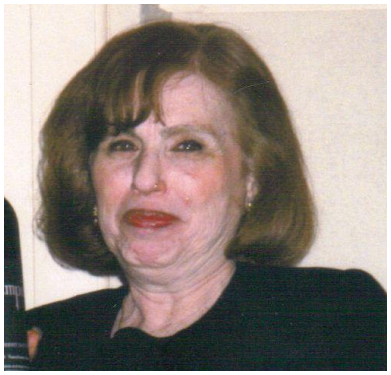
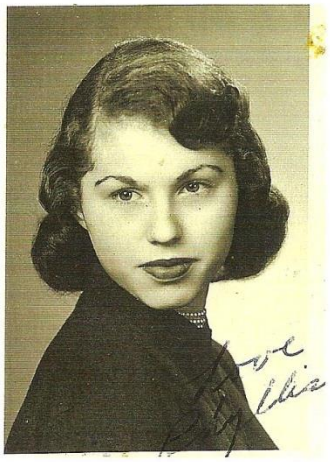
ILLINOIS ASSOCIATION OF BLOOD BANKS

The Phyllis Unger
Annual Case Studies Meeting

Thursday, November 4, 2021





This case studies meeting is dedicated to Phyllis Unger in memory of all the wonderful case studies she presented to students, technicians, technologists, residents, fellows and physicians. Phyllis was a dedicated blood banker who spent much of her time teaching and educating whether she was at Michael Reese, University of Illinois or LifeSource. She was always willing to answer questions or test a sample if you sent it to her. She inspired many blood bankers and gave them the desire to look further into a problem. Phyllis was the first Medical Technologist to be President of the ILABB. Prior to this only a physician could hold the office. She wrote many papers and contributed to a few books including "Blood Group System: MN and Gerbich." She had many things outside of blood banking that she enjoyed as well such as travel, music and bridge. Even these things helped give her blood banking perspective. She was known for never saying anything bad about anyone and always finding the best in them. We hope that this annual meeting will serve as a lasting memory to the knowledge she shared with all who came in contact with her over the years. Thank you Phyllis.

ILABB Case Studies 2021

Agenda

Presentations will begin promptly at 6:15pm via Zoom.

1. Title: Group O patient eluting anti-A following emergency use of group A liquid plasma
2. Title: Care Everywhere Conundrum
3. Title: Comparison of Adsorption Techniques: An Adjusted Process to Improve Efficiency and Sensitivity
4. Title: Identification of Anti-Yta in a Recently Transfused Patient with Multiple Alloantibodies
5. Title: Transmission of Cache Valley Virus through Red Blood Cell Exchange in Kidney Transplant Recipient with Sickle Cell Disease
6. Title: When Hemagglutination is Insufficient: The Use of Molecular Techniques in the Resolution of Ambiguous Rhesus D Results
7. Title: Passenger Lymphocyte Syndrome in a Liver-Kidney Double Transplant
8. Title: How much RHIG do you want to give that patient?
9. Title: What's Up with "U"? Transfusion Support for an African-American (AA) Patient with multiple co-morbidities and multiple red cell alloantibodies including alloanti-U
10. Title: Baron von Münchhausen's Visit to the Blood Bank and Apheresis Service

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Title: Group O patient eluting anti-A following emergency use of group A liquid plasma

Authors: Timothy Carll, MD, Geoffrey Wool. MD, PhD, University of Chicago Hospital

Background: Liquid plasma products are becoming recognized for their utility in emergency transfusion settings because of their hemostatic properties comparable to thawed plasma products and shorter preparation times. Liquid plasma is never frozen and is stored at refrigerator temperatures; storage life of 5 days after the expiration of the whole blood mother product. These units retain trace cellular content and should be uniformly irradiated. Hemolysis resulting from incompatible transfusion of liquid plasma has not been described.

Case Report: A woman in her 50s was admitted for a femoral fracture after motor vehicle collision. She had been transfused two units of group O-negative packed red cells at a referring hospital. At our institution, she underwent operative repair and was transfused two units of group O-negative packed red cells and five units of group A liquid plasma under emergency release protocol, as well as three units of type-specific group O-positive packed red cells. All subsequent blood typing at our hospital showed the patient to be group O-positive. Back typing was consistently 3+ to 4+ with A1 cells and B cells.

