Dear MABB Members,

In anticipation of the MABB 56th's Annual Meeting in September, 2010, the following is a summary of the 2009 presentations. The 2009 seminar was held on September 16-17 at the Schoolcraft College VisTaTech Center in Livonia.

**Wednesday, September 16, 2009**

Welcoming remarks were made by the 2009 MABB President, Suzanne Butch. Following that the first speaker was Dr John Gerlach, PhD. and MABB member and professor and director of the Biomedical Laboratory at Michigan State University. His lecture was titled *Molecular Diagnostics: Beyond NAT.*

*Molecular Diagnostics: Beyond NAT*

Molecular Diagnostics is the science that involves isolation of nucleic acid material i.e. DNA and RNA; Amplification of that material; Detection of what is in that material using gels, restriction endonuclease digestion and real time/quantization. Dr. Gerlach discussed the history of nucleic acid testing (NAT) in testing blood donors for HIV, HCV and WNV and the proposed testing for Parvovirus B19 in plasma products. What can be detected is limitless.....unless it requires FDA approval.

Genotyping of blood group antigens. There are 300 blood group antigens on the surface of the red cell. These are revealed by antigen specific antibodies. Fifty of these antigens are polymorphic at levels on consequence. Of greatest interest are those that cause antibody formation leading to transfusion reaction and hemolytic disease of the newborn.

Genotyping involves the isolation of SNPs, single nucleotide polymorphisms with one base difference. If the SNP changes the amino acid formed, this may be the basis of immune recognition. For instance group O is distinguished from group A1 most commonly by the deletion of G at codon 261.

Dr. Gerlach listed seven applications for blood group genotyping, They are: Fetal DNA typing; Extensive Blood Group typing of donors for allo-immunized patients; Determining the blood group of a recently transfused patients; Screening donors for rare antigens; Frequency/Demographic studies; Paternal RHD zygosity in HDFN; Blood grouping of patients with warm autoimmune hemolytic anemia.

Genotyping for HLA and chimerism was also discussed.

Dr. Gerlach described manual and automated methods for the isolation of the nucleic material. He discussed amplification of that material in Polymerase Chain Reaction (PCR) and how the material is labeled for detection and then further amplified using gel, PCR product digestion using restriction endonuclease, hybridization with a probe, microtiter plate assay, microarray solid phase and microarray liquid bead array, use of capillary electrophoresis and mass spectrophotometry.

Dr. Gerlach concluded his lecture with a brief quiz on the basics of nucleic acid chemistry. The applications of Molecular Diagnostics as they apply to the rest of the clinical lab are numerous.
Mandip Atwal, DO was the second speaker on Wednesday. Dr. Atwal is a surgeon and a member of the Department of Surgery at Mount Clemens Regional Medical Center in Mt. Clemens, MI. His lecture was titled *Emergency Blood and Massive Transfusion: A Surgeon’s Perspective*.

*Emergency Blood and Massive Transfusion: A Surgeon’s Perspective.*

Dr. Atwal’s agenda began with a brief history of blood transfusion starting with William Harvey who described blood circulation in 1628 through the concept of "Permissive Hypotension" introduced in 2003 by Kenneth Mattox, MD.

Hemorrhage is defined as acute loss of circulating blood. It is the most common cause of shock in a trauma patient. Massive Transfusion is replacement of 50% or more of the blood volume in 12-24 hours. How much blood loss can lead to shock? There are four classes of volume loss. Class 1 - donate one unit, Class 2 - uncomplicated but crystalloids are needed, Class 3 - Blood will be required and Class 4 - Death is pending. Other criteria defining these classes included volume lost, blood pressure, pulse and respiratory and CNS/mental state changes, amount of urine output and whether crystalloids or crystalloids with blood is needed. In hemorrhagic shock the need for blood is urgent as is the need to control the bleeding.

However transfusion is also bad. Transfusion can lead to increased acute lung injury, renal failure, coagulopathy, infections, volume overload and decreased O2 affinity.

What can be used to prevent transfusion? First there is recombinant factor VIIa (rFVII). This product is synthesized by amplifying human factor VIIa genes and then growing those multiple copies in baby hamster cells. Factor VII works by combining with Tissue Factor (TF). TF is released when the endothelium is injured. That combination converts factor X to Xa which converts prothrombin to thrombin which converts fibrinogen to fibrin. Fibrin accumulating in the aggregating platelets results in a primary platelet plug. There are multiple citations regarding the efficacy of rFVII in reducing the need for blood transfusion. However rFVII is expensive.

Dr. Atwal continued by discussing the lessons learned from the Gulf wars. First is the need to maintain the patient as hypotensive. Keeping the systolic at less than 80 prevents from happening the phenomenon referred to as "pop the clot".

Second there are two topical dressings. Quick Clot absorbs water from the clot allowing the clotting factors to concentrate over the injury. Second is HemCon containing negatively charged chitosan which bonds with positively charged red cells causing a seal to form over the injury. Finally there are old fashioned tourniquets.

