of Serology, Hungarian National Blood Transfusion Service [2]Department of Hematology and HSCT, St. Istvan & St. Laszlo Hospital [3]3rd Department Of Internal Medicine, Semmelweis University, Budapest, Hungary [4]Division for Stem Cell Transplantation and Immunology, University Hospital Frankfurt/Main, Frankfurt, Germany

Background: Steroid refractory graft-versus-host disease (GvHD) is a serious complication of allogeneic hematopoietic stem cell transplantation (HSCT). More experience accumulates in the immunomodulatory effect of mesenchymal stem cell (MSC) infusion in numerous immunopathological disorders – such as GvHD – and signals.

Aims: We have evaluated the efficacy of a novel MSC product, we exclusively used the licensed MSC-FFM (derived from bone marrow, "MSC-FFM" /Kuci et al. Haematologica 2016/ submitted on a named-patient basis) in cases of GvHD refractory to conventional immunosuppressive treatment.

Methods: Patients with steroid-resistant GvHD were treated with the MSC-FFM, 4 times per case weekly at a dose of 1 million cells/kg. This is a novel MSC product generated of the MNC of 8 volunteer donors generated in the University of Frankfurt am Main, Germany. Clinical response was assessed 28 days after administering the first dose. Complete remission was defined as the complete disappearance of symptoms. Partial remission was assessed by the significant relief of symptoms and by the general improvement of the patient's condition. We have evaluated the red blood cell and platelet concentrate needs of the patients before and after the treatment.

Results: Our 17 patients had received a total of 21 cycles of MSC-FFM-treatment (2–4 doses per cycle). The median age was 40 (19–56) years with a male/female ratio of 5:4. Distribution of the underlying malignancies (n): acute myeloid leukemia: 6; acute lymphoblastic leukemia: 4; myelofibrosis: 1; myelodysplastic syndrome: 2; multiple myeloma: 2; T-cell lymphoma: 2. Twelve patients had undergone allogeneic HSCT with matched unrelated donors, the other five had stem cells derived from HLA-identic relatives. The first episode of GvHD after HSCT was observed on the median 57rd (7–455) day. The involved organs were skin (5), gut (5), skin and gut combined (7) and lung in 3 cases. We applied an average of 3 lines of treatment (it varies from 1–5 lines) before we started MSC-FFM treatment. The median time of MSC-FFMs first infusion was 224 (45–1981) days after stem cell transplantation (HSCT) and 122 (15–1974) days after the first episode of GvHD. Six of the 17 patients treated with the MSC-FFM showed complete remission (35.3%) and 8 resulted in partial remission (47.06%). All of the patients GvHD NIH stage score was 3 before MSC-FFM infusions, and it decreased to a median of 1 after treatment. The overall survival on the 60th day after the first GvHD was 76%.

Summary/Conclusions: According to our observation MSC-FFM-therapy is an effective treatment for GvHD in the majority of the observed cases. The application of third-party MSC-FFMs offers a promising alternative in the therapy of GvHD and other GvHD-associated complications after HSCT. Further research is required to warrant the optimal start and dosage of the MSC-FFM treatment, along with the issue of long-term safety.

P-843

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P-844

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P-845

CURRENT PRACTICES FOR VIABILITY TESTING OF CRYOPRESERVED CORD BLOOD PRODUCTS: AN INTERNATIONAL SURVEY BY THE CELLULAR THERAPY TEAM OF THE BIOMEDICAL EXCELLENCE FOR SAFER TRANSFUSION COLLABORATIVE

M Takanashi[1,2], E Selogie[2], J Reems[2,3], D Stroncek[2,4], M Fontaine[2,5], J Girdlestone[2,6], H Garritsen[2,7,8], P Young[2,9], D McKenna[2,10] and Z Szczepiorkowski[2,11,12]

[1]Japanese Red Cross Society, Tokyo, Japan [2]Biomedical Excellence for Safer Transfusion Collaborative, Lebanon [3]University of Utah, Salt Lake City [4]National Institutes of Health, Bethesda [5]University of Maryland School of Medicine, Baltimore, United States of America [6]NHS Blood and Transplant, The John Radcliffe Hospital, Oxford, United Kingdom [7]Municipal Hospital Braunschweig gGmbH [8]Fraunhofer Institute for Surface Engineering and Thin Film IST, Braunschweig, Germany [9]Vanderbilt University, Nashville [10]University of Minnesota, Saint Paul [11]Dartmouth-Hitchcock Medical Center, Lebanon, United States of America [12]Institute of Hematology and Transfusion Medicine, Warsaw, Poland

Background: Viability testing is a common practice in laboratories. As cord blood for transplantation is cryopreserved, cord blood banks are required to validate the procedures for cryopreservation and thawing by measuring the post-thaw viable cell recoveries. Since processing of cord blood units typically involves concentrating the buffy coat fraction, this means that the total nucleated cellular fraction consists largely of neutrophils. Various methods are used for viability testing and the method used may affect the test results, leading to data inconsistencies among laboratories.

Aims: The goal of this study was to ascertain current laboratory practices internationally when performing viability testing of cryopreserved cord blood products, and glean information about how to standardize the method to improve inter-laboratory reproducibility.

Methods: A survey to evaluate current laboratory practices for viability testing was designed and distributed internationally. The question topics included sampling and testing methods, responses to unexpected results, rating the reliability of cord blood quality tests, together with expectations for standardization.

Results: There were 32 respondents to the survey, of whom 28 responded to the more detailed questionnaire about viability methods. Of the 32 participants, ten were with a cord blood bank only, 18 with a transplant centre only and four with both. Overall, responses indicated that various stains were used among the laboratories, and when multiple sites used the same viability stain the methods differed. The longest time allowed from thawing to viability testing varied from one minute to 60 min, with some laboratories not having a definite time limit. The acceptance limits for the viability assay results also varied from 35% of the CD45 population to 85% of the CD45/CD34 population with flow cytometry, and 50% or 70% with Trypan blue. Among cord blood assays, the TNC and CD34 counting data were regarded as very important by >60% of the participants, while the viability and CFU data were considered less valuable. Viability data was regarded as very important by seven out of ten participants with cord blood banks, but by only four out of 16 participants with transplant centres. The majority of the respondents were in favour of standardizing the viability testing methods. A wide variety of preferences were communicated about how to standardize the methods, but a majority did advocate the use of 7-AAD with flow cytometry.

Summary/Conclusions: The survey results revealed a variety of tests and inconsistent inter-laboratory practices for performing the viability assay. Flow cytometry with a 7-AAD dye was suggested as a first step towards standardization.

P-846

TREATMENT OF SKIN ULCERS WITH PLATELET RICH PLASMA GEL

E Borici[1], V Doci[1], E Kokalari[2] and N Borici[2]

[1]National Blood Transfusion Center [2]European Hospital Villa Maria, Tirana, Albania

Background: Cutaneous ulcers are commonly seen in people with diabetes, renal failure, hypertension and lupus, diseases that impair circulation and improper healing following accidents or trauma to the skin. Disorders that affect blood clotting, such as arteriolosclerosis, can cause skin ulcers too. Non infected skin ulcers are very difficult to treat especially when the cause of it is not possible to be corrected. Such wounds as diabetic ulcers, avascular necrosis, vasculitis are difficult to get closed and their treatment is a challenge. The use of platelet rich plasma (PRP) gel is becoming a good option of treatment for skin ulcers.

Aims: In this study we bring our experience on treating skin ulcerations by PRP gel aiming to prove its effective role on wound closure.

Methods: During the period of time January 2015 – January 2017 we treated 78 patients with non-infected cutaneous ulcers. There were 45 males and 33 females included in the study that passed the criteria for the treatment. We excluded all the infected wounds, wounds that had bones or tendons exposed, pregnant women and the patients suffered from cancer diseases. The mean age of the patients was 62 y.o. (51–81). The patients pathologies that had caused the ulcerations were: diabetes, vasculitis and avascular necrosis by trauma. We prepared the PRP gel from homologous blood donations by deriving the platelet from the plasma. Then in the plasma we provided the cryoprecipitate which mixed with the platelet and activated with thrombin and calcium chloride formed the PRP gel. We measured and photographed all the wounds before the treatment and once a week when the wound medication session was performed. After the cleaning wound with betadine and necrotomy if was necessary a PRP gel was applied onto the wound surface and then dressed correctly.

Results: We saw in every wound a granulation formed at 3rd or 4th medication session and the wound closure at 15th session (12–20 sessions). One patient acquired an infection during the treatment period that obliged us to exclude him from the study. In a diabetic foot patient the toe was necrotized and the amputation in its base was necessary and the wound was then closed after 12 sessions. All the patients had wound closure without performing other type of treatment.

Summary/Conclusions: We concluded that the PRP gel is a good option for treating skin ulcers. The treatment of non-infected wound by this method gives satisfied outcome and the patients feel comfort for using this non-invasive medication therapy.

