Greetings from the new Chair of the Pediatric Maternal Fetal Division!

I am honored to be writing to you for the first time in my new role. Many years ago, I was recruited to join this wonderful professional society, and I have found it a rich source of professional support, educational resources, academic and career opportunities, and importantly, friendships. I am grateful to AACC for all that it has offered me, and I hope I can give back, perhaps in modest ways, in turn.

The 2012 AACC Annual Meeting is just ahead, to be held in Los Angeles July 15-19, 2012, and for those of you who will attend, you are invited to two special events. First, we will continue our tradition of presenting our Division awards at our lively evening mixer. This will be held at the Annual Meeting, Tuesday, July 17, 2012, from 5:30-7:00 PM at the J.W. Marriott, in the Olympic 3 room. All members and prospective members are invited-the only requirement is an interest in Pediatric Maternal Fetal laboratory medicine! Noteworthy are the excellent submissions this year for our Annual poster awards; we received entries comprising AACC peer-reviewed, accepted papers from ten countries this year, including: the United States, Canada, Spain, Greece, Italy, India, Turkey, Belgium, Nepal, and Ghana. The awardees for our Division’s Best Poster and Best Student/Young Professional Poster and runner-ups for each category and our award for outstanding contribution to pediatric clinical chemistry are announced in this issue. For your future abstract submissions, do not forget to check our Divisions’ box to be considered for our honors and small honoraria.

Your second invitation is to a Dialogue with Industry regarding Advancing Pediatric Reference Interval Development. This event will be held Tuesday, July 17, 2012, 1:00-3:00 PM, at the J.W. Marriott in Diamond Ballroom Salon 5. This is an opportunity for AACC, clinical laboratories, commercial laboratories and medical device manufacturers to collaborate to develop new pediatric reference intervals. The National Institute of Health’s National Children’s Study (NIH-NCS) is underway, and will provide quality healthy children’s samples for candidate projects deemed appropriate to the NIH-NCS mission. The details of the event and venue are available by link in this newsletter. Do consider attending this event with your ideas, or follow up with us if attendance is not possible, as these projects offer potential value to patients, laboratories and industry partners alike.

This issue of our Newsletter offers an excellent review from David Carpentieri from Phoenix Children’s Hospital in Phoenix, Arizona, and his colleague Stephanie Souza regarding performance of procalcitonin measurements for the diagnosis of pediatric sepsis. This paper, which represents letter “P” in our ABCs in pediatric laboratory medicine series, is a timely update on a topic of considerable general interest: our collective search for the Holy Grail, a better laboratory test for definitive diagnosis of sepsis

Additional newsletter offerings include several “gems” from the very recent pediatric literature, as has been a longstanding tradition. This includes: a perspective on the positive impact of transcutaneous
bilirubin testing, new support for the role of cystatin C for early diagnosis of acute renal injury in children, and some exciting work using serum S100B in the emergent evaluation, triage and management of pediatric head trauma. Feel free to send us “gems” that you have discovered in your forays into the vast literature out there, or your own recently published papers that you would like to share with your colleagues, addressed either to speaghan@stanfordmed.org or to our editor Angela Ferguson, amferguson@cmh.edu.

This issue we have the spotlight on serum S100B measurements in infants, children and adolescents for our (newer-but-now-regular feature) Reference Interval Corner.

Hearty thanks to our two new Executive team members, Drs. Jon Nakamoto and Dean Carlow, for agreeing to join up! Jon comes to us from the commercial laboratory setting, Quest Diagnostics Nichols Institute, where he is Medical Director. The commercial laboratory arena has such an important role in serving so many patients, including our special populations, and we appreciate his contributions to our team. Dean hails from Children’s Hospital of Pennsylvania (CHOP), where he is Associate Professor of Clinical Pathology and Laboratory Medicine in the University of Pennsylvania’s Perelman School of Medicine’s Pathology and Laboratory Medicine, and comes with a record of both scholarly and clinical contributions. Are any of our readers ready to consider getting more involved in our Division management? If so, we are eager to hear from you.

Happy reading, and best wishes for summer rest and relaxation—it’s good for everyone!