On hospital day 8, antibody screen (gel, Ortho) was positive and anti-E reactivity was identified. Anti-IgG DAT (gel, Ortho) was 2+. Elution was performed (Gamma ELU-kit II, Immucor), and the eluate showed anti-E reactivity. Segments from the five red cell units transfused locally were tested, and one was positive for the E antigen. The eluate also reacted 3+ against A1 reagent cells (Ortho) and 2+ against A2 reagent cells (Albasyte). No reactivity was observed to B reagent cells. An aliquot of a group A1 single-donor unit which was negative for E antigen showed 2+ reactivity with the eluate.

Investigation: To evaluate the extent of red cell contamination in our liquid plasma supply, five such units were randomly selected, well mixed, and were sampled with an automated hematology analyzer (Sysmex XN-350). The average red cell count was found to be 1.4 k/µL (SD 0.55 k/µL). Assuming a maximal plasma unit volume of 300mL, and a maximal donor red cell mean corpuscular volume of 100fL, this corresponds to no more than 42□L of red cell volume per unit, or no more than 0.21mL of total major incompatible red cells in this presented case.

Case Outcome: The patient's postoperative course was uncomplicated and she was discharged on hospital day 28.

Discussion: The finding of an eluate reactive against group A cells was unexpected in this group O patient receiving only group O cellular products. Trace red cell contamination is common and can often be visually appreciated in liquid plasma. However, the contributing red cell volume is miniscule, and recovery in circulation is expected to be minimal in settings of transfusion to group O or B patients. It may be the case that antecedent hemorrhage and crystalloid resuscitation effectively reduced the titer of anti-A to the degree that transfused group A RBCs survived in circulation. As a final consideration, donor or patient weak A subgroup (Ax, AEL) appearing as group O could also potentially explain our findings.

ILABB Case Studies 2021

Title: Care Everywhere Conundrum

Authors: Colleen Aronson, Jordan Lenihan, Cindy Wenschhof and Nicole Roggeman

Background: A large 9 center hospital system moved to Epic computer system as part of a merger with another large hospital system that was already utilizing Epic for the hospital information system. As part of the Epic system, there is a function that allows access to some shared hospital records at other Epic hospitals. Transfusion Service (TS) have always struggled with patients who have red cell antibodies that move from one hospital to another even when it is within the same hospital system. There are multiple antibodies that are known to evince over time making these antibodies difficult to detect when patients arrive at a new location.

Case Report: 1. A patient with no transfusion history within our hospital system was given 1 RBC unit in an outpatient setting and had a transfusion reaction. Nursing staff was updating the patients record in Epic and saw on the patient Storyboard that there was a "Blood Allergy alert." When looking into the Blood Alert in Care Everywhere it was discovered that the patient had a history of Anti-Jka at another hospital location. 2. A patient had a positive antibody screen and antibody identification was performed where an anti-D and C were found to be present. A staff member happened to hear about the other story regarding the Anti-Jka so looked into Care Everywhere and later found that anti-Jka, S and Cob had been identified at another location in the metropolitan area. 3. A patient sample was received as a pre-operative sample 10 days prior to surgery but information was incomplete regarding recent transfusions. A new sample was received on the day of surgery and found to have a positive antibody screen. When staff were investigating the positive screen, it was found that the patient had received 4 RBC units about between 1 and 2 months prior at an outside hospital facility. Antibody ID found a new anti-Jka. Patient was scheduled for a Coronary Artery Bypass Graft that had to be delayed while work up was completed and 10 RBCs were found from the inventory units. 4. Patient arrived and found to have a positive antibody screen and as part of the workup investigation an anti-E was found to be listed at 2 other locations in the Care Everywhere system.

Discussion: Clearly there are multiple examples where Care Everywhere has been shown to yield clinically significant information regarding antibody and transfusion information but there are multiple issues with using this system for every patient. How do we validate the antibody ID information for accuracy? Phone call? How do we determine which patients we should look up in the system? With the current staffing that are available in the lab, there is not sufficient time to look up every patient specimen that is received to see if there is clinically significant antibody history in Care Everywhere. How do we determine what best practice is for using this system and information?