P-847

NEUROPROTECTIVE EFFECTS OF TRANSPLANTED MESENCHYMAL STROMAL CELLS–DERIVED HUMAN UMBILICAL CORD BLOOD NEURAL PROGENITOR CELLS IN EAE

M Kheirandish, H Rafieemehr and Z Asadpoor Dezaki

Immunology, Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background: Multiple Sclerosis (MS) is an autoimmune inflammatory demyelinating disease of the central nervous system.
Aims: The aim of this study was to investigate the neuroprotective effects of transplanted human umbilical cord blood mesenchymal stromal cells (UCB-MSC) derived neural progenitor cell (MDNPC) in EAE, an experimental model of MS.
Methods: To initiate neuronal differentiation of UCB-MSCs, the pre-induction medium was removed and replaced with induction media containing retinoic acid, b FGF, h EGF, NGF, IBMX and ascorbic acid for one week. The expression of neural genes was examined in comparison to control group by real-time PCR assay. Then, experimental autoimmune encephalitis (EAE) was induced using myelin oligodendrocyte glycoprotein (MOG, 35–55 peptides) in 24 C57BL/6 mice. After induction, the mice were divided into four groups (n=6) as follows: healthy, PBS, UCB-MSCs and MDNPC, respectively. At the end of the study, disease status in all the groups was analyzed using hematoxylin-eosin (H&E) staining of brain sections.
Results: We found that UCB-MSCs exhibit neuronal differentiation potential in vitro and transplanted MDNPC lowered clinical score and reduced CNS leukocyte infiltration compared to untreated mice.
Summary/Conclusions: Our results showed that MDNPC from UCB may be a proper candidate for regenerative therapy in MS and other neurodegenerative diseases.

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P-850

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P-851

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P-852

ESTABLISHMENT OF STABLE CHINESE HAMSTER OVARY CELL LINE CAPABLE OF EXPRESSING HUMAN RECOMBINANT HEMOPEXIN: A PROMISING THERAPEUTIC MODALITY AGAINST HEMOLYTIC ANEMIA

F Amiri[1], M Bahadori[2] and M Habibi Roudkenar[3,4]

[1]Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran [2]IBTO, Tehran [3]Medical Biotechnology Research Center, Paramedicine Faculty [4]Neuroscience Research Center, Guilan University of Medical Sciences, Rasht, Iran

Background: Hemolytic anemia is associated with intravascular heme release and oxidative stresses that lead to endothelial dysfunctions. Hemopexin (HPX) is a plasma heme-binding _1-glycoprotein, which plays a pivotal role in heme transfer to hepatocytes and iron recycling. Recently, HPX administration in hemolytic patients attenuated hemolysis-driven oxidative damages and endothelial disorders that led to a rise in the strategy of HPX therapy. Human HPX production using recombinant DNA technology could provide a real alternative to plasma-derived HPX.
Aims: The purpose of this study was to generate a stable Chinese hamster ovary (CHO) cell line expressing human rHPX.
Methods: Total RNA was extracted from HepG2 cells, and HPX gene was amplified by Real Time-Polymerase Chain Reaction (RT-PCR). Then, the HPX gene was cloned in pcDNA3.1 (+) shuttle vector. The recombinant pcDNA3.1-HPX was transformed to E. coli TOP10 strain. Gene cloning was verified by colony PCR, restriction digestion, and DNA sequencing. The CHO cells were chemically transfected with pcDNA3.1-HPX, and screening was performed by G418 sulfate effective concentration to develop stable single cell clones. The rHPX expression was verified by RT-PCR and Western blot.
Results: Cloning confirmation analyses showed that HPX gene was successfully cloned in pcDNA3.1 (+) vector. Screening of transfected cells with G418 sulfate enriched the population of single cell clones expressing human rHPX. The RT-PCR and Western blot analyses confirmed rHPX expression in CHO cell line both at transcriptional and translational levels.
Summary/Conclusions: Human rHPX protein was stably expressed in CHO cells. This study was a pioneering work for the future production of therapeutic rHPX.

P-853

TRANSFERRIN AND IRON COMBINATION THERAPY DOES NOT CORRECT ANEMIA OF INFLAMMATION

M Boshuizen[1,2], A Kim[3], E Khorramian[3], V Gabayan[3], E Nemeth[3], T Ganz[3], N Juffermans[1] and R van Bruggen[2]

[1]Intensive Care, Academic Medical Center [2]Blood Cell Research, Sanquin, Amsterdam, Netherlands [3]Department of Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, United States of America

Background: Anemia of inflammation (AI) occurs in patients with systemic inflammation caused by infections, cancer and auto-inflammatory disorders. In AI, high levels of hepcidin cause iron sequestration in macrophages and thus low serum iron availability for haemoglobin synthesis. Iron therapy for AI has been tested in several randomized clinical trials, but most of these studies did not show an increase in haemoglobin level in response to iron therapy. Another factor that limits the iron that is available for erythropoiesis in AI is a decrease in serum transferrin (Tf) levels during this condition. Therefore, the combination of iron and Tf therapy may be more effective in supporting erythropoiesis in individuals suffering from AI.
Aims: We studied the potential of a combination of iron and Tf therapy in an animal model of AI to support erythropoiesis and correct the anemia.
Methods: A mouse model for AI induced by an injection of heat-killed Brucella abortus (BA) was used. The mice received intraperitoneal injections of saline, iron dextran, apoTf or iron dextran + apoTf. The injections were given every other day, starting on the first day after BA injection. Mice were sacrificed at 7, 14 and 21 days after BA injection.
Results: Tf plus iron therapy does not correct anemia in AI (P=0.69). Tf therapy alone aggravates the anemia (P=0.005) compared to saline controls. In contrast, iron therapy alone increases haemoglobin levels (P=0.002). In accordance with the haemoglobin levels, reticulocytes are lower in Tf treated animals compared to saline treated mice (P=0.027). Iron therapy decreases iron restrictive erythropoiesis compared to saline treated animals, shown by decreased zinc protoporphyrin levels (P=0.01). Iron plus Tf therapy did not decrease iron restrictive erythropoiesis. Serum iron levels decrease at 7 days in all groups compared to healthy controls (P=0.003). Serum iron levels increase at day 14 in mice treated with Tf (+/- iron) compared to saline treated animals (P=0.004).
Summary/Conclusions: Tf therapy, either alone or in combination with iron therapy, does not correct anemia in an animal model of AI. In contrast, Tf without iron aggravates the anemia in our model. However, iron therapy does correct anemia in our model. These results suggest that the correction of AI is dependent on Tf saturation and not on total serum iron, given that the amount of iron administered was equal for the iron and the iron + Tf groups. We hypothesize that Tf therapy causes a lower Tf saturation and thereby increases the amount of monoferric Tf. Monoferric Tf has a lower affinity for transferrin receptor 1 (TfR1) than diferric Tf and consequently transports less iron to the bone marrow for erythropoiesis. Iron consumption may be lower in the Tf treated groups, causing the higher serum iron level in these groups. These results suggest that the decrease of Tf during inflammation is not the cause of anemia, but rather may be protective.

P-854

PERFORMANCE EVALUATION OF THE SPECTRA OPTIA APHERESIS SYSTEM MONONUCLEAR CELL COLLECTION FOR AUTOLOGOUS PERIPHERAL STEM CELL TRANSPLANTATION

T Jisr[1], G Rawas[1], M Elchaar[2], W Halabi[1], A Mekdad[1], A Youssef[1], A Mougharbel[1] and A Ibrahim[1]

[1]Makased Hospital [2]University of Balamand, Beirut, Lebanon

Background: The Spectra Optia (SO) apheresis system performs a wide range of therapeutic procedures, including peripheral blood stem cell (PBSC) collection in mobilized donors and patients (pts).

Aims: The device was studied to evaluate the cellular composition of PBSCs harvested in pts with multiple myeloma (MM), non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma(HL) planed for autologous peripheral stem cell transplantation (APBSCT), and to optimize the collection of PBSCs using the CD34+ precount and collection efficiency(CE2) of apheresis device.

Methods: In our study enrolled pts undergoing PBSC mobilization and planed for APBSCT. We evaluated SO system's mononuclear cell (MNC) collection performance, with respect to CD34+ cells and MNC collection efficiency, platelet reduction pre to post apheresis, and product purity in view of using prediction algorithms to optimize the procedure and predict the CD34+ yield, blood volume processed and platelets loss. We also evaluated neutrophil and platelet recovery in pts who underwent APBSCT.

Results: Between 30/3/2015 and 30/11/2016, 45 pts underwent PBSC harvesting by SO device. Median age was 46 y (20–71). There were 19 females and 26 males. Diagnosis was MM in 21 pts, HL in 17 pts and NHL in 7 pts. The number of apheresis procedures was 59. Mobilization consisted in G-CSF alone in 36 pts, chemotherapy and G-CSF in 8 pts, and G-CSF + CXCR4 inhibitor in one patient. Median count of CD34+ cells pre-collection was 58/µl (16.5–372). Median total blood volume processed was 12.4L (6.3–19.9). Median count of CD34+ cells collected was 4.1 106/kg (1–23.6). Median MNC collection efficacy was 48% (7–95). Median CD34+ cell collection efficacy was 45.5% (15–95%). Median platelet reduction pre to post apheresis was 30% (0–50%). Median product hematocrit and granulocytes product was 5% (3–9) and 52% (5–93), respectively. Twenty-six of the 45 pts underwent myeloablative high dose chemotherapy followed by APBSCT which was performed for MM in 18 pts, HL in 6 pts, and NHL in 2 pts. The median count of CD34+ cells infused was 2.5 106/kg (1.15–10.6). All the pts received G-CSF post-APSCT until neutrophil recovery. The median day for neutrophil recovery was 10 (8–14). Median duration of severe neutropenia (ANC < 0.5 109/L) was 7 days (4–10). The median day for platelet recovery was 10 (7–17). Median duration of severe thrombocytopenia (platelets < 20 109/L) was 5.5 days (2–14).