Dr. Atwal ended by describing the Red Chest protocol which is a massive transfusion regimen of blood products administered immediately. This regimen includes the 2:1 red cells to plasma protocol plus platelets and cryoprecipitate.

Following Dr. Atwal's lecture was a break to allow participants to enjoy refreshments and meet with the vendors.
Investigation of Drug-Induced Immune Hemolytic Anemia

The last lecture of the morning was the Kay Beattie lecture. This lecture is dedicated to serological topics. Pat Arndt was the guest speaker and recipient of the Kay Beattie Award.

Ms. Arndt is a Senior Research Associate from the American Red Cross Blood Services Southern CA Region. Her lecture was titled **Investigation of Drug-Induced Immune Hemolytic Anemia**. Drug Induced Immune Hemolytic Anemia (DIIHA) is rare. The reaction is associated with over 125 drugs including anti-microbials, anti-inflammatories and anti-neoplasics. There are three mechanisms. They are referred to as (1) Drug Dependent, (2) Drug Independent and (3) Non-immunologic protein adsorption. Of those most common drugs associated with DIIHA are cefotetan (second Generation cephalosporin), ceftriaxone (third generation cephalosporin) and piperacillin (semi-synthetic penicillin) in combination with taxobactam in zosyn.

Ms. Arndt listed those complications of each drug as reported in the literature. Ms. Arndt discussed the criteria to consider when deciding whether to do a workup for DIIHA. Ms Arndt concluded her lecture by describing four DIIHA clinical cases encountered at her institution. One case involved rapid hemolysis and death of a ten year old boy due to anti-ceftriaxone.

Prophylactic Platelet Transfusion

Following a wonderful lunch prepared by the culinary students at Schoolcraft, Dr. Kenneth Schwartz, MD, Professor of Medicine, Hematology and Oncology at Michigan State University discussed prophylactic platelet transfusion. Dr. Schwartz first outlined the topics for discussion which were indications for prophylactic platelets transfusion and the number or trigger to prevent or stop bleeding. Also discussed were platelet dose, unique clinical problems and the adverse effects of platelet transfusion.

In addition to the required minimum number of platelets in a whole blood derived (WBD) and a apheresis platelet concentrates (APC), Dr. Schwartz had a slide that showed the AABB and Council of Europe requirements total leukocyte count in non-leucoreduced and leucoreduced platelet products as well as the required pH at the end of the allowable storage.

Dr. Schwartz named three way to measure response to platelet transfusions which were (1) Absolute platelet increment, (2) Corrected count increment and (3) Percent platelet increment.

The World Health Organization describes four grade classifications of bleeding, grade four being the most severe. In a study done in 2008 using three doses of platelets, low medium and high doses, randomized patients in all grades were shown to be safely and effectively transfused with low doses of platelets in most cases.
Dr. Schwartz discussed the advantages of leucoreduction and ABO compatibility matching of platelets. Platelet refractoriness is defined as no increase in the one hour platelet count after two platelets transfusions. Factors involved were non-immune clinical, drug, and patient factors as well as immune factors and "other" factors.

Finally Dr. Schwartz discussed (1) neonatal autoimmune thrombocytopenia (NAT) best treated with maternal or antigen matched platelets, (2) heparin-induced thrombocytopenia for which platelet transfusion is not contraindicated and (3) Thrombotic Thrombocytopenic Purpura (TTP) and whether it is advisable to transfuse platelets or not.

Dr. Schwartz concluded with two slides showing the adverse consequences of platelet transfusion.

**Current Practices in Pretransfusion Compatibility Testing**

Katherine Downes, MD spoke about the *Current Practices in Pretransfusion Compatibility Testing*. Dr. Downes holds several positions. One is as the Associate Medical Director of the Blood Banking/Transfusion Medicine at University Hospitals Case Medical Center in Cleveland Ohio. Her goals in this discussion were to (1) Review required elements of pretransfusion compatibility testing (PCT), (2) Discuss available methods for PCT and (3) Present data regarding the current practice of PCT in North American laboratories.

The purpose of pretransfusion compatibility testing is to prevent the transfusion of incompatible red cells that might result in immune mediated hemolysis.

**Required Elements of Pretransfusion Compatibility Testing Include:**
- Specimen requirements
- ABO Group determination
- Rh(D) Type determination
- Antibody detection screen
- Antibody identification
- Selection of donor RBC units appropriate for recipient ABO/Rh(D) and antibody status
- Performance of crossmatch between recipient and unit to be transfused

Dr. Downes described Gel Column Methodology and compared it to Tube Testing. She summarized the advantages and disadvantages. They are listed below.
- Advantages are: Stable, well-defined endpoints of reaction; Reproducible interpretation of test results; Standardization of reading and grading agglutination reactions; Reduce mistyping errors; Easier training of staff; Decreased sample volume;
- Disadvantages are: Requires special incubators and centrifuges for the microtube cards; Specific pipettor; Semi-automated.