Sharie Geaghan M.D., Chair, Pediatric Maternal Fetal Division

Reference Interval Corner

Sharon M Geaghan M.D.

Serum S100B Levels in Pediatrics

S100B protein is produced primarily by astrocytes in the central nervous system. This specific protein is part of the S100 super family of proteins. These homodimeric structures have two Ca++-binding sites and one Zn-binding site on each monomer. S100B is a functional protein which acts on a variety of intra- and extracellular targets that include cytoskeleton proteins and those that are involved with cellular regulatory activities. Though not entirely specific to brain tissue, elevated serum levels are indicative of brain tissue injury. S100 protein is released either directly into the bloodstream or through a compromised brain-blood barrier. The reader is referred to a recent review of the S100B protein for a thorough analysis of this marker in biological fluids, current investigations and its clinical correlates¹.
Recently published studies of serum S100B measurements in healthy infants and children establish the S100B reference values associated with health in the pediatric population, which is quite distinct from adults\(^2\)-\(^8\). S100B levels are consistently inversely correlated with age in multiple studies. Cord blood has higher S100B levels than maternal blood levels in matched fetal-maternal pairs, and is higher in arterial cord blood compared with venous cord blood, which supports an independent fetal production of S100B\(^2\). High S100B levels are evident at birth, with one study indicating that the mode of delivery may have a statistically significant impact on S100 levels. Prolonged vaginal deliveries have higher levels than either usual vaginal or caesarean deliveries, consistent with possible minor head trauma associated with difficult vaginal birth\(^3\).

The generally higher levels in infancy compared with later childhood have been posited to reflect a more permeable blood-brain barrier, increased cell turnover and proliferation characteristic of growth and development of the child’s central nervous system, or as evidence of its role as a trophic cytokine. One investigation found an overall trend of high S100B values in the first year of life followed by a sustained decrease in levels, then from seven years onward, a progressive increase was observed, peaking again in adolescence. These findings led to their suggestion that S100B may serve a neurotrophic effect, since the levels surge, coincident with peak height growth velocity\(^8\). Although some studies have found gender differences in certain age groups, others have not; therefore, categories are not segregated by gender here.

A developing literature has focused on S100B and other potential biomarkers of central nervous system injury as a way to inform clinical evaluation and management of head trauma. A threshold cut-off value for serum S100 has been established to guide decision-making, together with clinical evaluation, to possibly avoid unnecessary hospitalizations and/or CT scans, with associated costs and radiation exposure which are particularly risky to the developing brain\(^10\). The short half-life of S100B of 25.3 ± 5.1 min (range 18.9-36.7 minutes) has limitations in application to clinical settings\(^11\). Some investigators have suggested urinary S100B measurements to assess brain injury, and a study of urinary levels in healthy children has been published\(^12\). In our Excerpt From the Literature feature this issue, we highlight the use of S100B for its negative predictive value in the management of pediatric brain trauma patients presenting to the emergency room. This type of test utilization- employing a test which has been demonstrated to add clinical and economic value in an evidence-based clinical algorithm- represents a rational strategy to apply more generally to diagnostic testing, and can be a key factor in successful resource conservation.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>Method</th>
<th>Manufacturer</th>
<th>Age</th>
<th>Mean (μg/L)</th>
<th>Maximum (μg/L)</th>
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</thead>
<tbody>
<tr>
<td>Neonates (2)</td>
<td>12</td>
<td>Double antibody immunoluminometric assay</td>
<td>Sangtec Medical AB Sweden</td>
<td>Cord blood</td>
<td>1.6</td>
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<td>24</td>
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<td>Roche Diagnostics</td>
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<td>0.67</td>
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<tr>
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<td>25</td>
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<td></td>
<td>27</td>
<td></td>
<td>Roche Diagnostics</td>
<td>Caesarean section</td>
<td></td>
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<td>Healthy children in first three years of life(4)</td>
<td>186</td>
<td>Electroluminescence immunoassay</td>
<td>Roche Diagnostics</td>
<td>0-3 mo</td>
<td>0.38</td>
<td>0.62*</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>4-9 mo</td>
<td>0.23</td>
<td>0.35*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10-24 mo</td>
<td>0.16</td>
<td>0.23*</td>
</tr>
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<td></td>
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<td></td>
<td>25-26 mo</td>
<td>0.11</td>
<td>0.17*</td>
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<td>Electroluminescence immunoassay</td>
<td>Roche Diagnostics</td>
<td>&gt; 3-18 yrs</td>
<td>0.10</td>
<td>0.16*</td>
</tr>
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<td>372</td>
<td>Electroluminescence immunoassay</td>
<td>Roche Diagnostics</td>
<td>1-2 yrs</td>
<td>----</td>
<td>0.21*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3-14 years</td>
<td>----</td>
<td>0.15*</td>
</tr>
<tr>
<td>Healthy children (7)</td>
<td>20</td>
<td>ELISA</td>
<td>Biovendor Laboratomi Medicina A.S.</td>
<td>&lt; 15 yrs</td>
<td>0.13</td>
<td>0.16**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean =51.5 mo</td>
<td></td>
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</tr>
<tr>
<td>Healthy children (8)</td>
<td>1004</td>
<td>Immunoluminometric assay</td>
<td>AB Sangtec Medical</td>
<td>0-15 yrs</td>
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<td>Biovendor Laboratomi Medicina A.S.</td>
<td>&lt; 15 yrs</td>
<td>0.13</td>
<td>0.16**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean =51.5 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults (9)</td>
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<td>Roche Diagnostics</td>
<td>adult</td>
<td>0.045</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* 95th percentile