Summary/Conclusions: The study results confirm that the SO apheresis system's MNC collection protocol is safe and effective. The neutrophils and platelets recovery in pts auto-transplanted was not inferior compared to historical controls. In addition, this system help to use prediction algorithms for whole blood processing to achieve a desirable and optimal yield based on CD34+ precounts and CE2 of the apheresis device.

P-855

PERIPHERAL BLOOD STEM CELL COLLECTION ON THE SPECTRA-OPTIA APHERESIS SYSTEM USING THE CONTINUOUS MONONUCLEAR CELL COLLECTION PROTOCOL PROVIDES SIMILAR CELL YIELDS IN HEALTHY AND AUTOLOGOUS DONORS

EJ Dann[1,2], T Mashiach[1], L Bonstein[1,2] and T Katz[1,2]

[1]Rambam Health Care Campus [2]Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel

Background: Currently, stem cell collection could be performed on the Spectra-Optia Apheresis Device using one of the two following programs. The mononuclear cell collection (MNC) procedure is fully automated, requiring intervention only in case of technical problems, such as clamping or incorrect interphase. Unlike MNC, in the continuous mononuclear cell collection (CMNC), the interface needs to be frequently checked to verify that the correct cell layer is being collected. At the Rambam Health Care Campus, a tertiary care center providing services to Northern Israel, only MNC has been used until 2017. At that point, the CMNC has been introduced for patients with a white blood cell (WBC) count of ≥20,000/µl, and the MNC program has been employed for patients with a lower WBC count on the collection day.

Aims: Comparison of the peripheral blood stem cell (PBSC) yield obtained in healthy donors and hematologic patients undergoing the CMNC procedure and evaluation of the impact of PB CD34^{+} count on the total PBSC collection.

Methods: Data were retrospectively retrieved from patients' PBSC collection reports in 50 consecutive CMNC procedures, including 36 autologous and 14 healthy donors. A sub-analysis compared results of patients with a PB CD34 count ≥20/µl or <20/µl with the results of healthy donors.

Results: In the CMNC, the following parameters did not statistically differ between autologous and healthy donors: mean collection time (323±23 and 308±74 min, respectively), the total blood volume processed (3.1±0.88 and 2.75±0.84, respectively) and pre-collection PB WBC count [median 48 (20–112) and 46(31–67), respectively]. Difference in the means collection efficiency-2 (CE-2), defined as the total CD34^{+} amount in the collection bag divided by the amount of CD34^{+} cells in the PB processed by the collection apparatus (57±21 and 63±13, respectively), did not reach statistical significance either. The following values were significantly different between autologous and healthy donors: percentage of PB CD34^{+} cells [median 0.08 (range 0.01–0.54%) and 0.13 (range 0.08–0.3) respectively; P=0.01], percentage of CD34^{+} cells in the collection bag (0.5±0.43 and 0.71±0.27, respectively; P=0.03) as well as the total CD34^{+} cell amount (399±278 × 10^6 and 585±171 × 10^6, respectively; P=0.008). Notably, when only the results of patients with a PB CD34^{+} cell count ≥20/µl were analyzed, they were found to be identical to those obtained in healthy donors.

Summary/Conclusions: The CMNC is highly effective in terms of the cell yield in both healthy and autologous donors with a PB CD34^{+} count ≥20/µl. Similar CE-2 is observed in both donors group. The total amount of CD34+ cells in the collections is found to directly correlate with the PB CD34+ count.

P-856

DOUBLE-VIRUS INACTIVATED (PSORALEN/UV-SOLVENT/ DETERGENT) HUMAN PLATELET LYSATE FROM EXPIRED PLATELET CONCENTRATES TO EXPAND BONE-MARROW MESENCHYMAL STROMAL CELLS

L Barro[1], Y Huang[2], F Knutson[3] and T Burnouf[4]

[1]International Ph.D. Program in Biomedical Engineering, College of Biomedical Engineering [2]Center for Cell Therapy and Regeneration Medicine, Taipei Medical University, Taipei, Taiwan, China [3]Clinical Immunology and Transfusion medicine IGP, Uppsala University, Uppsala, Sweden [4]Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering, Taipei Medical University, Taipei, Taiwan, China

Background: Experimental studies are convincingly showing that human platelet lysate (HPL) can be used, in place of fetal bovine serum (FBS), as a clinical-grade supplement of growth media needed for expanding mesenchymal stromal cells (MSCs) and reach clinically-meaningful number for transplantation. Recent work has further demonstrated the possibility to use expired platelet concentrates (PC), as well as PC subjected to a pathogen inactivation treatment, as source materials for the production of HPL. As the need for HPL for cell therapy applications is expected to develop sharply, production scale may also have to increase to meet the demand. Increasing the HPL pool size is one means to improve productivity but raises concomitantly the issue of virus safety. As is the case in the plasma fractionation industry, implementing double virus reduction treatments may become mandatory to provide a sufficient margin of safety to large-pool HPL.

Aims: Evaluate the possibility to expand bone-marrow derived MSCs (BM-MSC) ex vivo using as growth medium supplement with HPL prepared from expired PC pathogen-inactivated by psoralen/UV treatment, and further virally inactivated by solvent/detergent (S/D).

Methods: Expired psoralen/UV (Intercept)-treated PC (n =4) formulated in PAS/ plasma were prepared at the Uppsala University Blood Bank and frozen. The PC were thawed at 37°C and pooled. The Intercept-HPL (I-HPL) was prepared by 3 freeze-thaw (−80°C/37°C) cycles, and centrifuged. S/D-treated I-HPL (I-SD-HPL) was obtained by additional incubation with 1% (v/v) tri-n-butyl-phosphate (TnBP)-1% (v/v) Triton X-45 at 31°C for 1 h, followed by 10% (v/v) soybean oil extraction, C18 hydrophobic interaction chromatography, and sterile filtration. The HPL total protein concentration, protein profile (SDS-PAGE), and the content in growth factors (GF; ELISA) and PF4 were determined. The capacity of 10% (v/v) I-HPL and I-SD-HPL supplementation to expand BM-MSC was compared, using 10%FBS as control. Morphology, cell viability, cumulative population doubling (CPD), and differentiation capacity were evaluated.

Results: The mean total protein content of I-HPL and I-SD-HPL was 26.4 and 25.9 mg/ml, lower than that of FBS 35.3 mg/ml. The content in five GF (BDNF, PDGF-AB, EGF, FGF) and in PF4 was significantly lower in I-SD-HPL than in I-HPL, and that in IGF-1, TGF-b1, and HGF was essentially unchanged. BM-MSCs presented a more elongated spindle-shaped morphology with I-HPL and I-SD-HPL supplementation than with FBS. Cells were larger when expanded in I-SD-HPL than in I-HPL. Cell viability

was higher using I-HPL and I-SD-HPL than FBS. The CPD after four passages was higher using I-HPL than I-SD-HPL, and both better (P<0.0001) than FBS. The differentiation capacity into the chondrocyte and osteocyte lineages was more effective in I-SD-HPL but less pronounced towards the adipocyte lineage than when using I-HPL.

Summary/Conclusions: 10% I-SD-HPL promoted BM-MSC expansion better than 10% FBS. These data support the possibility to develop a double-virally inactivated HPL to substitute for FBS supplementation. The S/D treatment resulted in a change in the content of some GF, impacted cell morphology and CPD compared to the HPL treated by psoralen/UV only. Further studies are on-going to investigate the immunophenotype and immunomodulation properties.

P-857
PLATELET TRANSFUSION IN PATIENTS UNDERGOING STEM CELL TRANSPLANT – AN AUDIT

N Ali, U Shaikh and S Adil

Aga Khan University, Karachi, Pakistan

Background: Prophylactic platelet transfusion is considered standard practice for patients undergoing haematopoietic stem cell transplant. Platelet concentrates are the most frequently utilized blood product in our institution. In a developing country like ours, platelets are a limited resource and represent a significant cost to the patient and hospital.

Aims: We retrospectively analyzed platelet transfusion trigger in our patients undergoing stem cell transplant.

Methods: All consecutive adult and pediatric patients admitted at the Aga Khan University Hospital's bone marrow transplant unit between 2004 and 2017 were included in the study. Transfusions were monitored from the time of admission in BMT unit till discharge. Other variables to be analyzed included age, gender, type of transplant, underlying diagnosis, engraftment, bleeding diathesis and outcome of transplant. We followed institutional guidelines of prophylactic platelet transfusion and the threshold was a count less than $20 \times 10^9/l$.

Results: During the study period, we performed n=293 transplants. There were n=188 allogeneic transplants and n=105 autologous transplants. Male: female ratio was 1:2.5. The most frequent diagnosis was aplastic anaemia in n=63, β thalassemia major in n=36 and leukemia in n=66. Median age±SD (range) was 24±14.5 (2–64) years. Mean duration of stay was 26.7 days (Range: 4–50 days). Eighty percent of our patients engrafted. In 80% of the patients, we achieved the institutional benchmark of prophylactic platelet transfusion at a level of less than $20 \times 10^9/L$. In 16%, prophylactic platelet transfusion was done at a level above $20 \times 10^9/L$. Indications for this approach were sepsis (n=24), bleeding diathesis (n=5), intracranial bleed (n=4) and graft failure (n=14). In 4% of autologous transplant patients, the threshold was decreased to $10 \times 10^9/L$ mainly due to delayed engraftment. The overall survival rate was 70%.

Summary/Conclusions: We achieved the required benchmark in 80% of patients. The way forward will be to evaluate the safety and efficacy of lower platelet transfusion threshold i.e. $10 \times 10^9/L$ to ensure judicious use of this product in stem cell transplant patients.