Dr. Downes described Solid Phase Red cell Adherence methodology and compared it to Tube Testing. • Advantages are: Stable, well-defined endpoints of reaction; Reproducible interpretation of test results; Standardization of reading and grading agglutination reaction; Easier training of staff.
Disadvantages are: Requires incubators, centrifuges, light source; Semi-automated: Antigen phenotypes of antibody screening cells not recorded in system or correlated to agglutination results; Manual transfer of hemagglutination results to antibody identification antigen phenotype panels.

Pretransfusion Compatibility Testing

CLIA Regulated Analytes in PCT are regulated by the federal government. Performance Limits of Acceptability for Proficiency Testing Participants are listed.

• ABO grouping 100%
• Rhesus (D) typing 100%
• Antibody detection 80%
• Antibody identification 80%
• Crossmatching 100%

In 2001 the College of American Pathologists (CAP) started to capture information about the methodology used in PCT.

ABO and Rh testing showed a dramatic increase in gel testing 2001 through 2007. Automated gel and solid phase use for ABO and Rh determination both increased over tube in years 2005-07.

Next Dr. Downes discussed antibody screen methods. Manual Gel testing increased while tube-LISS testing decreased 2001-07.

Tube testing using Liss is predominant. Microscopic reading with tube was split 52% yes, 48% no.

Automated antibody screening increased in 2005-5007.

Regarding antibody identification over 67% will re-identify a previously identified clinically significant antibody. Over 14% will honor a previously identified clinically significant red cell antibody ONLY if detected in the current specimen.

In 2005 primary antibody panels were 50% gel, 48% tube and 2% solid phase. Dr Downes compared crossmatch methods for full crossmatch of alloimmunized recipients. Gel testing increase while tube LISS decreased in years 2001-07. Automated crossmatch use also increased in those years.

For the non-immunized recipient in 2001-06, Tube-LISS decreased, immediate spin remained the same while gel use increased.

Finally Dr. Downes discussed Electronic Crossmatch (EC), its requirements and advantages and disadvantages.

Advantages of EC: Technologist time savings; NO sample volume; NO biohazard exposure; Reduced false positive tests and interference due to cold agglutinins and rouleaux; Improved TAT.

Disadvantages of EC are: Requires a Laboratory Information System with software for blood bank applications; Requires resources to; Develop system to conform to AABB Standards & FDA requirements; Perform on-site validation.

Selection and Use of Automated Methods in the Transfusion Service.

After a break for refreshments and to visit the vendors’ exhibits, Dr. Downes continued with a presentation about the Selection and Use of Automated Methods in the Transfusion Service. Her goals were to review the process of selection of automated systems for PCT (PCT); present data regarding the current practice of PCT in North American laboratories; and introduce the CLSI Guidance Document on Validation of Automated Systems for Immunohematologic Testing. Automated Methods for PCT include; Column agglutination method (GEL); Solid phase red cell adherence method (SPRCA): and Electronic or computer crossmatch.

Automated Pretransfusion Compatibility Testing.
Applications are: ABO Group; Rh (D) Type; Antibody Detection (screen); Antibody Identification; Compatibility Testing (crossmatching). Under the consideration of cost containment of labor, included is the staffing of blood bank/transfusion service which is complex and challenging. There is the: (1) unpredictability of emergent transfusion; (2) variable work volumes-must be able to handle peaks; (3) not permitted delays; (4) 100% accuracy, documentation; (5) complexity of the testing; (6) set hours to correspond to clinical activity (OR times etc); (7) meticulous mapping of volume by time of day may provide useful data. Also there is the question of (8) cross-training versus specialists?; (9) determination of competencies and complexity of tasks; (10) testing, component preparation, inventory receipt, specimen accessioning; regulatory and accreditation requirements; (11) critical area of lab to urgent care sections of hospital.

Introduction of Automation in the transfusion service has financial and safety quality factors to consider. Automation provides cost savings by reduction of labor costs if fewer techs needed for testing and it addresses technologist staffing shortages. There is improved productivity in improved turnaround time, increased test menu and will help to handle volume growth and/or personnel loss. In order to determine if automation is right for your laboratory you should analyze your lab's testing, costs and workflow in order to prepare a "Request for Proposal" (RFP). In testing analysis, consider your test menu; test volumes, test turnaround time, and test growth opportunities (add new tests to menu). In cost analysis consider $$ spent on salaries, reagents, disposable, hazardous waste removal etc., select your own metric, cost per reportable result (CPRR). In workflow specimen testing analysis, consider peak volumes by time of day, number of FTE per shift, number of FTE required to cross-cover different testing areas of the laboratory, experienced versus inexperienced techs, time spent training new techs. Further workflow analysis in result reporting as in paper copy, HIS, LIS, BB information systems or combination, blood issuance/release documentation, blood administration, documentation, record storage media: electronic or paper, location: offsite or onsite, tracing/tracking. Analyzing the aforementioned elements of current operations enables you: to define and to prioritize requirements, to evaluate relative importance or value of various capabilities of systems, to determine cost/benefit ratio of different automation platforms.

