The Perinatal Gazette

Newsletter of the Regional Perinatal Center Maria Fareri Children’s Hospital at Westchester Medical Center

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The Case for Judicious Use of Antibiotics

Blood stream infections (BSI) are among the most common causes of mortality and long term morbidities in the neonatal, pediatric and adult patients. The incidence of BSI has been increasing steadily with particularly alarming rates of increase in multi-drug resistant bacterial sepsis. Various patient and practice related factors have been found to contribute to the development of BSI. In the neonatal period, the gestational age and the severity of illness have a direct effect on the immunologic response and the attendant outcome of sepsis. Maternal and perinatal infections, presence of central lines, duration of TPN and NPO state, infection control practices and antibiotic usage have been all also implicated. Consequently, the incidence, mortality and complication rates of neonatal BSI vary among institutions. Neonatal BSI are classified into early (EONS) and late (LONS) onset sepsis, of neonatal BSI vary among institutions. Neonatal BSI are classified into early (EONS) and late (LONS) onset sepsis, occurring before and after 72 hours of life respectively. A separate category of nosocomial sepsis, defined as blood stream infection occurring after 72 hour of hospitalization, is currently being used as a marker of quality of care and its reporting is mandated by law. Nosocomial sepsis accounts for approximately 45% of all deaths after 2 weeks of age in VLBW infants. EONS occurrence rate is 4 - 27/1000 live births with most common causative organisms being Group B streptococcus, Escherichia coli and Listeria monocytogenes, acquired predominantly in the peripartum period. LONS is caused by a wide variety of Gram positive, Gram negative and fungal organisms and vary among institutions (20 – 40%), with preterm infants having 30 fold higher infection rates than term neonates.

In suspected LOS, broad spectrum antibiotic coverage is begun empirically before the results of the blood culture. Commonly used antibiotics are Oxacillin or Vancomycin for Gram positive and Cefotaxime or aminoglycosides for Gram negative organism coverage. Vancomycin is the preferred choice in many centers due to the high prevalence of nafcillin/ oxacillin resistance of hospital acquired coagulase negative staphylococcus (CoNS) and other Gram positive flora. Vancomycin is well tolerated in the neonatal period. Neonatal nephrotoxicity is rare and reversible even in presence of other nephrotoxic agents and usually associated with high trough levels. Oto toxicity although extremely rare in humans, is irreversible. The newer preparations are safer, however strict through level monitoring should be done to prevent this completely avoidable untoward effect (level >80 mg/l).

Cefotaxime is a third generation cephalosporin, with broad spectrum bactericidal activity against most Gram negative and some Gram positive organisms. In recent years, Cefotaxime has become the preferred antibiotic for empiric broad spectrum coverage because of its safety and no need for serum level monitoring. However there are growing concerns with the broad use of 3rd generation cephalosporins, such as increase in the incidence of sepsis caused by fungal, cephalosporin-resistant and extended spectrum beta-lactamase producing Gram negative, and Vancomycin-resistant Gram positive organisms and outbreaks of Acinetobacter baumanii. Combination therapy with Vancomycin and 3rd generation cephalosporin has been reported in sepsis caused by Vancomycin resistant Enterococcus (VRE) and Staphilococcus aureus. P. De Man et al. (Lancet 2000) demonstrated that Ampicillin/ Cefotaxime combination was associated with 18 times higher colonization rates with resistant Enterobacter species. In the same study the patients in the Penicillin/ Tobramycin group had shorter length of stay.

In a recent survey in our NICU in MFCH, we found that 62% of LONS was caused by Gram positive bacteria, 32% by Gram negatives, predominantly Klebsiella and Enterobacter, and 6% by fungal organisms. We have also previously reported antibiotic induced selective inhibition of the normal intestinal flora of the preterm neonates and colonization with 3rd generation cephalosporin resistant Enterobacter species. These resistant pathogenic organisms may serve as a reservoir for blood stream infections through GI mucosal translocation.

Practice for LOS empiric antibiotic coverage in Australia,
UK and New Zealand have already changed to Nafcillin and aminoglycosides instead of cefotaxime after these publications. However, in a June 2000 survey conducted by the National Association of Children’s Hospitals, the Pediatric Prevention Network and CDC in 34 NICU with 278 participating clinicians, 75% of whom were attending neonatologists; 22% reported routine use of third generation cephalosporin as empirical anti-microbial therapy for suspected LONS, which increased to 39% in the presence of shock.