Clinical Immunogenetics – HLA in Transfusion Medicine

P-858
CLINICAL AND LABORATORY CHARACTERIZATION OF HEMATOLOGY PATIENTS WITH PLATELETS REFRACTORINESS: A SINGLE-CENTRE RETROSPECTIVE STUDY

A Basendwah, H Aljedani, A Greenshields, W Hasegawa, R Liwski, S Couban and C Campbell

Faculty of Medicine, Dalhousie University, Halifax, Canada

Background: Platelet refractoriness (PR) refers to a persistent, inadequate response to platelet transfusion in patients with hypoproliferative thrombocytopenia (HT). PR has been associated with both inferior clinical outcomes and significant cost to the healthcare system. The majority of PR cases are due to non-immunologic causes

(such as fever, infection, and drugs); a minority of cases (20% or less) are caused by alloimmunization against foreign human leucocyte antigens (HLA) induced by sensitization via pregnancy, transfusion, or solid organ transplantation. The calculated panel reactive antibody (cPRA) score is used in solid organ transplantation, and is indicative of the patient's HLA alloreactivity to the general donor population. The cPRA for platelet recipients can be similarly calculated by including only antibodies targeting platelet-expressed HLA-A and HLA-B antigens. Patients with a high cPRA (>70%) have multiple antibodies targeting common HLA antigens, and are predicted to be incompatible with a large proportion of platelet donors. The current standard of care is to provide HLA-matched platelets for these patients, as the administration of pooled or single-donor apheresis units would likely result in immunologic PR.

Aims: This study aims to review the correlation of clinical and laboratory factors with suspected alloimmune PR cases at our institution, including gender, cPRA and potential sensitizing events.

Methods: A retrospective review of clinical and laboratory charts was conducted for all hematology patients investigated for alloimmune PR between January 1, 2010 and July 31, 2017. Class I HLA antibody testing was performed by the Canadian Blood Services Platelet Laboratory using the LABScreen single antigen bead assay (One Lambda). cPRA was determined based on the HLA-A and B locus antibodies using the Canadian cPRA calculator.

Results: This review identified 51 patients with PR, of whom 46 (29 female, 17 male) had HLA antibody data available for analysis. Of the 29 female patients, only 4 (14%) were either non-sensitized (cPRA=0%; n=3) or mildly sensitized (cPRA=1.4%; n=1), while 25 (86%) patients were highly sensitized (cPRA>70%; mean=94.8±7.8%; median=98.3%). Of the 17 male patients, 5 (29%) were non-sensitized, 9 (53%) were mildly to moderately sensitized (cPRA=1–70; mean=25.1+±20.6%; median=17%), and only 3 (18%) patients were highly sensitized (cPRA>70%; mean=88.1±10%; median=92.7). Overall, the degree of HLA sensitization was significantly greater in females vs males (mean cPRA=91±20% vs 41±34%; P<0.001). The mean number of RBC units transfused was similar for female vs male patients (16.6±12 vs 21±21; P=0.37), as was the mean number of transfused platelet units (23+/- 14 in females vs 22±15 in males; P=0.86). The mean number of pregnancies was 2.5 (range=0–8) in highly sensitized female patients vs 1.7 (range=1–2) in non-sensitized or mildly sensitized females.

Summary/Conclusions: The vast majority of patients with immunologic PR who were highly sensitized (cPRA>70%) were female (25/28; 89.3%), most of whom had a history of pregnancy (91%). There was no difference in the number of RBC or platelet transfusions received by female vs male patients. These findings suggest that pregnancy, not transfusion, is the main cause of anti-HLA antibodies and subsequent alloimmune PR. Female patients with PR would therefore see the most benefit from the use of HLA-matched platelets.

P-859
REDUCTION OF HLA CLASS I EXPRESSION ON PLATELETS BY ACID TREATMENT AND EFFECTS ON PLATELET STORAGE

M Mirlashari[1], B Landmark[1], A Vetlesen[1] and G Hetland[2]

[1]Immunology and Transfusion Medicine, Oslo University Hospital [2]Immunology and Transfusion Medicine, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Background: Antibodies to foreign HLA class I molecules can form in patients exposed to allogeneic cells, for example during blood transfusion. In addition, around 30% of pregnant women have HLA antibodies in their plasma. During platelet transfusions, these anti-HLA class I antibodies can bind to transfused platelets and mediate their destruction, and thus lead to platelet refractoriness. Such patients need to be provided HLA-matched platelets, which require expensive typing of donors and time-consuming cross-matching. An alternative is to deplete platelets of HLA class I using a brief incubation in citric acid on ice at low pH, "Meinke, Transfusion, 2016". This treatment results in a reduction in HLA class I expression on the platelet membrane, and loss of reactivity to HLA class I-specific antibodies.

Aims: The present study was carried out to investigate whether the HLA class I expression reduction by acid treatment, might affect platelet storage.

Methods: Platelets (PLTs) from concentrates (5× pooled buffy coats) were pelleted 24 h after processing (1500 g, 10 min), cooled on ice, and resuspended at $1–1.5×10^9$ PLTs/ml in ice-cold citric acid buffer (equal volumes of 263 mmol/L citric acid and 123 mmol/L Na_2HPO4, resulting in pH 2.9 to 3.0). After 5 min, the acid was neutralized by dilution in excess volume (20-fold) platelet additive solution (SSP1, Maco-Pharma). The PLTs were centrifuged again, diluted acid was removed and PLTs were resuspended in their original supernatant (SSP1 + 30% plasma). PLTs were counted on ABX Pentra XL80, (Horiba Medical). Surface expression of HLA class I,β-microglobulin and HPA1a was analyzed on a Gallios flowcytometer (Beckman Coulter) using mouse

anti- HLA- A, B, C, anti-β-microglobulin (both Biolegend) and anti-CD61 (clone SZ21, Immunotech), "Killie, Transfusion and Apheresis Science, 2004". Spontaneous activation and residual activation potential was assessed on day 1, 2 and 5 after acid treatment, using anti-CD62P and anti-CD63 (BD Biosciences) before and after thrombin receptor activating peptide (TRAP)-stimulation.

Results: HLA class I surface and β-microglobulin expression was reduced 60–70% in acid- treated PLTs comparing to untreated ones from day 1 through day 5. Acid treatment did not induce significant change in the expression of HPA1a. Analysis of residual PLT activation potential (CD62P and CD63 expression) after TRAP stimulation showed no significant difference between acid-treated PLTs and controls run in parallel for 1 and 2 days after acid treatment, but the residual PLT activation potential was significantly decreased in acid-treated PLTs on day 5 compared to controls.

Summary/Conclusions: Our data suggest that the acid treatment induced reduction in HLA class I expression on PLTs without changing their residual activation potential, for at least 2 days of subsequent routine PLT storage.

P-860

COMPARATIVE EVALUATION OF DIFFERENT METHODS FOR THE DETECTION OF HLA ALLOANTIBODY

H Tang[1], F Chu[1] and L Chang[1,2]
[1]Department of Clinical Pathology, Far Eastern Memorial Hospital, New Taipei
[2]Asia-Med Medical Reference laboratory, Taipei, Taiwan, China

Background: Donor specific HLA Antibodies play an important role in allotransplant rejection and allograft loss. The sensitization status of HLA dramatically influences the waiting time of organ transplantation. Therefore, precise identification of anti-HLA antibodies is essential in current HLA laboratory practice for transplantation. For the detection of HLA antibodies, solid-phase tests using purified HLA antigens are increasingly used.

Aims: This study aimed to investigate the performance of different methods for the detection of %PRA and identification of antibody specificities.

Methods: A total of 15 sera were collected, including 5 sera from multiparous Taiwanese female blood donors who had developed HLA antibodies during pregnancy. All sera were first screened for the detection of HLA antibodies by One Lambda ELISA, Flow cytometry (FC), and LifeScreen Deluxe Kit (Immucor). FC, LifeCodes HLA Class I/II ID kits, and One Lambda ELISA kits were used to determine the PRA values. Antibody identification was performed utilizing LABScreen Single Antigen HLA Class I/II (One Lambda), One Lambda ELISA, and LifeCodes HLA Class I/II ID kits (Immucor).

Results: Both HLA class I and class II antibody screening test showed 100% concordance in 10 negative specimens and 5 positive specimens between FC and Luminex methods. ELISA method showed 86.7% concordance compared with the other two methods in the screening of HLA class I antibody. For the detection of %PRA, mean value of %PRA was 32% (25% to 42%) and 81% (61% to 91%) for class I positive and class II positive samples utilizing three methods. Luminex method exhibited highest sensitivity (a mean of 36% and 83% in class 1 and 2) than ELISA (a mean of 32% and 80%) and FC (a mean of 28% and 82%) method in detection of both class I and class II %PRA. There was 100% consensus on the assignment of DR10 and DR53 for each sample detected by three different methods. In terms of discordant results, DR1 was only detected by Immucor PRA/ID and ELISA method. Except for ELISA method, both Luminex Immucor PRA/ID and One Lambda single antigen had identified DQ8. Besides, DR7 and DR9 were only detected by One Lambda single antigen and ELISA method.

Summary/Conclusions: Immucor and One Lambda assays have a similar ability to detect anti-HLA antibodies. Although the correlation between the assays was present, some significant difference of detection for specific antibodies existed, which may be caused by test interference and/or loss of native epitopes. Further investigation is needed to clarify the possible reason for the phenomena.