Title: Comparison of Adsorption Techniques: An Adjusted Process to Improve Efficiency and Sensitivity

Author: Matthew Hukill, Rush University

Background: Panreactivity in patient serum may cause extended turn-around-time in identifying potential underlying clinically significant antibodies. Adsorptions are performed to resolve panreactivity and reduce the risks associated with transfusion. The standard adsorption procedure can be a lengthy process, dictated by the quantity of serial adsorptions required. The length of delay can be difficult to predict due to varying levels of circulating antibody and available antigen binding sites from patient to patient. Enzyme treatment of red cells makes binding sites for autoantibody uptake more available, allowing facilities to perform enhanced adsorption testing when a surplus of enhancement media is not always available, while reducing the risk of dilution of antibodies to undetectable levels.

Case Report: Specimens were tested in parallel with the standard adsorbing method outlined in the AABB Technical Manual and the in-house developed experimental method. Adsorbing cells were treated with papain or Zzap for all testing, as appropriate. Adsorptions were discontinued if panreactivity remained in adsorbed serum following six serial adsorptions.

Alterations were made to the adsorbing method in the experimental procedure to attempt to improve the efficiency and sensitivity of the process. The cells to serum ratio was increased to 3:1 with a maximum total volume of adsorbing cells plus patient serum of 1.5ml per adsorbing tube. Multiple adsorbing tubes may be used as necessary to achieve the desired total volume of adsorbed serum. Filter paper was utilized to absorb residual saline left behind in the adsorbing cells after the washing process to control for potential dilution. Incubation was performed in a water bath at 37°C for 60 minutes with adsorbing tubes placed horizontally, rather than vertically, to increase usable surface area and contact between antigens and antibodies, which also served to control for gravity induced separation. Adsorbing tubes were submerged in water and held in place by a test tube rack to counteract buoyancy.

Ninety-one of Ninety-three specimens achieved complete adsorption with the current standard method; ninety-three of ninety-three achieved complete adsorption with the experimental method. Adsorption by the experimental process revealed five additional antibody specificities not identified in the standard method. The average volume of adsorbing cells used for the standard method was 4.42ml while the experimental method was 3.2ml. The average turnaround time for the standard method was 197.7 minutes, while the experimental method was 81.4 minutes.

Conclusions: Fewer adsorbing cells were required on average with the experimental method, reducing enzyme usage and increasing longevity of the adsorbing set. The average turnaround time was significantly reduced by the experimental method, decreasing tech time required to perform the procedure and reducing delay in patient care. All five of the antibodies not detected in the standard method but detected in the experimental method have been reported

to cause hemolytic transfusion reactions. Failure to identify these antibodies by the standard method may be a consequence of antibody levels falling below detectable levels due to dilution from residual saline remaining after the washing phase when utilizing multiple serial adsorptions.

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Title: Identification of Anti-Yta in a Recently Transfused Patient with Multiple Alloantibodies

Author: Matthew Hukill, American Red Cross

Background: The Yta antigen is a high prevalence antigen that is expressed in 99.8% of all populations. The Yt(a-) phenotype is slightly more common in people of Israeli descent, at approximately 2% of the population. Yta was discovered in 1956 and its antithetical antigen Ytb in 1964, leading to Yt being classified as its own blood group system. The function of the Yta and Ytb antigens on red cells is currently unknown, but both are present on acetylcholinesterase (AChe), an important enzyme in neurotransmission.
Anti-Yta is typically an IgG antibody, and in some cases presents as IgG subclass 4 (IgG4). It is capable of binding complement and is most effectively identified at the anti-human globulin (AHG) phase. Yta is sensitive to disulfide bond reducing agents, such as dithiothreitol (DTT) and 2-aminoethylisothiouronium bromide (AET). Yta is destroyed by α-chymotrypsin and is resistant to trypsin and acid treatment. There has been reported variability with proteolytic enzymes, such as papain and ficin, which is believed to be dependent on the IgG subclass of the antibody.

Though not typically considered clinically significant, it has been reported to cause accelerated destruction of transfused Yt(a+) red cells and has been implicated in acute and delayed hemolytic transfusion reactions. Due to the rarity of Yt(a-) blood, performing a monocyte monolayer assay (MMA) to determine whether a demonstrating anti-Yta is predicted to cause overt destruction of transfused Yt(a+) red cells is recommended.