** Highest in range

**References**

The ABC’s of Pediatric Laboratory Medicine- P is for Procalcitonin

By David Carpentieri, Pediatric Pathologist and Biorepository Director, Phoenix Children’s Hospital

Stephanie Souza, Clinical Laboratory Specialist, Blood Systems Laboratories, Tempe, AZ

Background:

The history of Procalcitonin (PCT) dates back to the clinical association of toxic shock syndrome with hypocalcemia, and the discovery of a polymeric form of calcitonin in the mid 1970’s (10). The structure of PCT was described in 1981, but it was only in 1993 that the first association with the diagnosis of sepsis was published (2). Since then, the literature has produced almost 2,000 articles related to the
clinical utility of PCT and approximately 15% of these are related to pediatric diseases. In recent years, the measurement of PCT in serum or plasma has gained acceptance not only as a marker for the diagnosis and monitoring of bacterial sepsis (23, 26), but for other inflammatory conditions as well.

Molecular:

Synthesis of PCT is regulated by the CALC-1 gene which is composed of 6 exons located on the short arm of chromosome 11. PCT is comprised of 116 amino acids and is a precursor to the calcium regulating hormone calcitonin (3). This molecule contains an amino terminus (N-ProCT) composed of 57 amino acids, an immature calcitonin (CT) portion and a 21 amino acid C-terminus, also known as katacalcin moiety (Figure 1).

The serum of normal individuals contains several peptide fragments produced by post-translational enzymatic processing of the PCT molecule (3, 27) in the thyroid C-cells. Under normal physiological conditions, the C-cells produce CT by glucocorticoid, calcitonin gene related peptide, glucagon, gastrin and β-adrenergic stimulation. Somatostatin and vitamin D suppress CT production. However, during an inflammatory response, PCT production is induced by both bacterial toxins and cytokines in parenchymal cells. These cells lack the appropriate secretory storage and the ability to modify PCT into CT (24), resulting in elevated levels of PCT in the circulation. Under experimental conditions, bacterial endotoxins induce a PCT peak in 6 hours with a plateau between 8-24 hours (12). The PCT peak occurs after the elevation of tumor necrosis factor (TNF) and IL-6 but before the rise of C-reactive protein. It is suggested that TNF, IL-1, IL-2 and IL-6 may block the proteolysis of PCT to CT, resulting in the low levels of CT in the serum of patients with sepsis.