P-861

THE FREQUENCY OF HLA ALLOIMMUNIZATION IN PAROUS FEMALE BLOOD DONORS AND ITS IMPLICATIONS IN BLOOD SAFETY

P Arcot Jayachandran[1], R Sharma[2] and H Dhawan[2]
[1]Transfusion Medicine [2]PGIMER – Chandigarh, Chandigarh, India

Background: Various studies in the West has implicated that plasma causing TRALI are from females who become alloimmunized during pregnancy and the frequency

of sensitization to HLA was found to correlate with their parity score. No studies on prevalence of anti-HLA antibodies in parous female blood donors in India have been done till date. Hence a cross sectional study on the frequency of HLA alloimmunization in parous female blood donors was done.

Aims: To study the frequency of HLA alloimmunization in parous female blood donors. This shall help us to decide, if we should also adopt "male only plasma" strategy to decrease the occurrence of TRALI by selectively diverting female donor plasma for manufacturing plasma derivatives.

Methods: A total of 192 consenting voluntary blood donors from blood donation camps were enrolled in the study. Test group consisted of 96 parous female donors. The control group consisted of 48 nulliparous female donors and 48 male donors. HLA alloimmunization was tested by LIFECODES Life Screen Deluxe (LMX) screening assay to detect IgG antibodies to HLA Class I and Class II molecules of human origin. An MFI of more than 2000 was considered as a positive reaction, as the Luminex bead assay has a high sensitivity and can give an overestimate of the HLA antibodies in otherwise healthy population.

Results: Sixty-three out of 192 donors (32.8%) tested positive for Anti HLA antibodies. Twenty- three donors in the control group (23.9%) and 40 donors in the test group (41.6%) tested positive for Anti HLA antibodies (P−0.002). The rate of alloimmunization was 1.7 times higher in the test as compared to the control group of donors. On gender based comparison, 9 male donors (18.7%) and 54 female donors (37.5%) tested positive for HLA antibodies. HLA alloimmunization was significantly higher in female donors as compared to male donors (P-002). Although the frequency of HLA alloimmunization was higher in nulliparous female donors (29.1%) than male donors (16.6%), the difference was not significant. Based on increase in parity score, the frequency of HLA alloimmunization was found to be significantly correlated (P-0.002). On comparing the frequency of HLA alloimmunization based on the duration since the last pregnancy, the frequency of alloimmunization was higher in parity group of greater than or equal to 3 than a parity score of less than 3, but was not statistically significant. Higher frequency of HLA alloimmunization was observed in female donors with history of transfusion and bad obstetric history as compared to females with no history of transfusion and no bad obstetric history respectively, but the difference was not significant.

Summary/Conclusions: Hence the present study substantiates that plasma from parous female donors has a higher chance of containing Anti HLA antibodies. Hence in order to prevent transfusion related adverse events due to HLA antibodies, it is better to use plasma from these donors for fractionation rather than for clinical use.

P-862

HLA–A, –B, –C, –DRB1 AND –DQB1 ALLELE AND HAPLOTYPE FREQUENCIES OF 3580 VOLUNTEERS FROM THE ZHEJIANG PROVINCE, CHINA

N Chen[1,2], Z Han[1,2], W Wang[1,2], W Zhang[1,2], F Zhu[1,2] and W Hu[1,2]
[1]Key Laboratory of Blood Safety Research of Zhejiang Province [2]Blood Center of Zhejiang Province, Hangzhou, China

Background: The human leucocyte antigen (HLA) matching is critical for the success of hematopoietic stem cell transplantation (HSCT). HLA allele and haplotype frequencies are important especially in unrelated HSCT. It is known the distribution of HLA allele and haplotype is varied among different ethnic populations. Although the data for HLA allele and haplotype was reported in some population, the data for HLA-A, -B, -C, -DRB1 and -DQB1 loci with high resolution level in the Zhejiang Han population is limited.

Aims: To analyze HLA Allele and Haplotype Frequencies based on 3580 Volunteers from the Zhejiang Branch of China Bone Marrow Donor registry Program.

Methods: HLA-A, -B, -C, -DRB1 and -DQB1 loci were typed with SeCore sequencing commercial kits at high resolution level by polymerase chain reaction sequencing-based typing. The nucleotide sequences for exon 2–4 of HLA-A, -B, -C, exon 2 of HLA-DRB1, and exon 2–3 of HLA-DQB1 were amplified using locus specific primers. The sequencing reactions were processed with an ABI 3730 DNA Analyzer and the genotype of HLA loci for the sample was assigned by HLA SBT uTYPE software. The allele frequencies and the deviations from the Hardy-Weinberg equilibrium (HWE) were determined by Arlequin software. The haplotype frequencies and linkage disequilibrium (LD) between allele pairs were also analyzed based on the expectation-maximization (EM) algorithm with the Arlequin software. The level of significance for LD was set at $P < 0.05$.

Results: The frequencies of the HLA-A,-B,-C, -DRB1, and -DQB1 alleles and haplotypes were estimated among 3580 volunteer bone marrow donors of Zhejiang Han population in China. The total numbers of HLA-A, -B,-C, -DRB1 and -DQB1 alleles were 51, 97, 45, 53 and 27, respectively. Of these, the top three frequent alleles in

HLA-A, -B, -C, -DRB1 and -DQB1 allele, respectively, were A*11:01(23.90%), A*24:02(17.20%), A*02:01(11.30%), C*07:02 (18.23%), C*01:02:01G(18.17%), C*03:04(9.90%), B*40:01(14.09%), B*46:01(12.26%), B*58:01 (8.51%), DRB1*09:01 (17.45%), DRB1*12:02(10.54%) and DRB1*15:01(9.70%), DQB1*03:01 (22.72%), DQB1*03:03(18.20%) and DQB1*06:01(10.90%). A total of 135 HLA-A-C-B-DRB1-DQB1 haplotypes with a frequency of >0.1% were presented and the most common haplotypes with frequencies greater than 3% were A*02:07-C*01:02:01G-B*46:01-DRB1*09:01-DQB1*03:03(4.17%), A*33:03-C*03:02-B*58:01-DRB1*03:01-DQB1*02:01 (4.15%), A*30:01-C*06:02-B*13:02-DRB1*07:01-DQB1*02:02(3.17%). These three haplotypes overlapped with the three most frequent HLA-A-B-DRB1 and HLA-A-C-B-DRB1 haplotypes with frequencies greater than 3%. The most frequent HLA-A-C-B haplotypes were A*02:07-C*01:02:01G-B*46:01(7.56%) followed by A*33:03-C*03:02-B*58:01 (7.04%), A*11:01-C*07:02-B*40:01(4.33%), A*30:01-C*06:02-B*13:02(3.85%), and A*11:01-C*08:01:01G-B*15:02 (2.67%). The likelihood ratios test for the LD of HLA-A-C, -C-B and -DRB1-DQB1 revealed that the majority of the pairwise associations were statistically significant. The three most frequent HLA-A-C haplotypes were A*02:07-C*01:02:01G(7.99%), A*11:01-C*07:02(7.60%), A*33:03-C*03:02(7.12%). The most frequent HLA-C-B haplotypes were C*01:02:01G-B*46:01(11.54%) followed by C*03:02-B*58:01(8.35%) and C*07:02-B*40:01(8.25%). The three most frequent HLA-DRB1-DQB1 haplotypes were DRB1*09:01-DQB1*03:03(17.17%), DRB1*12:02-DQB1*03:01 (10.15%), DRB1*08:03-DQB1*06:01(7.67%).

Summary/Conclusions: The data presented in this study will be useful for selecting unrelated HLA-matched donor, planning donor registry and for anthropology studies.

P-863

Abstract has been withdrawn

P-864

DISTRIBUTION OF THE HLA SPECIFICITY IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

I Ramilyeva[1], Z Burkitbayev[1], S Abdrakhmanova[1], A Turganbekova[1] and E Zhiburt[2]

[1]Scientific-Production Center of Transfusiology, The Ministry of Healthcare of the Republic of Kazakhstan, Astana, Kazakhstan [2]National Medical and Surgical Center Named after N.I. Pirogov, Moscow, Russian Federation

Background: Acute lymphoblastic leukemia (hereinafter referred to as the ALL) is the most common tumor of hematopoietic tissue in children, accounting for 30% of malignant tumors of childhood. In patients younger than 15 years the ALL is diagnosed in 75% of AL cases. Peak incidence of the ALL falls at the age of 3–4 years, then its frequency decreases [1,2]. The ALL has geographical variations, averaging 30–40 cases per million people a year. As a result of numerous studies, a significant number of evidence have been obtained of the relationship between a liability to a number of human diseases and antigens of the main histocompatibility system. Most often, association of the HLA and diseases appears in form of associations. The HLA antigens associated with diseases can be considered as susceptibility antigens to diseases or as markers of locus linked to true antigens determining a liability to diseases, which allows for early diagnosis of oncohematological diseases. Thus, it is important to study the HLA phenotype peculiarities in patients with acute lymphoblastic leukemia in Kazakhstan, to search for a link between the development of this pathology and the HLA system antigens.

Aims: to study the peculiarities of HLA antigens in patients with acute lymphoblastic leukosis in Kazakhstan.