Case Report: A case presented of a 41-year-old Caucasian male admitted to the ED with a positive COVID-19 test, and bleeding from an open wound, with a Hgb of 6.6g/dl. The patient had been transfused 2 units of RBCs within 3 weeks of admission. A post-transfusion specimen was submitted to the Immunohematology Reference Laboratory (IRL) for antibody identification.

Testing of the patient's serum in the IRL demonstrated variable 2+ to 3+ reactivity with all reagent red cells and 1+ with the autologous control at AHG with polyethylene glycol (PEG) enhancement. The direct antiglobulin test (DAT) reacted 1+ with anti-IgG. Since the patient had been recently transfused, a reticulocyte separation was performed to isolate patient cells from the multiple donor red cell populations contained in the specimen. The DAT and autologous control were non-reactive with the patient's reticulocytes, suggesting that the positive DAT was due to antibody bound to donor cells only, indicating the probability of an antibody to a high prevalence antigen.
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After a serological phenotype was obtained using the reticulocytes, the patient's serum was tested against phenotypically similar reagent red cells, which reacted 1+ at AHG with PEG enhancement. Due to the variability in reaction strengths between the phenotypically similar reagent red cells and the random reagent red cells, additional specificities were suspected. A series of allogeneic adsorptions using papain treated donor cells of known phenotypes were performed, and the unknown antibody to a high prevalence antigen was removed from the serum. An underlying Anti-c and Anti-K were identified with the adsorbed serum, while antibodies to additional common red cell antigens were ruled out.
The patient's neat serum was tested against a ficin treated panel and 3+ to 4+ reactivity at AHG demonstrated with all cells. The patient's neat serum was then tested against a 0.2M DTT treated panel, and an Anti-c specificity demonstrated 2+ at AHG with PEG enhancement. All c- cells demonstrated no reactivity after DTT treatment. A selected cell panel of high prevalence antigen negative cells that are resistant to ficin and sensitive to DTT was tested against the patient's neat serum, and 3 of 3 Yt(a-) c- K- cells did not react. The patient's reticulocytes were tested against a plasma containing Anti-Yta, confirming the lack of Yta antigen on the patient's cells and the patient's ability to form an allo-Anti-Yta.

Conclusions: Anti-Yta was identified using standard tube techniques, proteolytic enzyme treatment, thiol reagent treatment, and allogeneic adsorptions. The commercial Anti-IgG used for testing at the AHG phase in the IRL is a murine monoclonal reagent that does not detect IgG4 antibodies; therefore, it is presumed this example of Anti-Yta is not IgG4. It has been suggested by MMA testing that IgG4 subclass Yta antibodies are not clinically significant and Yt(a-) blood is not necessary in these cases. MMA testing was recommended but declined by the hospital. Due to the scarcity of Yt(a-) donor red cells, the uncertainty of the clinical significance of this case of Anti-Yta, and the patient's clinical condition, the hospital declined to transfuse.

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Title: Transmission of Cache Valley Virus through Red Blood Cell Exchange in Kidney Transplant Recipient with Sickle Cell Disease

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Running title:
Transfusion-transmitted Cache Valley virus

Keywords:
Cache Valley virus (CVV), encephalitis, transfusion-transmitted infection, red blood cell exchange

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Abstract

Background: Cache Valley virus (CVV) is a mosquito-borne orthobunyavirus known to cause encephalitis.1,2 While the virus is distributed in mosquito populations throughout temperate North America, human cases are rare and all have occurred during late spring through early fall.

Alternative modes of transmission have not been recognized. We investigated the source of CVV disease in a kidney transplant recipient.

Methods: Patient cerebrospinal fluid (CSF) underwent clinical metagenomics next-generation-sequencing (mNGS) testing (University of California-San Francisco) and reverse transcriptase-polymerase chain reaction (RT-PCR) and viral isolation technique via cell culture (Centers for Disease Control and Prevention [CDC]). We reviewed transfusion records and traced donors and recipients of other co-components. As no retention segments were available from blood donors, follow-up serum samples were tested for CVV antibodies by plaque reduction neutralization testing (PRNT) (CDC). We investigated the organ donor by notifying the United Network for Organ Sharing/Organ Procurement and Transplantation Network, reviewing medical records and the pretransplant organ donor evaluation, testing archived donor serum, and investigating other organ transplant recipients.

