Rural Healthcare Quality Network

Hospital Peer Alert

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Hospital Peer Review *is a monthly newsletter sponsored by the Rural Healthcare Quality Network to alert Critical Access Hospitals regarding findings from the Peer Review Program. Summarized are a few of the key findings and best practices that would be helpful for other critical access hospitals to be knowledgeable about. This newsletter is edited by Myron Bloom, Medical Director and he can be reached at drmbloom@msn.com.*

Handling Hot Babes

Fever without apparent source in infants less than 3 months of age

A rectal temperature of 38°C (100.4°F) generally is regarded as fever in the neonate 0 to 28 days of age. The definition of fever in the one to three month-old varies from 38 to 38.2°C (100.4 to 100.7°F) depending on the study cited. All febrile neonates (age < 28 days) should be considered high risk, warranting a complete sepsis evaluation and hospital admission as 1 in 8 febrile neonates will have a serious bacterial infection [SBI]. But there is uncertainty about which baby in the second or third month of life can be managed safely as an outpatient at home by reliable caregivers and whether they should be empirically given antibiotics.

A meta-analysis of studies published between 1974 and 1990 found that 7.2 percent of all febrile infants with a temperature >39°C or 102.2°F under three months of age had an SBI [1]. A primary care office setting study from the Pediatric Research in Office Settings (PROS) network found that the incidence of both bacteremia and bacterial meningitis decreases with age: 3 and 1.1 % respectively in neonates, 1.4 and 0.4 % in infants in the second month of life, and 0.7 and 0 % in infants older than two to three months of age[2]. Current studies suggest that **well appearing** infants between 28 and 90 days of age categorized as low risk after a careful history and physical examination have an incidence of SBI somewhere between 0.5 to 1.1 percent[3]. But let's be clear about well appearing and low risk, which means not ill appearing and a statistical risk of SBI below the threshold of false positive testing results given a normal physical exam and negative past history, and paying attention to the details of the symptomatology and chronology of the present illness. Fever 39°C (102.2°F) or higher is the threshold above which evaluation for a source of occult infection, other than urinary tract infection (UTI), is often considered prudent[4].

Various protocols suggest it is safe to send home with close follow-up and without antibiotics febrile **well appearing** well hydrated term gestation infants older than a month, who were previously healthy (normal newborn nursery course and no previous illnesses) after careful history and physical examination.

Rochester protocol — no antibiotics for infants less than 60 days of age meeting these Laboratory criteria:

- WBC 5,000 to 15,000/microL with an absolute band count <1,500/microL
- UA <10 WBC/hpf and no bacteria seen
- Stool with <5 WBC/hpf if obtained
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Dagan R, Powell KR, Hall CB, et al. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. J Pediatr. 1985;107:855-60. Of 931 infants, 437 (47 percent) were categorized as low risk and five low-risk infants had an SBI (1.1%) with a negative predictive value of 98.9 percent (95% CI 97 to 100 percent) and there were no adverse outcomes, lending support to the consideration of less aggressive therapy in low-risk infants.

Philadelphia protocol — no antibiotics for infants between 29 to 60 days of age meeting these
Laboratory criteria:

- WBC 5,000 to15,000/microL with Band-neutrophil ratio <0.2
- UA <10 WBC/hpf and a negative urine Gram stain
- CSF <8 WBC/microL and a negative CSF Gram stain
- Chest radiograph without infiltrate if done
- Stool without blood and few or no WBCs on the smear

Baker MD, Bell LM, Avner JR. Outpatient management without antibiotics of fever in selected infants. N Engl J Med. 1993;329:1437-41. Categorizing 142 as low-risk infants (19 percent of the 747 study population), the sensitivity for identifying SBI was 98 percent (95% CI 92 to 100 percent); the specificity was 42 percent (95% CI 38 to 46 percent); the positive predictive value was 14 percent (95% CI 11 to 17 percent); and the negative predictive value was 99.7 percent (95% CI 98 to 100 percent). However, many well infants underwent excessive laboratory testing and many were managed as inpatients.