Methods: We have studied the incidence of I-class and II-class HLA antigens in patients with the ALL living in Kazakhstan. A total of 3 882 people were examined: 3 621 healthy blood donors and 261 patients with the ALL diagnosis. Genomic DNA for typing of HLA antigens was isolated from peripheral blood leukocytes by a proteinase method using columns with a silica gel membrane. The studies were carried out using a set of PROTRANS DNA BOX reagents (Protrans, Germany). Typing of patients (HLA-A, B, C, DRB1, DQB1) and blood donors (HLA-A, B, C, DRB1, DQB1) was performed by polymerase chain reaction. Commercial sets of Protrans reagents - PROTRANS HLA-A*/B*/DRB1* Cyclerplate System, PROTRANS HLA-C* Cyclerplate System, PROTRANS HLA-DQB1* Cyclerplate System were used. The average age of donors (control group) was 41 year (range from 18 to 64 years). Mean age of patients (trial group) was 25 years (range from 2 to 62 years). Distribution by sex among patients was as follows: men 166 (63.6%), women 95 (36.3%). Male patients prevailed over female 2136 (59%) and 1485 (41%) respectively. The results were evaluated using descriptive statistics, nonparametric χ2-criterion, odds ratio (OR) and 95% confidence interval (CI 95%).

Results: The study of the HLA antigens distribution in patients with the ALL has let to assume the existence of associative links between the HLA-A*30 presence (OR=1.72, CI 1.12–2.64, P<0.05), B*44 (OR=1.62, CI 1.19–2.21, P<0.01), C*16 (OR=1.95, CI 1.14–3.34, p<0.05), DRB1*07 (OR=1.33, CI 1.01–1.74, p<0.05), *16 (OR=1.72, CI 1.02–2.89, p<0.05) and the pathologic behavior. Presumably, the resistance to this disease in persons with (OR=0.77, CI 0.6–0.99, p<0.05), C*02 (OR=0.44, CI 0.27–0.72, p<0.01), DQB1*06 (p<0.05) in the HLA-A*02 phenotype was established.

Summary/Conclusions: The data obtained can be used to develop immunogenetic criteria for predicting the ALL development and to study various diseases associated with the HLA antigens.

P-865

Abstract has been withdrawn

P-866

LEVEL OF SENSIBILIZATION BY LEUKOCYTIC ANTIBODIES OF PATIENTS WITH ACUTE LEUKOSIS

A Turganbekova, Z Burkitbayev, S Abdrakhmanova and I Ramilyeva

Scientific and Production Center for Transfusiology of the Ministry of Health of the Republic of Kazakhstan, Astana, Kazakhstan

Background: Providing immunological safety of blood transfusions remains an important problem of transfusiology. In its solution, the main sense belongs to measures aimed at preventing allosensitisation of recipients and precaution of posttransfusion reactions and complications.

Aims: To study the sensitization of patients receiving blood platelet transfusions in Kazakhstan.

Methods: In the Scientific and Production Center of Transfusiology of the city of Astana, 23 patients with hematological diseases receiving blood platelet transfusions were examined to establish the level of sensitization. Blood sampling was carried out three times: on the first day when the patient entered the department and twice at an interval of 2 weeks. Samples of patient serosity were examined for the presence of leukocytic, aimed at the antigens of the first class the HLA system. A ductal cytofluorometry method was used on the LABScan 3D analyzer (One Lambda, USA).

Results: Screening of serosity obtained before platelet transfusion showed the presence of leukocytic antibodies to class I of HLA in 14 (61%) patients, 9 (39%) of patients without leukocytic antibodies were detected. Antibody monitoring among 9 patients with negative status showed that in 7 patients antibodies were detected in serosity obtained 2 weeks after the beginning of blood transfusion therapy. In 2 patients, a positive result was obtained after 4 weeks. Two and four-week monitoring of antibodies among 14 patients, with a positive status, determined an increase in the level of sensitization.

Summary/Conclusions: The study of monitoring leukocytic antibody sensitization on HLA I class antigens, found that multiple platelet transfusions lead to an increase in the percentage of patients sensitizing. Given this, it is necessary to transfuse platelets with individual selection, taking into account the HLA antigens of donor cells and the patient.

Histocompatibility in Stem Cell Transplantation

P-867

ALLELIC AND HAPLOTYPIC DIVERSITY OF HLA-A, -B, AND -DRB1 GENE AT HIGH RESOLUTION IN THE NANNING HAN POPULATION

Y Pei, J Lin, H Huang, L Li, J Chen and H Li
Nanning Institute of Transfusion Medicine, Nanning, China

Background: HLA has been found to be critical for infections resistance, autoimmune disease susceptibility, tumour resistance and immune responses to the allograft after solid organ or haematopoietic stem cell transplantation (HSCT).

Aims: : we investigated the allele and haplotype frequencies of HLA-A, -B, and -DRB1 loci in the Nanning Han population who live in Guangxi province of China. No doubt, a better and accurate characterization of HLA genotypes will improve CMDP and benefits transplant recipient patients.

Methods: The HLA-A, -B, and -DRB1 2nd-field genotyping was performed with SeCore® Sequencing Kits (life technologies™, Brown Deer, WI, USA). The nucleotide sequences for exon 2–4 of HLA-A and HLA-B and exon 2 of HLA-DRB1 were amplified using locus specific primers according to the manufacturers' instructions.

Results: A total of 26 HLA-A, 56 HLA-B and 31 HLA-DRB1 alleles were identified in 1124 Nanning individuals of Han ethnic group by sequence-based typing method. Of these, the three most common alleles in HLA-A, -B, and -DRB1 loci, respectively, were A*11:01 (32.12%), A*02:07 (12.54%), A*24:02 (12.01%); B*46:01 (14.41%), B*15:02 (13.61%), B*40:01 (11.48%); DRB1*15:01 (14.15%), DRB1*16:02 (11.57%) and DRB1*12:02 (10.14%). Departure from Hardy-Weinberg expectation was observed for HLA- DRB1 in this population. A total of 173 A-B-DRB1 haplotypes with a frequency of >0.1% were presented and the five most common haplotypes were A*33:03-B*58:01-DRB1*03:01 (6.12%), A*11:01-B*15:02-DRB1*12:02 (3.39%), A*11:01-B*15:02-DRB1*15:01 (3.22%), A*02:07-B*46:01-DRB1*14:01 (3.21%) and A*02:07-B*46:01-DRB1*09:01 (2.48%).

Summary/Conclusions: The phylogenetic tree and the principal component analysis suggested that Nanning Han population had a relative close genetic relationship with Chinese Zhuang population and a relative distant genetic relationship with Northern Han Chinese. The information will be useful for anthropological studies, for HLA matching in transplantation and disease association studies in the Chinese population.

P-868

CLONING AND EXPRESSION OF KILLER CELL IG-LIKE RECEPTORS (KIR) GENE IN BACULOVIRUS EXPRESSION SYSTEM

Y He[1,2], S Tao[1,2], J He[1,2], F Zhu[1,2] and W Hu[1,2]
[1]Zhejiang Provincial Key Laboratory of Blood Safety Research [2]Institute of Transfusion Medicine, Blood Center of Zhejiang Province, Hangzhou, China

Background: Killer cell immunoglobulin receptor (KIR) belonging to the immunoglobulin superfamily, mainly expressed on the surface of NK cells and T cells, KIR can with HLA-I molecules on the surface of target cells, regulating NK cells and T cell activity by transferring activate or inhibit signal conduction. It has been reported that different KIR molecules have different binding characteristic to their ligands, which will lead to different effects of NK cells.

Aims: In order to construct the Baculovirus expression system of KIR and obtain the recombinant KIR protein, which used for analyzing the binding characteristic between KIR and its ligands.

Methods: The KIR2DL1*00302 and KIR2DL3*00101 cDNA fragments consisting of complete coding sequences were obtained by the RT-PCR with the specific primers (Forward primer: CTATAAATACGGATCCATGTCGCTCTTGGTCGTCAG; Reverse Primer: GGCCGCCCGGGAATTCTCAATGATGATGATGATGTGGGCAGGAGACAA CTTTGG). The double restriction enzyme sites (BamH I/EcoR I) were added at both ends of the primer, and the tail of 6×His was added before the stop codon. The cDNA fragments were ligated with pBacPAK8 vector and the recombinant plasmids were extracted for sequencing. For the constructed plasmids with correct sequences, the virus was produced by using BacPAK Baculovirus Expression System (Clontech

Code No. 631402). The monoclonal cell strain was selected and sf21 Cell was infected to express small amount of the target protein. The target expressed protein were detected by western blotting with His-Tag antibody.

Results: The Baculovirus expression vectors with two common KIR alleles (KIR2DL1*00302 and KIR2DL3*00101)were constructed and the recombinant protein was obtained in sf21 cell at day 5 after infection with high titer virus. The result of western blotting showed that the target protein was correct.

Summary/Conclusions: The Baculovirus expression system of KIR gene was successfully established and the proteins with two common KIR alleles were obtained in this study. The recombinant KIR protein could be used for researching on the interaction between KIR and its ligands, which would help to explain the modulate on NK cell. This work was sponsored by National Science Foundation of China (81401732), Zhejiang Provincial Program for the Cultivation of High-Level Innovative Health Talents, and the Science Research Foundation of Zhejiang Province (LY18H080002).