Results: A 60-year-old woman with sickle cell nephropathy received a deceased-donor renal transplant in September 2020. She received 17 leukoreduced additive-solution RBC units perioperatively, mostly in 2 red blood cell (RBC) exchanges. Six weeks later she presented with weakness and impaired cognition progressing to aphasia and right hemiparesis. Encephalitis was diagnosed on neurologic evaluation and brain magnetic resonance imaging, but the cause was unknown until CVV was found by mNGS and confirmed by cell culture and RT-PCR on CSF obtained 3.5 months post-transplant. Archived organ-donor serum was negative for CVV by RT-PCR and PRNT. Four other organ recipients had no clinical evidence of CVV infection and all tested negative for CVV neutralizing antibody. Thirteen of 17 blood donors from Illinois and Wisconsin provided blood samples. One 42-year-old male Illinois donor's serum collected 7 months after donation had CVV neutralizing antibodies at a titer of 1:10. This donor's RBCs were collected in September 2020 and transfused on storage day 9 in a RBC exchange immediately before the kidney recipient's transplant. The plasma co-component was transfused to a pancreatic cancer patient with no subsequent neurological problems. Serum collected from this cancer patient 7 months post-transfusion demonstrated CVV neutralizing antibodies with a titer of 1:80. The blood donor was in good health with no history of illness at or after donation. The transplant recipient did not improve with intravenous immune globulin therapy and is in long-term disability care.

Conclusion: We demonstrated CVV transmission through blood transfusion during a RBC exchange procedure in an immunosuppressed organ transplant recipient. The RBC donor and recipient of the co-component both had laboratory evidence of CVV infection, providing strong evidence that the blood donor was the source of infection in the kidney recipient. The blood donor likely acquired CVV infection via mosquito-borne transmission. Initial diagnosis of this emerging infection in the transplant patient was made by an emerging technology, mNGS.3,4 Healthcare providers and blood bankers should be aware of the possibility of transfusion transmission of CVV and potentially other uncommon viruses.

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Title: When Hemagglutination is Insufficient: The Use of Molecular Techniques in the Resolution of Ambiguous Rhesus D Results

Author: Chinelo P. Onyenekwu, MD,[1] Angela Treml, MD.[1, 2]

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Background: Regulatory standards recommend Rhesus D (RHD) genotyping be performed in discordant RHD typing results. Herein, we present the findings from an O positive patient with anti-D antibody.

Case Report: A 29-year-old primigravida presented for routine prenatal care at 16 weeks gestation. Routine prenatal testing showed the patient was O-positive. Antibody screen performed on the Immucor Echo was positive demonstrating an anti-D antibody. The direct antiglobulin test (DAT) was positive (1+), IgG was 1+ and C3 was negative. The eluate-PEG showed the presence of an anti-D.

A review of patient's records confirmed the absence of a previous blood transfusion or RhIg administration. An impression of an O-positive with an unexpected anti-D antibody was made, with a plan to investigate for the presence of a partial D at the reference laboratory, and to administer O-negative products in the interim if required.

At the reference laboratory, initial reactivity of the patient's specimen with 4 FDA-licensed anti-D yielded a strong reaction on the immediate spin (IS) DAT tube techniques. Weak and variable results were obtained with the reagents, suggesting the presence of a variant antigen expressing quantitative or qualitative antigenic differences. Further testing for most frequent partial D alleles and common non-functional D alleles was performed using a laboratory developed end-point fluorescence detection of a sequence specific amplification polymerase chain reaction (SSP-PCR). The RHD*DAU allele and an unidentified RHD allele were detected. Thus, an impression of an unclear Rh type due to the presence of these two alleles were made, with a recommendation for further testing if the specific identity of these two alleles is required.
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At a second reference laboratory, RH genomic DNA and Sanger sequencing was performed. Sequencing of the 10 RHD exons and their flanking introns showed a genotype of RHD*01/RHD*DAU0.1.

It was deduced that the patient has one conventional RHD and was not at risk for an alloanti-D. The previously reported anti-D was most likely an auto-anti-D. Based on this, patient is Rh positive and will not require Rh negative blood products for transfusion.

