Conservation of Red Cell Mass in ELBW Infants

Within the first week of life, extremely low birth weight (ELBW) infants will lose up to 20% of their total body weight primarily as extracellular water volume. How timing and distribution of that loss occurs as shifts between intracellular, extracellular, and interstitial fluids is not easy to identify sequentially; therefore, as hemoconcentration can give inconsistent hematocrit (Hct) values, it is import to conserve red cell mass (RCM) in order to preserve the oxygen carrying capacity at an appropriate balance between oxygen consumption and oxygen delivery.

By maintaining ELBW infants in a safe zone of oxygen carrying capacity, we prevent them from approaching the critical oxygen delivery point where oxygen consumption exceeds the reduced oxygen delivery and altered blood flow and increased extraction can no longer meet metabolic demands. Some of the most common NICU practices to maintain this margin of safety include conserving RCM by, limiting the number of blood draws to only essential tests or by maintaining RCM by replenishing it with blood transfusions.1 While blood sampling and transfusions in an ELBW infant may be an unavoidable task, there are other clinical practices that can sustain RCM and/or avoid RCM loss. These practices include: delayed cord clamping (DCC), umbilical cord milking (UCM), and using the cord blood for admission labs. Applying these techniques are shown to reduce the need for RBC transfusion and thus can avoid the inherent risks of that procedure.2

Asymptomatic Symmetric SGA Infants - Is TORCH Work Up Really Required?

Congenital infections account for only 5-10% of all cases of fetal growth restriction. Infants afflicted with these infections often share clinical manifestations, like: IUGR, SGA, prematurity, hepatosplenomegaly, anemia, rash, cataracts and microcephaly. The similar clinical picture led to the creation by Nahmias in 1971 the famous acronym TORCH (Toxoplasma, Rubella, CMV, HSV and others). Since then the acronym has been expanded with the addition of Syphilis, Parvovirus, Enterovirus, HIV and HBV. During the last decades TORCH testing has been increasingly and inappropriately used, raising questions about the indication and cost-effectiveness of these tests.

The table shown below published in 2013 by DeJong summarizes current available TORCH tests. Most commonly, either serologic tests detecting specific antibodies or direct detection of genetic material by PCR are used.

<table>
<thead>
<tr>
<th>PATHOGEN</th>
<th>MATERIAL</th>
<th>METHOD</th>
<th>SENSITIVITY (%)</th>
<th>SPECIFICITY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>Serum (single sample)</td>
<td>IgM/IgA</td>
<td>61 - 68</td>
<td>67 - 100</td>
</tr>
<tr>
<td>Rubella</td>
<td>Serum (obtained before 3 mos. of age)</td>
<td>IgM/IgA</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Serum (obtained before 3 mos. of age)</td>
<td>PCR</td>
<td>20 - 70</td>
<td>100</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
<td>Blood, nasopharyngeal swab, conjunctival swab, CFS</td>
<td>PCR</td>
<td>99/100</td>
<td>100/100</td>
</tr>
</tbody>
</table>

In many centers total IgM level obtained from the neonate is the first screening step. It is known that there is no trans-placental transfer of maternal IgM, hence an elevated level would be indicative of fetal infection. The literature regarding total IgM testing was mainly published in the 1970-90s. Mahon et al in 1994 showed that out of 168 SGA neonates only 32 had elevated IgM levels, and only 6 had confirmed congenital infection. All 6 infants had other symptoms suggestive of infectious cause of their growth retardation thus prompting more specific investigations. Matthews et al did not find any unapparent cases of TORCH infection in nearly 1000 SGA babies with elevated IgM levels. Melish et al reported that many babies with CMV-uria had normal IgM levels. More recently, Khan et al in 2000 was investigating the diagnostic role of both IgM levels and specific TORCH testing.
Delayed Cord Clamping

Blood flow within the umbilical cord after birth is affected by the position of the infant in relation to the placenta before clamping. While a majority of obstetrical practices immediately clamp the umbilical cord of ELBW infants in order to provide the infant to the neonatal resuscitation team, benefits have been found by delaying cord clamping. When performing DCC, the infant is lowered below the perineum or cesarean section incision site. Blood is then passively transferred from the placenta to the infant primarily by uterine contractions over a period of 30-120s. This passive transfer has been found to increase infant blood volume by 10-20mL/kg. In a study specifically looking at DCC compared to immediate cord clamping (ICC) in premature infants 22-27 weeks gestation, infants with DCC were found to have higher hematocrit values in the first 72 hours of life and decreased number of total blood transfusions. The infants who underwent DCC were also found to have higher mean arterial pressures and were four times less likely to receive treatment for hypotension than the infants who underwent ICC. While physicians may be concerned about the risk of hypothermia from being outside of the radiant warmer and of jeopardizing or delaying resuscitation efforts in premature infants, this study found that there were no differences in cord blood pH or APGAR scores between DCC and ICC. In fact, admission temperatures in the infants undergoing DCC was higher than the ICC infants which was attributed to the fact that the providers were more vigilant with maintaining infant temperatures with warmed sterile towels while the DCC procedure was being performed.