(Cost effective answer for your lab may be NO automation!)
Serological Case Studies

Pat Arndt spoke again with the last lecture on Wednesday. It was titled *Serological Case Studies*. Unusual Autoimmune Hemolytic Anemia (AHA). Ms Arndt began by outlining the three types of AHA. They are Warm, Cold and a mixture of warm and cold. In warm AHA 60-80% of cases have IgG coating the red cells. Three to 11% have a negative DAT and rarely the protein is IgM or IgA.

Cold AHA is IgM protein in 8-25% of cases in cold agglutinin syndrome. Rarely, the protein is IgG as in Paroxysmal Cold Hemoglobinuria (PCH).

Ms Arndt detailed three cases. The first was a five year old boy suffering from IgA induced WAHA. The second was PCH in a two year old boy following a viral infection. Diagnosis of this case included performing the Donath Landstiiener Test. The last case described was of a IgM warm AHA. Ms Arndt compared the serological differences between IgG warm AHA, cold AHA and IgM warm AHA.

**Thursday, September 17, 2009**

Following remarks by MABB President Suzanne Butch, the second day's program began with Mr. Gerard Van Grinsven.

**Blue Ocean Strategy in a Difficult Economy**

Mr. Van Grinsven is president and CEO of Henry Ford Hospital West Bloomfield (HFHWB). As you are probably aware, HFHWB is innovative in its approach to patient care. Mr. Van Grinsven describes the philosophy or approach. In the introduction he explained that by offering customers something that had never been offered before, eventually the increase in sales will diminish the costs through economies of scale. He breaks down the differences between the traditional Red Ocean strategy of doing business versus the progressive Blue Ocean strategy of doing business. See below.
<table>
<thead>
<tr>
<th>Red Ocean Strategy</th>
<th>Blue Ocean Strategy</th>
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<tbody>
<tr>
<td>Compete in existing market space.</td>
<td>Create uncontested market space</td>
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<tr>
<td>Beat the competition.</td>
<td>Make the competition irrelevant.</td>
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<tr>
<td>Exploit existing demand.</td>
<td>Create and capture new demand.</td>
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<td>Make the value-cost trade-off.</td>
<td>Break the value-cost trade-off.</td>
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<tr>
<td>Align the whole system of a firm’s activities with its strategic choice of differentiation or low cost.</td>
<td>Align the whole system of a firm’s activities in pursuit of differentiation and low cost.</td>
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Using as an example the Cirque de Soleil, he explains how reducing below the industry standard or eliminating traditional standards factors while standard factors while increasing above the standard or creating new standards builds a new value curve.

**Eliminate-Reduce-Raise>Create Grid: The Case of Cirque du Soleil**

<table>
<thead>
<tr>
<th>Eliminate</th>
<th>Raise</th>
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<tbody>
<tr>
<td>Star performers</td>
<td>Unique venue</td>
</tr>
<tr>
<td>Animal shows</td>
<td></td>
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<tr>
<td>Aisle concession sales</td>
<td></td>
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<tr>
<td>Multiple show arenas</td>
<td></td>
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<tr>
<td>Reduce</td>
<td>Create</td>
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<td>----------------------------------</td>
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<tr>
<td>Fun and humor</td>
<td>Theme</td>
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<tr>
<td>Thrill and danger</td>
<td>Refined environment</td>
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<tr>
<td></td>
<td>Multiple productions</td>
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<td></td>
<td>Artistic music and dance</td>
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Mr. Van Grinsven explained that CEOs are moving Human Management to the top priority in order to survive in the face of an extreme workplace labor shortage. This is attained by focusing attention on the attraction, development and retention of employees. By increasing employees' engagement in the business over those who are not engaged or actively disengaged results in 50-60% higher success rates in associate retention, customer satisfaction and safety and 20-30% increase in productivity and profits. A 2006 Gallup survey concluded that actively disengaged employees costs the US economy about $238 billion.

The Value of Employee Engagement is Real.

**Annualized Net Gain**

<table>
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<tr>
<th>Turnover:</th>
<th>- 26%</th>
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<tbody>
<tr>
<td>Customer Satisfaction:</td>
<td>+ 12 percentage points</td>
</tr>
<tr>
<td>Safety Expenditure:</td>
<td>- 48%</td>
</tr>
<tr>
<td>Productivity per Employee:</td>
<td>+11%</td>
</tr>
<tr>
<td>Innovation (ideas and dollar value):</td>
<td>2.6x &amp; 3x</td>
</tr>
<tr>
<td>Engaged Workgroup Profitability:</td>
<td>+15%</td>
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Companies in the most engaged employee quartile have significantly better performance than those in the least engaged employee quartile. The higher quartile had lower absenteeism, turnover and safety incidents and had higher customer satisfaction, productivity and profitability.
Umbilical Cord Blood Donation was the title of the presentation by Suanne Dorr from the J.P. McCarthy Cord Stem Cell Bank which is a public, not-for-profit Cord Blood Bank in Detroit, MI. The objectives of the presentation were for the audience to understand the current clinical use of umbilical cord blood; how the umbilical cord blood is collected, processed stored and banked and what the difference is between public and private cord blood banking.