Genetic rearrangements in the RHD gene have resulted in more than 460 alleles that give rise to variants with normal and altered protein. There are 19 DAU alleles reported to date with the DAU0 proposed as the primordial allele of the cluster. This primordial allele is characterized by a single nucleotide polymorphism (SNP) c.1136c>T (p.Thr379Met) within the exon 8 of the RHD gene. Many DAU alleles encode partial D phenotypes however, the DAU0 has not been associated with a partial D. The Dau0.1 variant results in a non-synonymous as well as a synonymous alteration that affect the intramembranous portion of the RHD antigen.

Conclusion: In certain clinical circumstances, hemagglutination results are unreliable, requiring molecular methods to predict patient Rhesus type to overcome the limitations of hemagglutination. Some PCR assays may be insufficient for the identification of RHD alleles present in a patient. In such scenarios, gene sequencing may be explored for the complete identification of such alleles.

Title: Passenger Lymphocyte Syndrome in a Liver-Kidney Double Transplant

Authors: Hamideh Doozandeh, MD and Mark Pool, MD, Rush University Medical Center, Dept. of Pathology

Background: Passenger lymphocyte syndrome (PLS), occurs in ABO-mismatched hematopoietic stem cell transplantation and less frequently in ABO-mismatched solid organ transplantation with highest incidence heart-lung transplants, followed by liver, then kidney. Immunocompetent B-lymphocytes present within the donor graft are transferred to the recipient and produce antibodies directed against recipient RBCs with different surface antigen, causing alloimmune hemolysis. This is an uncommon condition, but the true incidence is unknown because many cases remain subclinical and undiagnosed. Therefore, there is a possibility of misdiagnosis and delay in patient care that can convert to a serious condition.

Case report: A 45-year-old group B, D+ male with a negative antibody screen, with alcoholic liver cirrhosis and consequent hepatorenal syndrome underwent dual liver and kidney transplant from a group O donor. On POD8, the hemoglobin dropped from a baseline of 8.6 g/dL to 6.3 g/dL without identifiable bleeding source. Haptoglobin was undetectable but LDH with within normal limits and total bilirubin was decreased from POD8. The DAT was negative. The patient had received 4 group B+ PRBC from POD8-10, but Hb dropped to 6.0 g/dL. On POD8, haptoglobin was still undetectable but LDH was increased and the polyspecific DAT and DAT-C3 were positive, but DAT-IgG was negative. However, on POD12, LDH, and total and direct bilirubin peaked and the DAT-C3 and –IgG were both positive. The eluate showed anti-B confirming the diagnosis of PLS. He then received two group O RBCs from POD13-14 and increased immunosuppression therapy, and the Hb increased to 8.0 g/dL.

Conclusion: Unexplained hemolysis following an ABO–mismatched solid organ or HSC transplant should raise the suspicion of passenger lymphocyte syndrome even if an initial DAT is negative and repeat DAT should be performed.
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Title: How much RHIG do you want to give that patient?

Authors: Colleen Aronson, ACL Laboratories, Advocate Hospitals; Nicole Roggeman Advocate Lutheran General Hospital

Background: A 31 year old pregnant female was admitted to our facility in active labor. Patient delivered 2 health male infants via Cesarean section. An Rh Immune Globulin (RHIG) work up was requested as the patient's blood type was AB negative and both infants were Rh positive. A fetal screen was performed by the Transfusion Service (TS) and was found to be positive. The patient sample was forwarded to the hematology lab for a Klehauer Betkhe (KB) or Fetal Stain test to quantify the number of fetal cells present. Testing showed that 230 cells out of 4000 were fetal cells which was 5.8% content. Calculations were performed automatically as part of the testing which recommended 11 vials of RhIG. This seemed to be an excessive amount of RHIG for a patient when there were no issues with the delivery or the infants. The high number of calculated RHIG vials was questioned by the TS staff and concerns were pushed to the TS Supervisor for further evaluation.