Laboratory Analysis and Interpretation:

PCT has a half-life of approximately 24 hours and can be measured in serum and plasma (EDTA or heparin). No publications have reported the analysis of PCT in other body fluids. The first monoclonal antibodies used in the detection of PCT were developed in 1988 and allowed for plasma analysis without cross-reactivity to mature CT. Recently, antibodies binding PCT (but not other post-translational fragments such as free CT, free katacalcin or free N-procalcitonin) were patented, but their clinical utility remains unknown. These antibodies might have different functional properties and half-lives in vivo. Therefore, the potential exists for future diagnostic applications superior to those currently available (35).

There are several commercial quantitative and qualitative immunoassays for PCT (33) which utilize a variable combination of antibodies targeting katacalcin and CT. The random access automated PCT Kryptor from BRAHMS was only approved for use in the United States within the last decade. The BRAHMS automated assays (31) have an analytical sensitivity ranging from 0.04-0.1 ng/mL with a functional sensitivity ranging from 0.05-0.3 ng/mL depending on the platform. Roche and Siemens systems are currently pending FDA approval, and the manual point of care method (PCT-Q) is only available in Europe (17).

The analytical performance of the Kryptor automated platforms has been described (20, 35) by users in Europe and Korea. These studies revealed coefficients of variability of up to 20% with reduced precision at lower values. Bias due to interferences from bilirubin, hemoglobin and triglycerides are automatically corrected by the instruments.
The PCT molecule is stable when stored at 4°C over 4 days. This is significant when considering the common practice of requesting additional analysis, a frequent occurrence in the management of pediatric patients.

A major pre-analytical issue to consider when interpreting PCT results in infants is the physiologic peak of PCT during the first 48 hours post-delivery. PCT values may increase during the first 24 hours post-trauma, in patients with circulatory shock, and in transplant patients receiving pan T-cell antibody (29) or anti-thymocyte globulin therapies (5). PCT appears to be a reliable marker of serious bacterial infection in the setting of recent vaccinations (13).

Importantly, the historical reference range (Table 1) utilized in the interpretation of PCT for the diagnosis of sepsis can lead to significant interpretative uncertainty about the optimal cut off values in the management of pediatric sepsis. Therefore, we recently reviewed our data on hospitalized children utilizing positive and negative bacterial culture results as the gold standard for the determination of sepsis/bacteremia.

In our first analysis (6) of 98 patients, PCT values were associated with 37 positive and 61 negative blood cultures. If not previously tested, PCT values were determined in samples obtained within 6 hours from the time of a culture collection. The positive predictive value (PPV) and the negative predictive value (NPV) for sepsis/bacteremia at the cut off value of 2.0 ng/mL were 60% and 75%, respectively. No positive culture was seen with a PCT value below 0.09 ng/mL. The second analysis (7), based on data collected from patients with the clinical suspicion of sepsis, contained 452 PCT and associated blood culture results. PCT had a poor positive predictive value (9%) for sepsis/bacteremia at levels above 2.0 ng/mL, possibly biased by the low number of positive cultures (18). In contrast, the negative predictive value of PCT for sepsis/bacteremia at levels below 2.0 ng/mL was between 95-100%. The lowest PCT value in this setting associated with a positive culture was 0.05 ng/ml.

**Clinical Pediatrics:**

PCT, among other biomarkers, has the potential to improve our ability to ascertain the diagnosis of sepsis or serious bacterial infections (SBI), regardless of age or clinical context (32, 38, 39). As an example, PCT analysis had a high sensitivity and specificity for the detection of early-onset sepsis in the first 48 hours of life, despite the expected physiologic peak (11). Similarly, PCT had a high sensitivity (95%), and reliably detected SBI in the neonatal period (less than 90 days old) at the cutoff value of 0.12 ng/mL (25). The analysis of cord blood may also be of value for this population, when prenatal infection is suspected (19). PCT has also been shown to be a useful marker of sepsis for children in immediate cardiac post-operative care (1).