Stem cells have much potential. It can differentiate into other blood cells including red cells, white cells and platelets.

There are three sources of Hematopoietic Stem Cells (HSC) for Transplant. They are: Bone Marrow, Peripheral blood and Umbilical Cord Blood.

To harvest bone marrow the procedure needs an operating room, the donor undergoes anesthesia. One-two liters of fluid are collected from the hip. Peripheral Blood Collection is through pheresis. Umbilical cord Blood collection is convenient. It is a normal medical waste product that does not alter the birthing experience. Requirements are (1) it should not be collected if there is any risk to the mother or baby; the gestation must be 34 weeks or greater and it must be a single birth.

Requirements for public banking are that the FDA requires infectious disease testing of the maternal blood within 7 days of donation (delivery). The national stem cell registry requires an in depth medical history of the donor family. Federally sponsored research states that consent must be signed before collection.

For in-utero cord blood collection, supplies needed are a collection bag with needle and guard with clamp and 3 povidone-iodine swabs. The procedure states to wipe the cord if necessary to visualize the vein. Then it is necessary to swab the cannulation site with povidone-iodine. Next the cord is stabilized in order to insert the needle. Blood should start to flow into the donor bag as soon as the vein is punctured. It will take about 3-5 minutes to completely drain.

The cord blood unit is shipped to the Processing laboratory. It is processed under special conditions. The volume is reduced to 25 mls for storage.

The advantages of cord blood for HSC transplant are:

- Non-controversial source of stem cells
- Limitless supply (4.1 million births annually)
- Testing and storage up front making it available on short notice for shipment to the transplant center.
- There is no donor attrition compared with adult cell bone marrow registry.
- Ethnic diversity is easier to achieve.
- It is painless collection of the stem cells from a medical waste product
- There is higher proliferation capacity of the cells therefore there is lower dosage needed.
- There is a lower rate of graft versus host disease
- There is the ability to transplant at a lower rate due to "naive" cells.

The disadvantages of using cord blood for HSC are:

- There is the inability to obtain additional donor cells for a possible second transplant
- There are fewer cells due to smaller volumes
There is slower engraftment in the recipient.

Matching the donor is by HLA type. There are 3 HLA antigens used in typing on Chromosome 6. They are HLA A, B and DR. Each of us gets one set from our mother and our father. Therefore each sibling has a 1:4 chance of a 6:6 match.

According to the National Marrow Donor Program, bone marrow transplants have increased annually since 1987. In 2000 more than 3300 were performed.

Some of the disease states treated with cord blood include cancers, bone marrow failure syndromes, hemoglobinopathies, inborn error of metabolism and immuno-deficiencies.

What is the difference between Public and Private cord blood storage? In the public the donor is entered into a National Registry for search. Public is not for profit but relies on funding from the government and foundations. In private donation the use is for personal family. Private is for profit. Some private banks have a two sided model of private and public banking.

There are tips for how to find the best private Blood Bank. There include is the blood bank accredited by the AABB or FACT? How much umbilical cord blood is typically collected and stored? How many transplants have they facilitated? How long will they store the cord blood? The vision for the future is that there will be routine education about the option to bank cord blood and it will become routine at delivery. There will be expansion of the stem cell population for multiple dose therapies and/or treatment of patients with larger body mass to assist with transplant. There will be ability to differentiate cells into other tissues such as neural, cardiovascular and endocrine.

What's My Type

What's My Type was the title of John Judd's presentation. Dr. Judd is Professor Emeritus at the University of Michigan (UM). Dr. Judd began by summarizing tube and gel reagents and expected reactions of ABO types. Listed below are conditions where there is no anti-A or anti-B. They are: Newborn, Elderly/Immune Impaired, Bone Marrow Transplant in Chimerism, para Bombay, alpha and beta prozones, total parental nutrition (TPN), and dilution.

In three cases of TPN where the child had little or no dietary exposure to bacterial antigens in their diet that are critical to the formation ABO antibodies, they subsequently did not form those antibodies.

Dr. Judd described the change in a group A sickle cell recipient receiving a bone marrow transplant from a group O donor.

There are also conditions where there is no or weak detectable antigens. There are weak antigens as in a subgroup or leukemia, where there is minor cell population as in chimerism, ruptured ovarian cyst (serum suspended red blood cells) and in secretions but not on the red cell as in para-Bombay.