Umbilical Cord Milking

UCM is an alternate method to increase RCM in ELBW infants. This procedure is shorter in duration and therefore, is less of a concern in delaying resuscitation efforts of either the mother or the infant. With UCM, the cord is pinched as close to the placenta as possible and milked toward the infant. This process is recommended to be performed over a 2 second duration and repeated 4 times, but it has been found to be effective in as little as 5 seconds. In a study comparing DCC to UCM in premature infants less than 32 weeks gestation delivered by cesarean section, infants who underwent UCM were found to have higher hemoglobin at birth, higher blood flow and blood pressures, and improved urine output when compared to infants who underwent DCC.

Cord Blood Work

Admission blood work can require up to 3.5mL of blood. With total body blood volume at approximately 80mL/kg, 3.5mL in a 500g infant is approximately 10% of the infant's total blood volume. But is the infant the only place to draw admission blood work labs? Cord blood is fetal blood, and therefore, admission blood work can be drawn from the umbilical vein. Labs that can be drawn from the cord include, but are not limited to, CBC, blood culture, and type and screen. Minimal differences in hemoglobin levels have been found between infant and cord blood. For blood cultures, if the cord is properly sterilized, a significantly larger volume of blood can be obtained which will be much more likely to identify low concentrations of circulating organisms. As for the type and screen, while the AAP has recommended cord specimens for the purpose of hyperbilirubinemia, few studies have evaluated the use of cord blood specimens for transfusion purposes.

Conclusion

RCM must be maintained in order to insure ELBW infants a margin of safety in meeting changes in metabolic demands over the full range of possibilities defined by the oxygen delivery curve. By performing DCC or UCM and drawing admission labs from the umbilical cord, we increase RCM, reduce losses and thus, delay the need for transfusion. While changes in RCM and blood volume are demonstrable, most investigators feel that this approach will likely provide short as well as long term outcome benefits with minimal risks to the infant, however, clear evidence for this is yet to be accumulated.

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REFERENCES:
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titers in a cohort of neonates with growth restriction. Most of the patients (85%) had no other clinical findings besides growth restriction. All serological testing was negative and only 1 asymptomatic infant had CMV in the urine. Interestingly two infants who had positive head ultrasound findings (calcifications, hydrocephalus) had negative serology and urine. In the authors’ opinion serological work up proved to be of no value in elucidating the etiology of growth restriction, and only generated additional costs.

In 2010 Van der Welden et al were trying to evaluate to co-occurrence of congenital TORCH infections in asymptomatic SGA infants. All infants and mothers tested negative for IgM titers for Toxoplasma, Rubella, CMV and HSV. Two asymptomatic neonates had positive urine culture for CMV, with negative CMV IgM titer.

These finding suggests that a selective approach to TORCH testing with a focus on CMV would be more prudent.

CMV is the most common cause of congenital infections worldwide. The incidence ranges from 0.5-2% of all births. The majority of the infected infants are asymptomatic (85-90%) but have high risk for developing late onset sensorineural hearing loss (10-15%). Treatment of asymptomatic CMV infection with ganciclovir and valgancyclovir is effective in preventing hearing loss. Al-Hareth et al in 2010 investigated the role of selective CMV testing (CMV IgM, IgG and DNA PCR) in low birth weight infants as compared to healthy controls. CMV IgM antibodies were not detected in any of the patients but the majority of both LBW infants and controls had CMV IgG antibodies. Presence of CMV DNA was found in 3 of the LBW infants and in 1 control. The authors concluded that CMV PCR testing could be a rapid, noninvasive and sensitive diagnostic method. In 2014 Wei et al published a study investigating selective CMV testing in SGA neonates. Only 2/117 of them had positive IgM antibodies: one for CMV and one for HSV. The CMV IgM positive infant had persistent positive CMV urine cultures (5/7) and additional clinical findings of microcephaly, hydrocephalus, thrombocytopenia, hepatosplenomegaly, arthrogryposis. Total of 296 urine samples were obtained and 6 neonates had at least 1 positive urine CMV culture. Treatment was administered in 2/6 infants based on additional clinical findings.

The search for other options for selective CMV testing led Boppana et al to investigate dried blood spots (JAMA 2010) and saliva (NEJM 2011) as alternative sources for CMV PCR testing. Especially the saliva PCR assays had high sensitivity and specificity in CMV detection and seem very promising for the future.

Isolated SGA is a rare symptom of a congenital infection and does not warrant laboratory testing with total IgM and TORCH specific titers or imaging, unless there are other clinical findings. If testing is performed it should be, at most limited to CMV. As of now, urine CMV culture is considered gold standard for diagnosis but new techniques such as PCR are emerging and could be utilized more broadly in the near future.

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Morgan’s FunDay to Fight Necrotizing Enterocolitis

The First Annual Morgan’s FunDay was held on Sunday April 24, 2016

Morgan’s FunDay is a special day of fun and fundraising for The Morgan Leary Vaughan Fund a nonprofit organization that raises money to treat and prevent Necrotizing Enterocolitis (NEC) in premature and medically fragile babies.