PCT has also been evaluated as a biomarker in other conditions. Among these, serum levels have been well correlated with the prediction of acute pyelonephritis, creating the potential to reduce unnecessary cystographies in febrile children with suspected urinary tract infections (4, 22, 28). When compared to other inflammatory biomarkers, PCT has a greater specificity for the diagnosis of bacterial infections (34, 40) including tonsillolaryngitis (16). In addition, PCT values are also directly correlated with the clinical outcome of children admitted with the diagnosis of meningitis (9, 15) or E. Coli O157:H7 induced hemolytic-uremic syndrome (14). However, the role of PCT in the evaluation, diagnosis, and management of pediatric patients with lower respiratory infections, febrile neutropenia (21, 37), hemophagocytic lymphohistiocytosis, and fungal septicemia (among other disorders with inflammatory changes) is not conclusive, and will require additional studies.
Final Comments:

Caution is recommended when interpreting PCT values in the screening of children with suspected sepsis/bacteremia. In this context, the sensitivity and specificity of the PCT result appears to be related to which clinical gold standard was applied to each study. Furthermore, future studies may reveal different critical cut off values/reference ranges for PCT in children (30) based on different ages (8), clinical diagnosis (36) and emerging methodologies. In our experience, PCT trends appear to be a more useful predictor for antibiotic therapy compared to PCT absolute values. However, PCT absolute values appear to reflect the severity of an infectious process and may be predictive of mortality (9, 14). Finally, one needs to carefully evaluate the cost effectiveness of PCT considering the increased cost versus other available biomarkers.
Table 1: Historical reference range

<table>
<thead>
<tr>
<th>PCT VALUE</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.05 ng/ml</td>
<td>Not supportive of sepsis. A repeat analysis is indicated in 24-30 hours. Rising values should be correlated with clinical information and antibiotic resistance data.</td>
</tr>
<tr>
<td>(0.05-2) ng/ml</td>
<td></td>
</tr>
<tr>
<td>&gt; 2 ng/ml</td>
<td>Probability of sepsis is high.</td>
</tr>
</tbody>
</table>

References:


Acknowledgment:
Charles Mitchell (Blood Systems Laboratories, HLA lab) for the PCT graphic
AACC Division Poster Winners

Congratulations of the winners of the Pediatric and Maternal Fetal Division 2012 poster session awards. Please check out their posters at the annual meeting!

**Best poster:** Brad Karon, Mayo Clinic, Rochester MN

Impact of a universal inpatient transcutaneous bilirubin screening program on the distribution of serum bilirubin values among healthy neonates at a single institution

**Runner up:** Victor Margalet, Virgen Macarena University Hospital, Seville, Spain

Increased expression and phosphorylation of the RNA binding protein Sam68 in the placenta from women with gestational diabetes mellitus (GDM)

**Student and Young Faculty Award:** Eduardo Martinez Morillo, Mount Sinai Hospital, Toronto ON

Development of selected reaction monitoring assays for quantification of biochemical markers of Down syndrome in amniotic fluid samples

**Runner up:** Yu Chen, Horizon Health Network Fredericton, New Brunswick, Canada

Performance Evaluation of Siemens ADVIA Centaur and Roche MODULAR Analytics E170 Total 25-OH Vitamin D Assays

**Award for Outstanding Contributions to Pediatric and Maternal-Fetal Clinical Chemistry**

Dennis J. Dietzen, Ph.D., DABCC, Associate Professor of Pediatrics
Washington University School of Medicine
On July 17, 2012 we will honor Dr. Dennis J. Dietzen as this year’s recipient of our highest Division Award, for outstanding contributions to our specialized discipline of pediatric maternal fetal clinical chemistry. We will share more about Dr. Dietzen in our next issue.

Congratulations to all the award winners.

2012 AACC Annual Meeting

Once again, it is time for the AACC Annual Meeting. Here are some sessions of interest for members of the Pediatric and Fetal Maternal Division.