An example of a patient who forwarded as an O but reversed as a group A was resolved when the red cells were suspended in serum. After washing, the red cells forwarded as group A.
Dr. Judd listed the carbohydrates in the red cell, types 1 and 2 chains and how A and B antigens become attached to the red cell membrane. He included one slide defining the difference between a para and true Bombay phenotype. See below.

BOMBAYS

TRUE

- mutated $H$ gene
- $Se \vdash ABH$ in secretions
- type 1H (and A/B) on RBCs
- weak anti-H in serum
- $Le_b$ if $Le$ present
Dr. Judd explained a case where a patient had a case of Alpha/beta prozone. The patient had no agglutination in the forward or reverse test immediate spin. After room temperature incubation there was complete hemolysis in both reverse tests. Causes of prozone are:

- Seen with (1) high titer IgG Anti-A (alpha) and anti-B (beta);
- Due to steric hindrance of agglutination by the C1 component of human complement;
- Not seen with EDTA plasma or reagent RBCs in EDTA;
- Manifested by 5% of sera left at RT for 2 minutes.

Extra reactivity is another cause of ABO typing problems. These include cold agglutinins, alloantibody, subgroups (anti-A1 in A2), antibody to reagent constituent; cis- AB including B(A) phenotype. How to differentiate A1 and A2 phenotypes was defined. The characteristics of B(A) phenotype were listed.

Dr. Judd mentioned polyagglutination as in T* and Tn activation and acquired B. These problems are seen in patients with sepsis.

Mixed field reactivity in transplant, transfusion, genetic chimerism, leukemic change and A3 phenotype was discussed.

Dr Judd concluded his presentation with a reminder of the importance of protecting the patient starting with the requisition containing the right reason, patient and product; the right patient identification; the sample with right name, number and blood in the tube; and the transfusion of the right patient for the right reason with the right product.
Beating Burnout with Balance

Amy Dixon followed with *Beating Burnout with Balance*. Amy is a Senior Development Technologist at William Beaumont Hospitals. Amy’s objectives were that participants be able to recognize how you respond to stressors, be able to be more aware of your choices, moment to moment and identify at least two things that you can do to achieve greater balance.

You might be burned out if.... *Every* day is a bad day, You tell folks you are “retired”, but mean that you have been getting tired of the same things over and over, You feel like nothing you do makes a difference, You feel sick and tired...of being sick and tired!, You’ve noticed your lack of energy, Your friends and family have noticed your lack of energy, the clerk at the grocery store has noticed your lack of energy...

There’s a difference between Stress and Burnout. **Stress** = too much (work, tasks, appointments, pressure, etc.)  Note: We’re ALL stressed! **Burnout** = not enough (feeling empty, lacking motivation, not caring). Sources of stress are Internal or external “triggers” or positive or negative events or experiences.

One-fourth of employees view their jobs as the number one stressor in their lives. (Northwestern National Life).

Three-fourths of employees believe the worker has more on-the-job stress than a generation ago (Princeton Survey Research Associates).

Problems at work are more strongly associated with health complaints than are any other life stressor- more so than financial or family problems. (St. Paul Fire and Marine Insurance Co.)

Other stressors include Work - Life balance, relationships, financial, aging parents, and health issues.

Burnout in Action includes Lack of control over your work / life, Lack of recognition for good work, unclear job expectations, Overly-demanding expectations, Monotonous or unchallenging work, Chaotic / high-pressure environment, Being too many things to too many people and Lack of close relationships.

The theme is lack of control and personal and emotional impact. Amy lists eight tools to use in order to bring balance back into your life. They are (1) Spot & Stop, (2) Adjust your Focus, (3) Voice a Choice, (4) Concern Returns, (5) Renew Your YOU, (6) Prioritize, (7) Plan your Day and (8) 3 Minute Vacation.

Career Opportunities for CLS/MT : Syllabus not available

ABO’S and Ob(stetrics)

Dr. Dorothy Halperin is the Medical Director of the Transfusion Service at Mount Clemens Regional Medical Center. The title of her presentation was *ABO’S and Ob(stetrics)*.

Dr Halperin began with discussing the testing and issuance of blood products to the mother if there is hemorrhage ante and post partum. The cause of antepartum hemorrhage includes (1) placenta previa, (2) placental abruption, (3) Vasa previa [condition in which the fetal blood vessels, unsupported by either the umbilical cord or placental tissue, traverse the fetal membranes (bag of waters) across the lower segment of the uterus between the baby and the
cervical opening. (This condition has a very high fetal mortality rate (50-100%) due to fetal exsanguination resulting from fetal vessels tearing when the amniotic membranes rupture or because the vessels become pinched off as they are compressed between the baby and the walls of the birth canal.), (4) Ectopic Pregnancy, (5) hydatiform mole (A non-viable, fertilized egg implants in the uterus, and thereby converts normal pregnancy processes into pathological ones.) and (6) abortion.