Aminoglycosides have high Gram negative effectiveness, low resistance rates and low cost (Gentamicin: 2.80$/day vs Cefotaxime: 52.23$/day). They irrevocably inhibit protein synthesis in the microbial ribosomes. They have rapid bactericidal activity against wide range of Gram negatives, some activity against Gram positives and a post-antibiotic effect. Concerns with their use are the need to monitor serum levels to prevent adverse effects such as nephrotoxicity, ototoxicity (rare but irreversible, very strongly associated with Amikacin) and neuromuscular blockade (extremely rare). Another precluding factor for their wider use is the reported poor penetration into the CSF. Although with meningeal inflammation, gentamicin penetration in the CSF has been shown to improve, a normal CSF cell count and chemistry should be obtained prior to selecting gentamicin in empiric Gram negative sepsis coverage. The currently recommended regimens for gentamicin administration at once daily in full term neonates and Q 48 hours in preterm neonates lead to excellent therapeutic serum levels. Once sepsis is excluded by the 48 hours negative blood culture, the antibiotics can be stopped without serum level monitoring. Monitoring must be done at a steady-state if gentamicin treatment is continued, as the bactericidal activity is trough-level dependent while the toxicity is peak-level dependent. Theoretical concern exists about potentiating nephrotoxicity when combining Vancomycin and gentamicin. Although reported in adults after prolonged use, it is very uncommon in pediatric and neonatal patients and reversible after discontinuation of treatment.

In conclusion, judicious use of antibiotics (selective initiation, early discontinuation and limiting of 3rd generation cephalosporins) will prevent further increase in resistant organisms as pathogens or colonizing flora in the hospital settings and in the community. Ongoing surveillance of the microbiologic epidemiology and antimicrobial susceptibilities should be part of the infection control practices. The empiric antibiotic coverage for suspected BSI must be based on hospital, unit and community specific bacterial prevalence and antibiotic susceptibility patterns. The antibiotic treatment for confirmed sepsis should be adjusted as soon as the causative organism and the sensitivity are identified.

Based on our review of the current evidence and the prevalence and antimicrobial susceptibilities at our NICU and hospital flora, we recommend the following Antibiotic Protocol:

**Table 1: Antibiotic Protocol**

<table>
<thead>
<tr>
<th>CBC, BCx, + LP and UCx</th>
<th>Clinda, Amp/Genta</th>
<th>Vancomycin + Cefotaxime</th>
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</thead>
<tbody>
<tr>
<td>Meningitis (seizures, abn CSF)</td>
<td>Add gentamicin if shock Consider fungus or other pathogens</td>
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<tr>
<td>NEC</td>
<td>Add meropenem if GN bacilli, then Adjust antibiotics per susceptibility Duration of tx per organism and site of infection</td>
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<td>Duration of tx per organism and site of infection</td>
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**The Maria Fareri Children’s Hospital RNICU Welcomes 3 New Fellows**

We warmly welcome the following fellows who have joined our neonatal fellowship program at the MFCH at WMC RNICU as of July 1, 2006

**Caroline Chua** – Caroline came to us from Flushing Hospital Medical Center after completing her residency there. While in the Philippines, she worked as a pediatrician in private practice and was responsible for the direct management of pediatric patients at Ton Yen General Hospital in Taiwan. Caroline is fluent in English, Chinese Dialect, Mandarin and Tagalog.

**Portia Groening** – Portia has completed her residency from Schneider Children’s Hospital in New Hyde Park, NY. She was on the Dean’s list at Meharry Medical College and won outstanding student award in biochemistry there. In working toward her M.S. in biology, her thesis was on imaging DNA using atomic force microscopy. She spent one year after graduate school researching genetics of hypertension in African American families.

**Jessica Kalia** – Jessica will be joining us as a 2nd year fellow, having completed her first year at the Robert Wood Johnson University Hospital in New Jersey. Her residency was completed at Newark Beth Israel Medical Center. Her scholarships and awards included a program for the medically underserved scholarship, an award for dedication to osteopathic medicine and a medical education scholarship from the student osteopathic medical Association foundation. Jessica’s research interests are in epidemiology and biostatistics.