In contrast, the Boston protocol for infants 29 to 89 days of age uses higher white cell counts and ceftriaxone intramuscularly before being sent home with scheduled follow-up visit by 24 hours.
Laboratory criteria:

- WBC 5000 to 20,000/microL
- UA <10 WBC/hpf and a negative urine Gram stain
- CSF <10 WBC/microL and a negative CSF Gram stain if done
- Chest radiograph without infiltrate if done

Baskin, MN, O'Rourke, EJ, Fleisher, GR. Outpatient treatment of febrile infants 28 to 89 days of age with intramuscular administration of ceftriaxone. J Pediatr 1992; 120:22. Categorizing infants with a WBC count between 15,000 and 20,000/microL as low risk was more liberal than in other studies, and 27 patients (5.4 percent of 503) had an SBI identified during follow-up. Nevertheless, there were no adverse outcomes; all infants with SBIs received an appropriate course of antimicrobial therapy and were well at follow-up.

Viral infections are the most common cause of fever in neonates and young infants while the morbidity from viral infections is higher than in older children. Viruses that can cause significant infection include herpes simplex, varicella, enteroviruses, some adenoviruses, influenza virus, and respiratory syncytial virus. Bacterial pathogens that cause significant infection in the neonate are Group B streptococcus, Escherichia coli, and Listeria monocytogenes. Streptococcus pneumoniae and Haemophilus influenzae type b begin to rise in incidence in the second month and become the major bacterial pathogens by the third month of life. Sources of serious bacterial infection (SBI) among neonates and infants less than three months of age are urinary tract infections, bacteremia, bacterial gastroenteritis, bacterial meningitis, and cellulitis

Fever without a source in infants 3 to 36 months of age who appear well the following testing and treatment strategies have been suggested:

For most children three to six months of age, and for most children <36 months who have not been completely immunized-

- CBC and UA with urine culture.
- Blood culture and parenteral ceftriaxone if WBC ≥ 15,000/microL.
- CXR if WBC ≥ 20,000/microL.
- Follow-up with the primary care provider within 24 hours is recommended.

For children over six months of age who have received three doses each of Hib vaccine and PCV7-

- UA and urine culture for girls < 24 months and uncircumcised boys < 12 months
- No routine testing for girls >24 months of age
- No routine testing for uncircumcised boys >12 months of age
- No routine testing for circumcised boys greater than six months of age
- No empiric antibiotics for patients after 3 doses each of Hib vaccine and PCV7

In contrast the Guidelines from the Cincinnati Children's Hospital recommend that well-appearing children three to 36 months of age with a fever without an apparent source, who can receive excellent follow-up and who have completed their appropriate series of recommended vaccinations, may be considered for outpatient observation without any initial laboratory testing or empiric antibiotics. Paraphrasing their 2003 recommendations from the National Guideline Clearinghouse web page:

"Decision to conduct laboratory studies is dependent on results of clinical assessment: viral infections are the most likely cause of FUS; most children do not need testing but in select children, depending on season and clinical presentation, viral studies for rapid diagnosis and/or culture for influenza, RSV or enterovirus may modify management. Routine CBC or blood culture is not recommended for well-appearing child with unremarkable history. However, it is recommended that a practitioner have a low threshold for obtaining both a urinalysis and a urine culture. UTI is the most common SBI in this age group with risk factors: male, especially uncircumcised or <6mo; female <2 yr; Caucasian race; fever >39° C. Absence of risk factors does not preclude presence of UTI and positive nitrite screen, positive leukocyte esterase or positive microscopic

exam presume a UTI diagnosis and use of appropriate antibiotic treatment, while pending results of culture. It is recommended that a CBC with differential and a blood culture be performed on any child who is ill-appearing or if the practitioner determines the child to be at high risk for occult SBI. It is recommended that chest X-rays, stool culture, or lumbar punctures be performed only if there are clinical signs and symptoms indicative of specific SBI. Observation without antibiotic treatment is recommended for: well-appearing children in whom testing was not performed due to a low risk clinical assessment or well-appearing children with positive viral tests or well-appearing children with normal laboratory studies."

Restating <u>minimum</u> recommended workup for Well Appearing infants:

- Neonates get full septic workup and admission for observation and antibiotics
- 29-90 days old: CBC and UA
  - No antibiotics if WBC 5,000 to 15,000 without bandemia and clear urine
- Over 90 days
  - Males <6 months: check urine in both circumcised and uncircumcised.
  - Uncircumcised Males check urine until 12 months old
  - Circumcised Males >6 months no routine urine
  - Females: check urine until 24 months old
- High white count, bandemia or pyuria demand cultures before antibiotics
- By definition, well-appearing infants being evaluated for fever without a source should not have clinical findings suggesting the need for lumbar puncture or chest xray.