Causes of post partum hemorrhage include trauma at the time of delivery such as C-section, instrumentation, episiotomy, genital tact laceration and uterine rupture. Other causes include placental abnormalities. These include the “Creatas” which is a severe obstetric complication involving an abnormally deep attachment of the placenta, through the endometrium and into the myometrium (the middle layer of the uterine wall). There are three forms of placenta accreta, distinguishable by the depth of penetration. There are multiple variants, defined by the depth of their attachment to uterine wall:

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Percent</th>
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<tbody>
<tr>
<td>placenta accreta</td>
<td>An invasion of the myometrium which does not penetrate the entire thickness of the muscle. This form of the condition accounts for around 75% of all cases.</td>
<td>75-78%</td>
</tr>
<tr>
<td>placenta increta</td>
<td>Occurs when the placenta further extends into the myometrium.</td>
<td>17%</td>
</tr>
<tr>
<td>placenta percreta</td>
<td>The worst form of the condition is when the placenta penetrates the entire myometrium to the uterine serosa (invades through entire uterine wall). This variant can lead to the placenta attaching to other organs such as the rectum or bladder.</td>
<td>5-7%</td>
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</table>

Another placental abnormality is retained portion of the placenta.

Two maternal factors that cause post partum hemorrhage include uterine atony which is a loss of tone in the uterine musculature. Normally, contraction of the uterine muscle compresses the vessels and reduces flow. This increases the likelihood of coagulation and prevents bleeds. Thus, lack of uterine muscle contraction can cause an acute hemorrhage. Clinically, 75-80% of postpartum hemorrhages are due to uterine atony. Uterine inversion is a second rare complication of vaginal delivery in which the uterus partially or completely turns inside out. Complete inversion is when the uterus is turned completely inside out, with the very top of the uterus protruding through the cervix. The entire uterus rarely prolapses out of the vagina. Other post partum bleeding episodes are caused by obesity, previous post-partum hemorrhage and Native American ethnicity. Finally coagulation defects can cause post partum bleeds. Definition of blood loss at delivery is 500 ml loss in vaginal delivery or 1000 ml loss after C-section.
Within twenty-four hours of delivery a blood loss of 1500ml or a 4 g/dl or greater drop in Hgb is considered to be hemorrhage.
Treatment of obstetrical hemorrhage depends on etiology and timing i.e. antenatal involves the baby.

Management of hemorrhage include pharmacologic intervention, interventional radiology, surgery, fluids and transfusion.

Prenatal testing includes maternal ABO and Rh but NOT including Weak D testing, antibody screen for and identification of clinically significant red cell antibodies. Dr Halperin explained the confusion that arises with Weak D positive patients/recipients and donors. Regarding clinically significant red cell antibodies, they can cross the placenta and cause hemolytic disease of the newborn (HDN). Thus it is important to recognize the presence of these antibodies in order to alleviate the HDN. Antibody screen should be repeated at 28 weeks gestation of an Rh negative mother preceding Rh Immune Globulin administration. In Rh positive mothers the antibody screen should be repeated if the is abdominal trauma, for transfusion ad if the is another clinically significant red cell antibody present.

Dr. Halperin discussed Rh Immune Globulin (RhiG) which is a high titer IgG anti-D solution derived from hyper-immunized human volunteers. RhiG should be given to Rh negative patients at various times or following various episodes. The times are antepartum at 28 weeks gestation and post-partum delivery of an Rh positive or Weak D positive infant. Episodes would include invasive procedures, following abortion, vaginal bleeding or threatened abortion. A full dose of RhiG is 300 micrograms which protects against up to 30 mls of fetal whole blood bleed into the maternal system.
The mechanism of RhiG is not known but is does not work by saturation of the maternal Rh positive antigen sites. RhiG “Pearls” are (1) It should be given within 72 hours of delivery; (2) It will not work after primary immunization; (3) It will not suppress secondary response; (4) It has a half life of 21 days; (5) Enough must be given. The amount given depends on the extent of Fetal- maternal bleed of the Rh positive fetus into the Rh negative mother.

Means to detect the amount of FMH are the qualitative rosette test to detect Rh positive cells in the maternal Rh negative circulation. If the rosette test is negative, only one dose if RhiG is indicated. If fetal cells are detected, the next test is the quantization of the Rh positive fetal cells by using the Kleihauer-Betke (acid-elution) test. Fetal cells are resistant to acid and remain pink. Adult cells are sensitive to the acid and become “Ghost” cells. Once the number of fetal cells in the maternal whole blood circulation is determined, that number is divided by 30 to calculate the number of RhiG doses indicated. Another way to calculate RhiG dosage is through the use of flow cytometry. Dr. Halperin listed the risks of receiving RhiG which are low for infectious disease transmission and rare for fever and pain at the injection site. Antibody titer is the last test Dr. Halperin described. Antibody titer is the reciprocal of the highest dilution of plasma that gives a 1+ reaction. Three methodologies are (1) Traditional or
classical, (2) Uniform method - CAP and (3) Cell Selection. Some Include in the results reported the score which considers the strength of all the positive reactions in the titration.