Histocompatibility in Organ Transplantation

P-869

Abstract has been withdrawn

P-870

EFFECTIVENESS OF PLASMAPHERESIS FOR REDUCING DSA IN ORGAN TRANSPLANTATION

J Nakamura[1], M Matsuhashi[2], M Kawabata[1], Y Nagura[1], S Sone[1], J Kaneko[3], N Akamatsu[3], K Hasegawa[3], O Kinoshita[4], K Nawata[5], M Ono[5], T Ikeda[1], N Tsuno[6] and H Okazaki[1]
[1]Department of Transfusion Medicine, The University of Tokyo, Tokyo [2]Department of Health Sciences, Saitama Prefectural University, Saitama [3]Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, University of Tokyo [4]Department of Cardiac Surgery, Graduate School of Medicine, University of Tokyo [5]Department of Cardiac Surgery, Graduate School of Medicine, University of Tokyo [6]Laboratory Department, Japanese Red Cross Kanto-Koshinetsu Block Blood Center, Tokyo, Japan

Background: Donor-specific antibody (DSA), detected pre- or post-transplantation, is an important predictive factor of the humoral (antibody-mediated) rejection reaction in solid organ transplantation, and desensitization treatments, such as plasmapheresis, have been applied. However, different results have been reported on the effectiveness of the antibody-removal effect of plasmapheresis, and its clinical efficacy remains to be elucidated.

Aims: In the present study, we aimed to investigate on the effectiveness of plasmapheresis in reducing DSA titers, and for this purpose, we evaluated the antibody titers pre- and post-plasmapheresis in patients receiving organ transplant.

Methods: Among the patients who were admitted to our university hospital in the period of March 2008 to June 2016 with the intent to receive liver or heart transplant, we analyzed 4 DSA-positive patients who received plasmapheresis for the removal of DSA. LabScreen Single Antigen (One Lambda) was used for the measurement of DSA. Antibody titers were expressed as the mean fluorescence intensity (MFI) and compared.

Results: One patient received plasmapheresis pre-transplant, but since the reduction of the antibody titer was not achieved, the transplant was canceled. Among the 3 cases who received organ transplantation, one case of liver transplant received plasmapheresis in the post-operative day (POD) 3, and the antibody titers decreased by 97.9%, 99.8%, 96.4%, 99.6% and 95.4%, respectively, for anti-A2, -A24, -B35, -B54, and -DR4 antibodies. The cases 2 and 3 were heart transplant recipients, who started MMF administration pre-transplant, and plasmapheresis was started intra-operatively. The DSA (IgG) titers in case 2 decreased by 75.5%, 86.8%, 40.5%, and 73.8%, respectively, for anti-A24, -A26, -B56, and –B61 antibodies, and in case 3, 83.6%, 31.6%, and 82.6%, respectively, for anti-A24, -B13, and –DR7 antibodies. Relatively high titers of antibodies against HLA-B13, -B44, -DR4, and DQ6, which are high frequency HLA types in Japanese, were identified, but neither case developed clinically evident episodes of antibody-mediated rejection reaction. In addition, IgM antibodies were tested but not detected at any time point in cases 1 and 3.

Summary/Conclusions: The antibody titer reducing effect of plasmapheresis varied according to the cases, but most of the DSA are presently at undetectable levels. On the other hand, most of the non-DSA antibodies still persist at high titers, especially those against the high frequency antigens in Japanese. This discrepancy between DSA and non-DSA suggests that among the non-DSA there may be some that are not true antibodies. Also, it is known that in ABO-incompatible kidney transplant, plasmapheresis removes IgM type antibodies more efficiently than IgG type ones. However, in our cases, IgM antibodies were almost not detected, so we could not confirm if plasmapheresis is also superior in removing anti-HLA antibodies of IgM than IgG type. The differences in the removal rate according to the antibody specificity, the possible mechanisms causing these differences, and the other desensitization treatments will be discussed.

P-871

HUMAN LEUCOCYTE ANTIGEN ANTIBODY DETECTION BY SINGLE ANTIGEN BEAD ASSAY IN KIDNEY TRANSPLANT CANDIDATES – WHICH IS THE MOST COMMON HLA-ANTIBODY FOUND?

SM Teixeira[1], I Alonso[2], S Tafulo[3], M Carvalho[1], C Monteiro[1], L Gonçalves[1], C Mendes[3], F Freitas[3], M Ramalho[1], I Machado[1] and C Koch[1]

[1]Department of Transfusion Medicine and Blood Bank, Centro Hospitalar São João, EPE [2]Department of Transfusion Medicine and Blood Bank, Centro Hospitalar Vila Nova de Gaia/Espinho [3]Histocompatability Center of the North, Portuguese Institute of Blood and Transplantation, Porto, Portugal

Background: Pre-formed HLA - antibodies against graft antigens may lead to acute or chronic transplant rejection. Therefore is current practice to study the receptor for potential antibodies that may lead to organ rejection. xMAP technology is the most sensitive and plays a major role in the study of kidney transplant (KT) candidates.
Aims: Our aim was to evaluate the most frequent HLA- antibodies found in kidney transplant candidates, registered in 2017, in the Transplantation Center responsible for the northern region of Portugal.
Methods: We studied the results of KT candidates samples subjected to Luminex Single Antigen (LSA) beads I and II, through 2017, in order to calculate the most frequent antibodies found. Patients with previous KT were excluded and the test was considered positive if the standard medium fluorescent intensity (MFI) was >1000. We also evaluated if patients had previous transfusion or pregnancy history.
Results: In a total of 340 patients, 191 (56, 2%) were male and the mean age was 52, 2 years (SD±11, 8). Only 3 female patients had a history of pregnancy and 101 patients had a history of transfusion. A total of 353 LSA I and 355 LSA II assays were analyzed. In LSA I the most frequent antibodies found were B76 (16.4%), B57 (10.2%), A66 (10.2%), Cw17 (9.9%) and B82 (9.9%) and in LSA II were DR16 (11.6%), DR4 (12.1%), DQ7 (12.4%), DP1 (12.1%), DQ8 (11.6%).
Summary/Conclusions: The HLA antibodies frequencies found do not represent HLA antigen frequencies in the Portuguese population, illustrating that HLA antibodies assignment based only on SAB assay with 1000 MFI cut-off can be misleading, emphasizing the technical limitations associated with this methodology. Even though it has an important number of false positives, testing HLA antibodies remains essential in transplantation risk assessment as it allows to perform virtual cross-matching. The improvement of this technology seems of the utmost importance, due to the key role in these patients evaluation.

P-872

PREVALENCE OF HLA ANTIGENS AMONG PATIENTS AWAITING RENAL TRANSPLANT COMPARED TO RENAL DONORS, TESTED AT NATIONAL BLOOD CENTRE OF SRI LANKA

GS Manchanayake

Blood Bank, National Hospital of Sri Lanka, Colombo, Sri Lanka

Background: End stage renal disease (ESRD) has become a major public health problem worldwide and it is a chronic debilitating disease that requires renal transplantation as a permanent therapy. Chronic kidney disease of unknown aetiology is a major health problem in the North Central Province of Sri Lanka. Many studies have been performed on various populations to assess the association between HLA alleles/ haplotypes with the development of ESRD.

Aims: To determine the association of HLA antigens with the development of End stage renal failure among patients awaiting renal transplantation tested at National Blood Centre, Sri Lanka.
Methods: This descriptive study was carried out at the histocompatibility laboratory of National Blood Centre, the only ISO approved HLA laboratory of the country, for a period of one year from 1st of June 2015 to 31st of May 2016. At the time of study, HLA typing was performed by serological method (complement dependent cytotoxicity test) using commercially available typing plates. HLA typing results were collected from Sri Lankan patients with renal failure awaiting transplant. HLA typing data of kidney donors with Sri Lankan origin were taken as the healthy group. Both HLA class I and class II typing results were considered for the study. HLA antigen frequencies of HLA-A, -B, -C, -DR and -DQ loci were assessed in both patient and donor groups relation to the ethnicity (Sinhalese (S), Tamils (T) and Moors (M)).
Results: A total data of 978 was collected from the patients with ESRD (S- 75.77%, T- 10.63%, M-13.29%) and 1172 was from renal donors (S- 73.72%, T- 14.68%, M-11.77%). The five most frequent antigens of HLA-A locus were HLA-A33, -A24, -A2, -A11 and -A1 in both patient and donor categories in all three races. In both groups, -A33 in Sinhalese and -A24 in Moors were the commonest. In Tamils, -A24 among renal patients and -A1 and -A2 (with equal frequencies) among donors were the commonest. The most frequently occurring HLA-B antigens of both patients and donors were HLA-B57, -B51, -B35, -B7 and -B44. HLA-B57 and -B51 were having the highest frequencies in donors of all three races and patients with Sinhala and Tamil origin. In patients of Moors origin, -B51 and -B35 were the commonest. HLA-C7, -C6 in HLA-C locus, HLA-DR15, -DR7 in -DR locus and DQ5, DQ6 in HLA-DQ locus were the commonest in both categories in all three races. The most frequent HLA antigen combinations detected in renal patients were HLA-A33,-B57,-DR7 and HLA-A33,-B44,-DR7. HLA-A33,-B44,-DR7 and HLA-A1,-B57,-DR7 combinations were the commonest among renal donors. HLA-A1,-B57,-DR7 combination was commonly detected in all three races, both among patients and donors. HLA-A26 in Sinhalese and HLA-B7 in Tamils were associated positively with ESRD. HLA-B57 and HLA-C3 were negatively associated with the development of ESRD in Moors.
Summary/Conclusions: There is a significant positive as well as negative associations between the occurrences of HLA antigens with the development of ESRD. Once molecular HLA typing technologies are available, a similar well designed study should be conducted on large study population.