- Indicates a ticket is required for the session

Sunday July 15

Opening Plenary: Wallace H. Coulter lecture by Eric Green, MD, PhD
“Entering the Era of Genomic Medicine: Research Opportunities and Challenges”

AACC University:

Advances in Prenatal Risk Assessment for Down’s Syndrome and other Abnormalities

Genetic Testing: Principles Applied to Case Studies

Monday July 16

Plenary: Robert Roberts, MD, “9p21 DNA Variants Associated with Coronary Artery Disease Risk”

Brown Bag Sessions:

Demystifying Metabolic Testing: Amino Acid Analysis

Blood, Sweat and Tiers: Screening and Diagnosis of Cystic Fibrosis

Application of MicroRNA to Maternal Fetal Medicine

Symposia:

eGFR in the Context of Drug Dosing for Pediatric Patients

Current Topics in Thyroid Disease

Short courses/Interactive Workshops:

Reference Intervals: Practical Approaches

Contemporary Fetal Lung Maturity Testing: How to Validate the lamellar Body Count/LBC

Tuesday July 16

Plenary: Panel Discussion, The Ethics of Human Tissues in Research

Brown Bag Sessions:

Update on Preeclampsia Diagnosis

Demystifying Metabolic Testing: Organic Acid Screens

Diagnosis of Bacterial Vaginosis, Available Testing Technology?

Symposia:
Debate on the Diagnosis of Gestational Diabetes Mellitus

Applications for Measurement of Arginine and its Methylated Derivatives (ADMA and SDMA) in Adult and Pediatric Disease

**Special Events:**

Pediatric and Maternal Fetal Division Dialogue on Advancing Pediatric Reference Ranges

Pediatric Maternal Fetal/Industry/Clinical Translational Science Divisions Joint Mixer and Abstract/Poster Awards

**Wednesday July 17**

**Plenary:** Elaine Mardis, PhD, “Whole Genome Sequencing in the Clinical Laboratory”

**Brown Bag Sessions:**

Past, Present and Future of Newborn Screening

Anti-Mullerian Hormone (AMH): Fertility Assessment and Beyond

Role of Therapeutic Drug Monitoring in Pediatric Cancer Chemotherapy

Demystifying Metabolic Testing: Acylcarnitine Screens

False-Positive hCG Results: What Every Lab Should Know

**Symposia:**

Update on Thyroid Disease in Pregnancy

**Short Courses/Interactive Workshops:**

The PATH Towards Accurate Steroid Hormone Testing

Contemporary Prenatal Testing for Down Syndrome: A DNA-Based Approach

**Thursday July 18**

**Plenary:** Alice Lichtenstein, D.Sc, “Diet and CVD Prevention, Where Should the Emphasis Be”

**Symposia:**

New Developments in Metabolic Disease Testing
Excerpts from the Literature

Compiled by S. Geaghan MD


This prospective study aims to evaluate the utility of serum S100B measurement in the management of mild traumatic brain injury (mTBI) on a large cohort of children. Children less than 16 years of age who presented at a pediatric emergency department within 3 h after TBI had venous blood samplings to determine serum S100B concentrations. The serum S100B concentration differences in children with closed head trauma—446 children, divided into 3 groups on the basis of TBI severity (minimal, mild, and severe)—were found to be statistically significant. This biomarker correctly identified patients with either positive findings on CT scan (100% sensitivity at a cutoff threshold of 0.18 μg/L) and correctly identified those with “bad” clinical evolution (CE) (100% sensitivity at a cutoff value of 0.19 μg/L). The low specificity for S100B for each of these clinical findings of positive CT scan and bad CE underscores that this is a nonspecific marker.

S100B has a short half-life of 120 min so any proposed future algorithm must include the caveat that a venous sample must be taken within 3 h after the TBI. Delayed serum S100B measurements following a head trauma may lead to false negative interpretations, and underestimate extent of central nervous system damage. These results, when fully validated in multicenter trails, support the potential value of serum S100B determination during the first 3 h of management of children with mTBI. A proposed new management algorithm for triage and classification of patients by interview and clinical examination, together with S100B measurement, could provide both economic and health benefits, such as reduction of the number of CT scans and associated irradiation, and hospitalization cost savings.