The Morgan Leary Vaughan Fund (AKA “Morgan’s Fund”) was started after Stephanie Vaughan (President & Co-founder) and Jeff Vaughan delivered premature twin boys (Shaymus and Morgan) and Morgan developed Necrotizing Enterocolitis.

The event was held on a beautiful day at the Mahopac Golf Club. While over 30 children watched the magic show, had their faces painted and got lots of exercise doing summersaults and back flips on the tumbling mats the adults sipped their refreshments and listened to the guest speakers who had been affected by Necrotizing Enterocolitis in profound ways.

Katie and Frank Pedro shared their story about their micro preemies Lucas and Lily born in 2012 and who both developed NEC. Although the doctors did all they could, Lily earned her angel wings and now watches over her twin brother Lucas and her parents from heaven.

The Lily Pedro Award for Excellence was established in memory of Lily Marie Pedro who lost her battle with NEC in 2012. This award recognizes individuals or organizations who exemplify the mission, vision, and ideals of The Morgan Leary Vaughan Fund.

This year’s award was presented by Jennifer Degl to Dr. Edmund LaGamma, Chief of Newborn Medicine of the Regional Neonatal Intensive Care unit at the Maria Fareri Children's Hospital, Westchester Medical Center, because of his extensive research and dedication to NEC and premature babies.

Jennifer Degl is the author of the blog from which this information was excerpted (micropreemie.net) and her book entitled “From Hope to Joy; A Memoir of a Mother’s Determination and Her Micro Preemie’s Struggle to Beat the Odds”. It is her memoir describing the journey of her decision to have another child, to the birth of her micro preemie (Joy) at twenty-three weeks and who battled NEC. Joy is now a thriving and active 4 year old which Jennifer thanks and credits Dr. LaGamma, and the other neonatologists and nurses at Maria Fareri Children’s Hospital for the reason her daughter is alive.

Please visit The Morgan Leary Vaughan Fund’s website to learn more about Necrotizing Enterocolitis and how they are using the monies to research new treatments and prevention of this devastating condition.

http://www.morgansfund.org

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Congratulations!
Please join in congratulating Dr. Lyndsey Garbi and Dr. Heather Brumberg.

Lyndsey Garbi, MD, Neonatologist
Triple congratulations are in order for Dr. Lyndsey Garbi! In May of this year Lyndsey graduated with a certificate in Pediatric Bioethics from Children's Mercy Bioethic's Center in Kansas City. The Children's Mercy Center for Bioethics offers the only pediatric bioethics certificate program in the world. The nine-month course begins and ends with an intensive three-day session and students become knowledgeable in pediatric bioethical issues such as the role of ethics committees, ethics consultations, futility and moral distress, end-of-life decisions, research ethics, and much more. Close on the heels of her bioethics certificate graduation, Lyndsey completed her Neonatology Fellowship program at Maria Fareri Children's Hospital, Westchester Medical Center. Though these are significant accomplishments, Lyndsey's most cherished “accomplishment” occurred this June 7th with the birth of her son!

Wishing you all the best Dr. Garbi in each of your future endeavors!

Heather Brumberg, MD, MPH, FAAP
Congratulations to Dr. Heather Brumberg on being elected as Vice President of the American Academy of Pediatrics – Chapter 3, District 2. Upon completion of her 2 year term Dr. Brumberg will assume the position of President Chapter 3, District 2 at the American Academy of Pediatrics.

Warm Congratulations to Dr. Brumberg.

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Please visit www.westchestermedicalcenter.com/RPC for information about the Regional Perinatal Center at the Maria Fareri Children's Hospital at Westchester Medical Center and to locate previous issues of The Perinatal Gazette.

Maria Fareri Children’s Hospital Celebrates a Very Special First Birthday!

Tamaya Berry weighed only 9 ounces when she was born 15 weeks early in April of 2015 at St. Luke’s Hospital in Newburgh, NY, an affiliate of the Westchester Medical Center Health Network.

Immediately after her birth Tamaya was transferred to the Regional Neonatal Intensive Care Unit (RNICU) at Maria Fareri Children's Hospital. As one of the smallest (lowest in weight) babies to survive extreme prematurity and also the lightest baby to be cared for and graduate from the RNICU at Westchester Medical Center, Maria Fareri Children's Hospital, Tamaya spent the first 6 months of her life fighting many challenges due to her extremely low birthweight and extreme prematurity of 25 weeks. It was a momentous occasion when Tamaya graduated from the NICU in October, 2015 weighing 7lbs., 12 ounces - almost 14 times her birthweight!

A special first birthday celebration was hosted by the Maria Fareri Children's Hospital Regional NICU for Tamaya and her family. Present to share in the celebration was Dr. Edmund LaGamma, Chief of Newborn Medicine at MFCH, Sue Malfa, RN, Nurse Manager of the RNICU, MFCH and many of the physicians, nurses, and other NICU staff who are to be credited for working tirelessly as a team caring for Tamaya throughout her stay in the neonatal intensive care unit.

Tamaya's parents describe Tamaya as a happy little girl, always smiling, clapping, full of life and promise!