Case Study: It is known that patients with hemoglobinopathies may continue to make fetal hemoglobin into adulthood to compensate for a hemoglobinopathy such as Sickle Cell Disease or Thalassemia. The quantity of fetal hemoglobin that continues to be produced by these types of patients varies considerably. Sickle Cell disease patients can have a range from 1-25% fetal hemoglobin as an adult and Thalassemia adults can range from 1-10%. The diagnosis history of the postpartum patient was evaluated and found to include "D56.9 Thalassemia, unspecified." Based on the patient diagnosis and known probability of autologous fetal cells a pre-delivery specimen was located and sent for the KB testing. The pre-delivery sample was found to contain 4.3% of fetal cells with a calculated dose of 8 vials of RHIG. The TS Medical Director was consulted, and it was determined to give the patients a total of 3 vials of RHIG rather than the originally calculated 11 vials.

Conclusion: A questioning attitude by the Transfusion Service Team and knowing the diagnosis of this patient was key to determining the possibility that the mother's autologous fetal hemoglobin was likely causing the extremely high fetal cells being detected by the KB test. It was also helpful in this case that our hospital system current obtains a Type and Screen (TAS) specimen when a Mom is admitted to the Labor and Delivery area. The fetal screen test did detect the Rh positive cells from the newborns but is not quantitative, so the KB test is needed to measure the volume of a larger postpartum bleed. The KB Test detects fetal cells but not cells that are Rh positive. Having a pre-delivery specimen enabled staff to show that the large volume of fetal hemoglobin detected in the post-partum KB test was partially autologous and partially the newborns. Calculating the difference between the pre and post delivery fetal cell volume saved the patient from receiving a large volume of RHIG that was not needed to
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remove the Rh positive RBCs in her blood stream. This also saved the cost of the additional doses of RHIG.

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Title: What's Up with "U"? Transfusion Support for an African-American (AA) Patient with multiple co-morbidities and multiple red cell alloantibodies including alloanti-U

Authors: Phillip J. DeChristopher, MD, PhD, Kristina Gvozdjan, MD, Dianna Rodheim, MT (ASCP), Loyola University Health System, Maywood, IL; Margaret A. Keller, PhD, National Molecular Laboratory, American Red Cross

Background: The highly complex MNS blood group system currently includes 46 antigens, carried on glycophorin A (GPA) and glycophorin B (GPB), single-pass membrane sialoglycoproteins, encoded by two homologous genes (GPA and GPB) on chromosome 4. Whereas anti-M and anti-N are well known to be clinically insignificant, antibodies to S, s and U on GPB have been associated with moderate to severe transfusion reactions and HDFN. Patients with an S-s-U-negative phenotype lack GPB, can make alloantibodies to any high-prevalence GPB antigen, and is commonly associated with deletion of GPB (GYPB*01N). However the S-s- phenotype is encoded by two distinct molecular backgrounds in individuals of African descent, alleles GYP*03N.01 and/or GYPB*03N.02 that express splice variants which result in low level expression of Uvar, which can make "U-like" antibodies which are difficult to distinguish from alloanti-U using standard serologic methods. Caucasians and AA's are 99.9+% positive and ~ 1% positive, respectively, for the U antigen.

Case Report: A 43-y/o AA man, a chronic nursing home invalid, had multiple co-morbidities, a PMH of SLE, HTN, hyperlipidemia, Type 1 DM, multi-microbial wound infections, a cardiac arrest and hypoxic respiratory failure. He was admitted to LUHS via the ED after a fall associated with a blood glucose of 24 mg/dL and comatose-altered mental status. On admission he had GN bacteremia (blood cultures positive for Kelbsiella and Enterococcus sp.) and an aspiration pneumonia. Hypoglycemia work-up revealed hyperinsulinemia associated with a tumor at the head of the pancreas, probably an insulinoma causing ectopic insulin secretion. Admitting H & H were 8.7 g/dL & 26.5%. During a 28-day MICU admission, a progressive anemia with a nadir H & H of 4.3 g/dL and 12.7% developed, prompting increasingly more urgent demands for RBC transfusion.