This prospective cohort study asked several questions: can early cystatin C levels predict acute kidney injury associated with cardiopulmonary bypass in pediatric cardiac surgery patients? Can these levels predict pediatric-modified RIFLE (Risk, Injury, Failure, Loss, End-stage kidney disease) class, renal injury and estimated glomerular filtration rate? Can ultra filtration during cardiopulmonary bypass effect cystatin C levels? These are important questions, as acute kidney injury is frequent and a serious complication of cardiopulmonary bypass. Serum creatinine measurements are used to detect acute kidney injury in children, whereas cystatin C has been shown to have superior predictive value (as
compared with serum creatinine) for predicting acute renal injury in adults following cardiopulmonary bypass. In these 100 pediatric patients who underwent cardiac surgery with cardiopulmonary bypass, cystatin C levels decreased with removal of fluid volume by ultra filtration and was predictive of acute kidney injury in children after cardiopulmonary bypass. Cystatin C was predictive of pediatric RIFLE classification and of decreased estimated glomerular filtration rate after cardiopulmonary bypass. This study represents a contribution to the difficult diagnostic area of laboratory measurement of pediatric renal function, and suggests that serum cystatin C may be equally good as a biomarker in the laboratory evaluation of acute kidney injury in children, as has been demonstrated in adults.


This perspective from Dr. Maisels, a favorite lecturer at AACC Annual Meetings and a distinguished neonatologist, highlights the advantages of TcB measurements. These include: noninvasive and painless measurements, elimination of wait time for the infant’s bilirubin concentration, facilitation of multiple measurements within a day (allowing for the calculation of rise in bilirubin concentration to better inform clinical evaluation), reduction of TSB measurements, probable cost reductions and patient safety improvement. Maisels discusses the Wainer et al. report (Pediatrics 2012;129:77-86) of the introduction of routine TcB measurements to discharge care for 14,796 neonates discharged from three nurseries in Calgary, compared with a historical cohort of 14,112 neonates for whom visual inspection was utilized. The technology implementation yielded a 55% reduction in the incidence of TSB values >20 mg/dL (> 342 μmol/L). TSB draws were reduced by 23% and the overall phototherapy rate decreased from 5.27% to 4.3%. The authors’ conclusion, underscored by Maisels: implementation of TcB measurements in the public health program offered improved patient safety and a concordant decrease in resource utilization.

Maisels projects greater use of TcB measurements inside and outside of acute care settings in the future, and calls for change in the oversight of these measurements to fall under the clinical laboratory, which is not currently the standard in the U.S.

**SAVE THE DATE**

A Special Invitation: Industry-AACC Pediatric Maternal Fetal Division Dialogue on Advancing Pediatric Reference Intervals

Tuesday July 17th, 2012
The Pediatric/Maternal-Fetal Division and Pediatric Reference Range Committee (PRRC) invite you to attend this special session at the 2012 AACC Annual Meeting.

The Opportunity:

The session will focus on opportunities for AACC, clinical laboratories, commercial laboratories and medical device manufacturers to partner together to develop new pediatric reference intervals. The National Institute of Health’s National Children’s Study (NIH-NCS) has been launched, which has and will provide a unique resource of quality pediatric samples for potential projects deemed appropriate to the NIH-NCS mission.

Learn about the Pilot Study:

You can hear about the AACC-sponsored pilot study, an 'adjunct' to the NIH National Children's Study, designed to advance pediatric reference ranges for certain amino acids and steroids. We hope this is the beginning of a much broader effort.

Projects Offer Potential Benefits to Patients, Laboratories and Industry Partners Alike

AACC believes the time is right for all potential stakeholders with an interest in developing global reference range values throughout childhood to join us in this important initiative. The Division and PRRC are hoping more associations, manufacturers and laboratories will partner with us to provide improved clinical data for physicians to make better decisions affecting children's health, and these efforts also allow commercial entities to develop added value in competing for the pediatric sector. To learn more about AACC Pediatric Reference Range Initiative, please visit the study web page at http://www.aacc.org/resourcecenters/resource_topics/pediatric_reference_range/pages/default.aspx#.

We hope to see you there!

Sharon Geaghan, PhD
Chair, PMF Division

Mike Bennett, PhD
Chair, Pediatric Reference Range Committee