Discussion:

A history of fever should be carefully evaluated, even if the infant is afebrile at arrival. Response to antipyretics can not be used to rule out infection. If the cause of fever is suspected to be due to bundling, the infant can be unbundled for 30 minutes and considered afebrile if the repeat temperature is normal and the infant remains well-appearing and has not received other antipyretic therapy. Bundling generally causes only an elevation in skin temperature and a fever >38.5°C (101°F) should not be attributed to bundling.

Urinary tract infection — The most common source of bacterial infection among febrile infants and young children is the urinary tract. Urine testing in half the children in the PROS study found the urinary tract was the most common source of infection occurring in 19 percent of uncircumcised boys, 13 percent of girls, and 17 percent of infants of either gender with prolonged illness[2]. In a prospective observational report describing infants eight weeks to six months of age who were evaluated for fever >37.9°C, bacteriuria was diagnosed in 36 percent of uncircumcised males and in 2 percent of those who were circumcised[5]. Therefore, not routinely obtaining a catheterized urine in circumcised boys over six months of age is supported by the low incidence of UTI.

WBC and ANC counts are imperfect markers— Studies have identified an increased risk of occult bacteremia (particularly with S. pneumoniae) among children with WBC ≥ 15,000/microL and absolute neutrophil count (ANC) ≥ 10,000/microL [6,7]. However, as many as 20 percent of patients with occult bacteremia may have a WBC <15,000/microL [8]. A retrospective study found 81 percent of those with bacteremia from Staphylococcus aureus had WBC ≤ 15,000/microL while another study of children with adenovirus infection found 54 % had WBC ≥ 15,000/microL [9]. In a study of 256 patients between three and 36 months of age, an absolute neutrophil count (ANC) of 10,000 or more cells per mm3 (10 × 109 per L) was as predictive of SBI as a WBC count of more than 15,000 cells per mm3, with a sensitivity of 69 % and specificity of 79%[10]. However, using a test with a sensitivity less than 70% as the sole determinant of SBI is questionable at best because it will miss more than 30 percent of patients with SBI.

In a study of a large cohort of children 3 to 36 months of age presenting to a primary care provider with a febrile illness, an infectious syndrome, usually caused by a virus, such as croup, bronchiolitis, varicella, or roseola, was identified in 4 percent of cases [11]. Similarly, among a large group of children 3 to 36 months of age with fever ≥ 39ºC seen in the emergency department of an urban tertiary care children's hospital, 6 percent had a recognizable viral syndrome [12] .

Serious, and often readily apparent, bacterial infectious syndromes that occur in children 3 to 36 months of age include meningitis, pneumonia, and cellulitis. In one series (prior to the introduction of Hib and pneumococcal conjugate vaccines) of 996 febrile children less than 36 months of age, <1 percent had meningitis, 30 percent had pneumonia, and 10 percent had focal soft tissue infections [13] . However, the introduction of vaccines to prevent Haemophilus influenza type b (Hib) and pneumococcal disease has dramatically lowered the incidence of occult bacteremia. A retrospective California case study of over 37,000 blood cultures obtained between 1998 and 2003 in emergency departments or clinics from children 3 to 36 months of ageshowed that the incidence of bacteremia declined 67 percent (from 1.6 percent to 0.7 percent) after the introduction of PCV7 in 2000. Many of the children with positive blood cultures had foci of infection or were ill-appearing at the time blood cultures were obtained. In the final two years of the study, E. coli was the most common pathogen recovered from blood and all children with E. coli bacteremia also had a positive urine culture. The rate of isolation of a contaminant from blood culture remained 1.8 percent throughout the study period. [14]

When the rate of pneumococcal bacteremia was >1.5 percent, WBC plus selective blood culture and antibiotics was a cost-effective approach. With a rate of pneumococcal bacteremia now <0.5 percent, strategies that utilized empiric testing and treatment are no longer cost-effective. With lower rates of bacteremia, clinical judgment has become more useful in selecting a high-risk population that might benefit from selective testing and treatment[15].