**Free Online Source of Perinatal Health**

[www.marchofdimes.com/PeriStats](www.marchofdimes.com/PeriStats)

Developed by the March of Dimes Data Center with funding from the National Library of Medicine. This site provides free access to US, state & local maternal & infant health data.
Annual Perinatal Day Symposium a Great Success!

The Annual Perinatal Day Symposium was held this year at the The Maria Fareri Children’s Hospital on the campus of Westchester Medical Center and New York Medical College on May 4, 2006. It was graciously sponsored by the Committee on Fetus and Newborn and the Perinatal section for New York Chapter 3, District II of the American Academy of Pediatrics (AAP). It was attended by approximately 160 physicians, nurses, nurse practitioners, physician assistants, and respiratory therapists. This 2006 Annual Perinatal Day Symposium heard from a number of distinguished, internationally-renowned speakers about a number of “hot topics” in neonatology.

Following a welcome from Dr. Sheila Palevsky, the vice --president for NY Chapt. 3, District II of the AAP, Dr. Jonathan Faranoff, a neonatologist and lawyer who is the associate director of the Rainbow Center for Pediatrics Ethics at Rainbow Babies and Children’s Hospital in Cleveland, OH opened the conference with his presentation on “Neonatal ethics at the verge of viability.” Dr. Ragansamy Ramanathan, from the University of Southern California and Keck School of Medicine then delivered a presentation entitled: “Inhaled nitric oxide and preterm infants: when to say yes to “NO” and no to “NO”?

The Harry S. Dweck M.D., FAAP Memorial lecture was delivered by Dr. Ramanathan following remembrances of Dr. Dweck, who had attended Dr. Ramanathan’s NICU rotation. Dr. Ramanathan graciously agreed to deliver this presentation on minimal notice when it was learned that Dr.Ola Saugstad from Norway would be unable to attend because of an illness in his family. Dr. Ramanathan captured the interest of the audience when he presented evidence of the ill effects of supplemental oxygen delivery to newborns.

Following lunch and tours of the MFCH, De. Jacob Aranda, Professor of Pediatrics and Pharmacology at the Children’s Hospital of Michigan, Detroit, MI, reviewed the evidence for using: “Intravenous Ibuprofen for the newborn infant.” This medication has recently been approved by the FDA for the treatment of patent ductus arteriosus.

Rounding out the program was Dr. Robert Ambler, who is a pediatrician, and is Dean of the School of Public Health at the New York Medical College. He gave an inspirational talk on: “Infant survival disparities-opportunities and obligations.”

Much was learned by all and we look forward to next year’s symposium with great enthusiasm!

5th ANNUAL HUDSON VALLEY REGIONAL PERINATAL FORUM CONFERENCE

Sponsored by The Maria Fareri Children’s Hospital at Westchester Medical Center, the March of Dimes, Maternal Infant Services Network and the Lower Hudson Valley Perinatal Network

The Interplay of Stressors in Perinatal Health: Racism, Obesity, and Violence

November 1, 2006

Mariott Westchester, Tarrytown, NY

9a.m – 4 p.m.

Keynote Speaker: David Satcher, M.D.PhD:

Guest Speakers: Camara Jones, M.D, MPH, PhD & Janet Rich-Edwards, ScD

The Lower Hudson Valley Perinatal Network - LHVPN

The Lower Hudson Valley Perinatal Network (LHVPN) summer edition of their quarterly education and networking meeting was held June 20th, 2006 in Dutchess County at the Casperkill Golf Cub. The meeting hosted more than 100 guests who came to learn about and address the issues of Prematurity and Developmental Outcomes. The LHVPN was honored to have Dr. Karla Damus, RN, MSPH, PhD and Dr. Jordan Kase, M.D. as presenters on this very important topic. Karla Damus provided a HuGE update on preterm birth prevention, research, and the national campaign. Dr. Kase spoke about Prematurity outcomes right here in the Hudson Valley. During the county round table discussions, each of the four counties were able to outline the barriers their communities face in obtaining proper prenatal care, as well s devise action plans to eliminate those barriers. The LHVPN thanks all who were part of this very important and informative educational initiative. Please continue to check the LHVPN website lhvpn.net for links to perinatal resources in the lower Hudson valley and upcoming events.

*We would like to thank Respironics and GlaxoSmiathKline for supporting this event.

Cheryl Hunter-Grant, Executive Director at hunter-grantc@lhvpn.com or call 914-4936435.
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http://www.nymc.edu/neonatology