Results: Initial antibody screen was positive due to alloanti-Jka and an apparent alloanti-U. The DAT's (PS & IgG) were 2+, an eluate of which showed a warm IgG panagglutinating antibody. Serologically, the patient was negative for C-, E-, K-, Fya-, Fyb-, S-, s- and Jka-antigens. Absent obtaining extended phenotypically-matched, XM-compatible RBCs, 2 units of crossmatch-incompatible C-, E-, K-, Jka-negative RBCs were transfused using the emergency release protocol. The Hgb temporarily incremented to 7.4 g/dL for 3-4 days. An alloanti-Fya subsequently developed. RBC genotyping showed a complete deletion of the GLYB gene; the patient was S-s-U-negative. The genotyping also revealed a SNV in the GATA-1 binding site in the promoter gene encoding for the FY antigens (i.e., the GATA box mutation silences the allele
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encoding the RBC Fyb antigen). Although < 1% of donors are negative for U, we made a request through the American Rare Donor Program for genotype-matched RBCs. After 3 – 4 weeks, Fya, Jka, U-negative units were unable to be found, so the search was abandoned.
Conclusions: The patient's complicated clinical course ultimately prompted a decision that he was not a surgical candidate for insulinoma resection. The patient's hyperinsulinemia was partially managed medically using the drug diazoxide (Proglycem®). However, due to the combination of SLE (requiring steroids) and DM, wild, symptomatic hypoglycemic-hyperglycemic swings continued, prompting more hospital admissions. Intermittent treatment with erythropoietin has maintained the Hgb at 8 – 9 g/dL.

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Title: Baron von Münchhausen's Visit to the Blood Bank and Apheresis Service

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Background: A real-life German nobleman, Hieronymus Karl Friedrich von Münchhausen, was a soldier who fought in the Russo-Turkish War (1735-1739). After retiring in 1760, he was a celebrity in German aristocratic circles for telling outrageous tales of his military career. In 1785, German writer Rudolf Raspe authored the awkwardly entitled, Baron Munchausen's Narrative of his Marvelous Travels and Campaigns in Russia. The fictional Baron's exploits included untruthful, dramatic and impossible achievements, such as riding a cannonball, fighting a 40-foot crocodile and travelling to the Moon. For over 200 years, the fictionalized von Munchausen character appeared in scores of books, in plays, and on radio and TV comedies. In 1951, Munchausen's Syndrome was introduced to the medical literature. In modern parlance, the syndrome is now known as factitious disorder imposed on self.

Case Report: A 35-y/o, 110-Kg male, self-identified as non-Hispanic origin, was admitted via the ED on a Friday night with an acute onset of right-sided UE, LE and facial weakness and numbness. His "stroke symptoms" reportedly began on a Greyhound bus En route from Oregon to Florida. He stated h/o sickle cell disease (per patient, "I'm homozygous SS"), previously complicated by 3 ischemic strokes and prior RBC exchange transfusions for strokes and acute chest syndromes. He also c/o severe pain in his legs and back. On admission, a left arm PICC line was noted and H & H were 10.7 g/dL & 32.2%. Reported co-morbidities included Protein C deficiency and hyperlipidemia. Admitted to the Neuro-ICU where the acute ischemic stroke protocol (90 mg IV tPA (Activase®) began. The Apheresis Service was consulted for imperative RBC exchange transfusion. Medications included chronic hydroxyurea (3000 mg daily), aspirin, clopidogrel enoxaparin, atorvastatin, hydromorphone (Dilaudid®, 3 mg IV, q 2 hours) and Benadryl (50 mg, PO). Head CT and MRI scans were performed. A RIJ vein CVC was placed after two failed placement attempts (femoral veins).

Results: We allocated 10 units of RBC (Group B, Rh-positive, negative antibody screen, serologically phenotyped C-, E-, and K-negative). The RBC exchange was successfully accomplished without adverse effects. The fairytale gradually fragmented: prior Florida
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hospitalization check was disavowed. Disparate documented EMR histories from the ED and ICU emerged. His tone of care changed, belligerently refusing the exchange without premedication ("I always get 50 mg of IV Benadryl for all my exchanges.") Head CT and MRI scans showed no acute stroke or bleed, only a left occipital encephalomalacia consistent with an age-indeterminate infarct. Shortly, pretransfusion Hgb fractionation showed % Hgb A, A2, F and C as 91.6, 2.5, 0.5 and 5.4%, respectively. NO Hgb S was found. On Hospital Day 4, he left against medical advice.

Conclusions / commentary: This patient had no radiographically-documented acute stroke and no laboratory evidence of a sickling hemoglobinopathy. Annotations will be provided illustrating some outlays of healthcare expenses, updated DSM-5 diagnostic criteria of factitious disorder, epidemiologic remarks about Munchausen's Syndrome and some clues and behaviors making it easier to spot.

NOTES