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CHARACTERISTICS OF HLA AND ANTI-HLA ANTIBODIES OF PAIRED KIDNEY DONORS AND RECIPIENTS FROM 2011 TO 2017 AT CHO RAY HOSPITAL, VIET NAM

MN Le Pham[1], H Thu Thi Nguyen[2], B Van Tran[1], O Hoang Le[1] and S Truong Nguyen[1]

[1]Cho Ray Blood Transfusion Centre, Cho Ray Hospital [2]School of Biotechnology, International University, Ho Chi Minh City, Vietnam

Background: Today, renal transplantation has widely been considered as the best treatment for patients with end-stage renal disease (ESRD). It can significantly improve survival and life quality of those who have successful kidney grafts. In Vietnam, that most kidney donation is from related donors rather than unrelated ones results in numerous patients in the waiting list. Therefore, kidney donation from unrelated donors including deceased and cardiac-dead is the best solution for the high demand of transplantation. However, lack of understanding on the characteristics of HLA and anti-HLA antibodies of kidney donors and recipients in Vietnam causes lots of difficulties in finding matched donors in due time.
Aims: In this study, HLA and anti-HLA antibodies profiles of 425 pairs of kidney donors and recipients during 2011 and 2017 were investigated as pre-kidney transplantation screening at Cho Ray Blood Transfusion Center (Cho Ray BTC), Cho Ray Hospital, Ho Chi Minh City, Vietnam.
Methods: 425 pairs of kidney donors and recipients including 498 males and 352 females have the average age of donors and recipients ranging from 31 to 40 and 51 to 60 years old, respectively. The donors and recipients were tested for HLA-A, B, DRB1, DQA1, and DQB1 typing using Labtype SSO-PCR with Luminex technology. Anti-HLA antibodies of recipients were tested using Onelambda Labscreen Panel Reactive Antibody (PRA) on class I and class II with Luminex LABscan 100 analyzer system. The cross-matching tests between donors and recipients were performed using Complement Dependent Cytotoxicity (CDC) assay.
Results: Among 425 pairs, there were 295 consanguinity pairs, all with 100% negative results in cross-matching tests and 130 un-consanguinity pairs in which 3.85% were positive in cross-matching tests. The rate of 3/6 allele mismatch pairs was of

majority (30.59%). The most common HLA-A, B, DRB1, DQA1 and DQB1 types were HLA-A*02 (23.24%), A*11 (28.94%), A*24 (18.65%), B*07 (9.71%), B*15 (24.18%), B*46 (9.53%), DRB1*04 (9.94%), DRB1*12 (32.24%), DRB1*15 (10.41%), DQA1*01 (31.71%), DQA1*03 (18.59%), DQA1*05 (7.18%), DQB1*03 (54.59%), DQB1*05 (22.41%) and DQB1*06 (10.34%). There were 381 recipients (81.63%) recorded negative with anti-HLA antibodies and 79 positive (18.37%) with anti-HLA antibodies. The most common anti-HLA antibodies found were anti-HLA-A*02 (2.11%), A*33 (2.11%), B*78 (2.51%), B*81 (2.91%) and DRB1*09 (2.11%).

Summary/Conclusions: It is the first study in Vietnam providing HLA and anti-HLA antibodies profiles of paired kidney donors and recipients. The obtained data are particularly helpful not only in finding out the matched unrelated donors for future transplantation but also generating very first Vietnamese database on HLA and anti-HLA antibodies which can be helpful in other immunological and epidemiological research and application.

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HLA GENOTYPING USING THE NEXT-GENERATION SEQUENCING IN TRANSPLANTATION IN POLISH POPULATION

A Bukowska, A Bogacz, M Bukowska, K Olbromski and H Skalisz
Blood Center in Poznan, Poznan, Poland

Background: The immunogenetic compatibility between the donor and the recipient is an important issue in the transplantation, which is conditioned by the amino acid sequence in HLA (human leukocyte antigen) molecules. This is reflected in the donor's and recipient's genotypes at the DNA level. The incompatibility of HLA or amino acid sequences within peptides presented in the context of HLA molecules promotes the occurrence of serious immune and infectious complications after transplantation and worsens the survival of recipients. In order to detect HLA antigens, genetic methods such as a polymerase chain reaction (PCR) for DNA analysis are used. The use of modern molecular biology techniques for HLA typing in recipients and donors resulted in a significant improvement of the results in allogeneic transplantation. New generation technologies allowed to provide the highest possible resolution and to obtain unambiguous results of HLA genotyping due to the high degree of complexity of the HLA system.

Aims: The aim of the study was to determine the frequency of polymorphic variants of HLA loci (HLA-A, -B, -C, DRB1/3/4/5, DQA1, DQB1, DPA1, DPB1) in patients based on the high resolution using the next-generation sequencing method using the MiSeq system (Illumina).

Methods: The study included a group of 120 patients of both sexes, aged between 18–60 years. Genetic studies which determined the prevalence of polymorphic variants of HLA loci were made on the basis of high resolution using the next-generation sequencing method. DNA was isolated from peripheral blood using a commercial column kit. The preparation of the sequencing library was carried out using the TruSight HLA Sequencing Panel test (Illumina). The analysis of the HLA typing results was performed using the Conexio software, while statistical analysis was performed using the SPSS17.0 PL program.

Results: The analysis of high resolution HLA typing using next-generation sequencing (NGS) showed that the most common HLA class I variants among the studied group of patients were: HLA-A* 02:01:01 (n=52), HLA-B* 08:01:01 (n=31) i HLA-C* 07:01:01 (n=41). In case of the HLA genotyping for class II, the most common variants were: HLA-DRB1*07:01:01 (n=34), HLA–DRB3*01:01:02 (n=56), HLA-DRB4* 01:03:01 (n=59), HLA-DRB5*01:01:01 (n=40), HLA-DQA1*05:05:01 (n=40), HLA-DQB1* 03:01:01 (n=46), HLA-DPA1*01:03:01 (n=208), HLA-DPB1*04:01:01 (n=108).

Summary/Conclusions: 1. Preliminary results confirm the legitimacy of using the DNA sequencing method to obtain unambiguous genotyping results in the HLA system. 2. By using next-generation sequencing and widening the HLA typing panel with additional loci, it is suggested that it will be possible to extend the survival time for patients after the transplantation.

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CORRELATION BETWEEN THE POSITIVE SINGLE ANTIGEN ASSAY AND THE NEGATIVE CDC CROSSMATCH AS A PREDICTIVE VALUE IN THE REJECTION OF THE RENAL GRAFT OF THE CMN SXXI IMSS MEXICO FROM 2010 TO 2016

J Martínez Álvarez[1], G Rivera Aguilar[1], M Arrazola García[1], R Fuentes Landa[1], V Juárez Barreto[2] and G Benitez Arvizu[3]
[1]HLA Laboratory, IMSS [2]Blood Bank, HIM [3]Blood Bank, IMSS, CDMX, Mexico

Background: Renal transplantation has been shown to be the best treatment for the final stages of chronic kidney disease, since it allows the restoration of renal function as a whole. One of the causes of loss of grafts of immunological origin are acute rejections, which may be of cellular and humoral origin. Despite advances in the understanding of the mechanisms responsible for cellular immunity in renal rejection and the development of new immunosuppressive drugs, rejection mediated by humoral immunity (antibodies) appears to be a danger for graft survival in the short and long term. Performing transplants in highly sensitized patients results in a recognized higher risk of rejection, graft loss and lower long-term graft survival, however, this risk is associated with the presence of Donor-Specific HLA Antibodies (DSA) rather than the degree of sensitization per se. Desensitization protocols can be effective to change a crossmatch from positive to negative and enable a transplant in highly sensitized patients, however to achieve the success of the transplant it is a priority to know the magnitude of the alloimmune response, information that will help to make therapeutic decisions. Survival of the graft in this situation is probable in the vast majority of cases, however, long-term survival is still uncertain.

Aims: Establish the relationship between the positive Single Antigen assay (SA) with or without the presence of DSA and a negative Complement-dependent cytotoxicity (CDC) Crossmatch in the rejection of the renal graft

Methods: For this study, records of patients who presented positive single antigen assay were used with or without the presence of a DSA against some antigen C-I and/or C-II of the HLA system and a negative CDC Crossmatch

Results: The total of patients included in the study were 337, 121 (35.9%) presented DSA, and only 86 (25.5%) presented rejection of the renal graft. Of the total of 86 rejections, 39 (45.3%) patients presented humoral type rejection, 12 (13.9%) cellular rejection and 6 (6.9%) presented both types, 28 (32.5%) patients had rejection due to other causes (thrombosis of the graft, hyperacute rejection due to anastomosis, lymphocele, and opportunistic infections such as cytomegalovirus, polyomavirus, and pneumonia), and only one patient showed humoral rejection in conjunction with a viral infection. All episodes of rejection were determined by analyzing biopsies, according to Banff's classification (2013).

Summary/Conclusions: At the end of the present work, we can conclude that the CDC crossmatch and the single antigen assay are mutually complementary for the decision of the transplant. The CDC crossmatch is decisive when the result is positive since it contraindicates the transplant, and as it could be demonstrated in this work, the single antigen assay provides a very useful tool for the decision of the transplant, the treatment and the course of the success of the graft. The result measured in Mean Fluorescence Intensity of the presence of DSA qualifies the prognosis and success of the transplant, since it indicates the antibody titer, which is translated into the immunological status of the patient. The ideal scenario for the transplant protocol is a negative CDC Crossmatch and a value of 0% of Donor-Specific HLA Antibodies, however, we know that in these types of patients it is not possible to avoid all alloimmunization events to which they are exposed (pregnancies, transfusions and previous transplants).