TITLE: NICU Late-Onset Sepsis Antibiotic Practice Guideline

Purpose: Timely and appropriate treatment of late-onset sepsis with antibiotic will result in decreased mortality, morbidity, and better patient outcomes.

Decreasing the unnecessary use of all antibiotics and especially the wide-spectrum antibiotics will decrease the neonatal morbidity and mortality associated with growth of drug resistant organisms(1).

Scope: All physicians, neonatal nurse practitioners, RNs, pharmacists that participate in direct patient care in the NICU.

Policy: This guideline will be used in NICU for infants who have developed late-onset sepsis. The antibiotic guideline includes which antimicrobial agents should be used first-line, as well as alternatives based on suspected organism involvement.

Definitions:

LOS: Late-onset sepsis. Sepsis occurring after 72 hours of life.
CLABSI: Central Line-Associated Blood Stream Infection
CONS: Coagulase-Negative Staph

Background

Most of these infections occur in VLBW infants (BW < 1500 grams) and there is significant variability of the organisms found in the blood cultures. Most of these infections are associates with central lines (CLABSIs). The frequency of these infections and the variability of organisms is very likely associated with care practices of each unit to prevent these infections(2).

Reviewing the literature, the most common organisms in late-onset sepsis are: Staph species, E coli, Klebsiella, Pseudomonas, Enterobacter, Group B Streptococcus, Serratia, Acinetobacter, Proteus, anaerobes, and Candida.

A recent publication from a large database for 14,628 episodes of LOS found that the majority of organisms (61.2 %) were gram positives(2). The table compares the results of that study with the organisms found in our NICU. We compared two periods (2005-2008 with 2012-2015) and we noted that there was a significant decrease in the incidence of CLABSIs during the most recent period. Staph aureus, methicillin sensitive and E. coli were the most frequent organisms causing LOS. Another interesting observation is that in our NICU, sepsis due to CONS is a rare event.
<table>
<thead>
<tr>
<th>Organism</th>
<th>SJH 2005-2008</th>
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<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Methicillin-sensitive S. aureus</td>
<td>7 (21.5)</td>
<td>5 (45.5)</td>
<td>2258 (15.4)</td>
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<tr>
<td>Staphylococcus NON-aureus</td>
<td>7 (21.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative Staph (CONS)</td>
<td>5 (15)</td>
<td>1 (9.0)</td>
<td>4133 (28.3)</td>
</tr>
<tr>
<td>E. coli</td>
<td>5 (15)</td>
<td>3 (27.3)</td>
<td>900 (6.2)</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>3 (9)</td>
<td></td>
<td>1001 (6.8)</td>
</tr>
<tr>
<td>Group B Strep</td>
<td>2 (6)</td>
<td></td>
<td>448 (3.1)</td>
</tr>
<tr>
<td>Candida</td>
<td>1 (3)</td>
<td></td>
<td>1528 (10.5)</td>
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<tr>
<td>Methicillin-resistant S. aureus</td>
<td>1 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin-resistant S. NON-aureus</td>
<td>1 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serratia</td>
<td>1 (3)</td>
<td></td>
<td>363 (2.5)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>2 (18)</td>
<td>3997 (27.2)</td>
</tr>
<tr>
<td></td>
<td>33 (100)</td>
<td>11 (100)</td>
<td>14628 (100)</td>
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</table>

**Practice Guideline:**

**Cultures:**

- At least one ml of blood from a single site should be sufficient to document “true” Gram positive, Gram negative or yeast (fungal) sepsis in neonates.

- If the infant has a central venous catheter, attempt to obtain a second blood culture from the central line.

Obtain urine, and CSF specimens for culture, if clinically
indicated.

**Initial Empirical Antibiotic Treatment:**

An effort should be taken to use the following antimicrobial agents for initial treatment of late-onset sepsis, based on the prevalence of organisms in our NICU. The most common pathogens involved in late-onset sepsis are *S. aureus* and gram-negative organisms.$^{(2, 4-7)}$

First Line Antibiotics: Nafcillin + Gentamicin (according to Neofax). Provider will order antibiotics to cover the first 48 hours of treatment.


b. Gentamicin: Gram-negative coverage (*E coli, Proteus, Serratia*)

**Organism Driven Antibiotic Treatment:** If initial culture is positive and other organisms are considered:

- For GBS and *Enterococcus*: use gentamicin in combination with ampicillin
- For MRSA or Coagulase-negative *Staph* suspected: Vancomycin: Gram-positive cocci coverage (*Staph. Strep. Enterococcus*)
- For Gram-negatives: Cephalosporins, Cefotaxime will cover Gram-negative and GBS

**Alternate agents:**

a. Anaerobes: Clindamycin, metronidazole

b. Yeast (fungal): Fluconazole, amphotericin B

c. Viral: Acyclovir

Always adjust antibiotic appropriateness and dose for meningitis.

In cases of “true” bacteremia, and a decision to continue antibiotics is made, obtain two blood cultures, at least 72 hours after the initiation of antibiotic treatment, to document effective clearance of the bacteremia. This date will be useful to the determination of duration of antibiotic treatment.$^{(8)}$

In cases of CLABSIs when no other IV access is available or the placement of another central line is extremely difficult, treatment of bacteremia without the removal of the central line may be
attempted, unless persistent bacteremia is documented\(^8\).

Length of treatment for LOS, after a negative blood culture:
Bacteremia without an identifiable focus of infection is generally treated for 10 to 14 days (14 days for Staph aureus infection).
Uncomplicated meningitis attributable to GBS is treated for a minimum of 14 days. Other focal infections secondary to GBS (cerebritis, osteomyelitis, endocarditis) are treated for longer durations. Gram-negative meningitis is treated for a minimum of 21 days. Treatment of gram-negative meningitis should include Cefotaxime and an aminoglycoside until susceptibility is known\(^9\).

**Documentation Requirements:**
Documentation of indication for treatment, antibiotic type, and length of treatment in Neodata and eSummit.

**References:**
Document Control

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<td>Approved</td>
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