Hemolytic Disease of the Newborn (HDN) was first described in 1609. In 1921 hydrops and kernicterus were associated with the disease. In 1932 the disease was described but not he cause. In 1940 Landsteiner and Weiner identified Rh positive and Rh negative blood types. The causes of HDN are isoimmunization, congenital defect of red cells and acquired defects of red cells. There are many red cell antibodies that can cause HDN. They all occur as IgG in protein nature. The pathophysiology is that the fetal red cells have a paternally derived antigen which become coated by the maternal antibody. The antibody-coated fetal red cells then undergo destruction before and after birth. The symptom are kernicterus, erythroblastosis and hydrops.

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The sources of maternal red cell antibody due to exposure to foreign red cells are: (1) previous pregnancy; (2) previous transfusion; and (3) transplant. The question is will a pregnant patient with a clinically significant red cell antibody develop HDN and if so, how severe. Course of action is to discern the patient's history, perform initial and serial antibody titers, do ultrasound to look for hydrops including cardiac symptoms and size and the size of the liver and the spleen. Also the paternal phenotype and genotype can be determined and there can be analysis of the amniotic fluid to determine the concentration of bilirubin pigments with application to the Liley and Queenan charts.

Fetal testing is done through PUBS = cordocentesis. Tests are for ABO, the incriminating antigen, direct antiglobulin and hemoglobin. Risks to the fetus include amnionitis, fetal bradycardia and fetal loss. Also tested is the Peak Systolic using MCA Doppler Velocity. With fetal anemia this is increased.

For patients with severe fetal HDN and it's too early to delivery, there is intrauterine transfusion (IUT). It can be via intraperitoneal, intravascular and intracardiac.

Donor red cell must be antigen negative, irradiated, CMV negative and HbS negative and the must be crossmatch compatible with the maternal sample. Other treatments to decrease the antibody level include IVIG and intensive plasma exchange.

After the HDN baby is born there is increased bilirubin production and anemia. Unconjugated free bilirubin leads to neurotoxicity. Treatment is phototherapy to convert the unconjugated bilirubin to an H2O soluble form that can be directly excreted in urine or bile. The baby's eyes must be protected and the baby must be monitored every 6 hours.

Finally there is the option of performing exchange transfusion which removes the bilirubin and removes and replaces the coated red cells with antigen negative red cells. A normal level of hemoglobin and hematocrit is achieved. Indications for exchange are a bilirubin of 20mg/dl, severe anemia (HGB<10g/dl), cord bilirubin > 4mg/dl, increased bilirubin and increased serum bilirubin/albumin ratio. In exchange the red cells must be antigen negative for the corresponding maternal antibody; they should be O negative or ABO compatible, CMV negative, Irradiated, HbS negative, CPDA-1 and a young unit. The plasma must be compatible or group AB.
The exchange is accomplished through the umbilical cord via catheter in slow increments with close monitoring. Albumin may be given prior to the procedure. Complications involve cardiac, hematologic, infectious, metabolic, vascular and systemic.

An ImPRESSive Mimic

An ImPRESSive Mimic was the final presentation of the day presented by Dr. Laura Cooling, Associate Medical Director at University of Michigan (UM) and Dr. Melissa Bombery. This clinical case was regarding a patient admitted to UM hospital after a four day stay at an outside hospital. The patient's symptoms included frontal headache, blurry vision, photophobia, nausea, vomiting, nocturnal nosebleeds, "dark" small volume urine, fluctuating periorbital and peripheral edema. This patient had c-section for an uncomplicated pregnancy six months prior. However there was post-partum hemorrhage requiring one unit of blood to be transfused and prolonged bed rest. She was treated with progesterone. In physical exam she was pale, afebrile, had new hypertension and tachycardia. Her admission chemistries included decreased haptoglobin and increased LDH. The peripheral blood smear revealed microcytic anemia, moderate anisocytosis with red cell fragment. There was polychromasia and moderate thrombocytopenia. Urinalysis showed blood and protein. She was diagnosed with HUS/TTP and started on dialysis, steroids, ritulin and daily Total Plasma Exchange for 15 days. However the patient suffered hypertension, volume overload with pulmonary edema and seizure. She was transferred to UM with the diagnosis of refractory TTP. At UM the exchange was held but steroids and dialysis were continued.

After two days there were further complications. The patient had a signal abnormality noted in the occipital and parietal lobes. This leads to the diagnosis of PRES which is Posterior Reversible Encephalopathy Syndrome. Symptoms of this diagnosis include clinico-radiological edema, neurotoxicity, mental status changes, vomiting, seizures and visual changes. Dr. Bombery further described the clinical conditions associated with PRES as well as the treatment and follow up. This patient has had continued complications and is currently awaiting kidney transplant.