

## **Empiric Antibiotic Therapy for Sepsis in the Intensive Care Nursery UCSF Benioff Children's Hospital San Francisco**

This guideline applies to use of antibiotics in the Intensive Care Nursery for empiric treatment of presumed perinatal (early-onset,  $\leq 72$  hours of age) or hospital-onset infections in infants at  $> 72$  hours of age who have been hospitalized since birth (late-onset).

### Recommendations:

Refer to the following algorithms for antibiotic selection guidance in infants presenting with clinical signs concerning for sepsis:

- *Empiric Antibiotic Therapy for Sepsis in the Intensive Care Nursery (ICN)*
- *Necrotizing Enterocolitis: Antibiotic Selection and Duration of Therapy*
- *Neonatal Dosing Guidelines* for all antibiotic dosing

For situations in which a neonatal clinician would previously have considered empiric use of vancomycin and gentamicin, we now recommend nafcillin and gentamicin except in those infants with history of prior MRSA colonization or infection, or for infants with sudden and inexplicable severe illness.

Prior history of MRSA can be identified as follows:

1. Review infant's Microbiology history for prior isolation of MRSA or detection of MRSA via nasal swab screening (performed if transferred from another hospital).
  - a. This information can be located in APeX Microbiology Summary report
2. If an infant has any MRSA isolate or positive MRSA nasal swab, documentation of the result is recommended in team sign-out communication.
3. Decolonization may be considered and can temporarily eliminate MRSA colonization but recolonization is possible.

### Rationale:

The goal of these guidelines is to reduce avoidable vancomycin exposure among hospitalized neonates. Previously, vancomycin has been included in empiric late onset sepsis (LOS) therapy to cover coagulase-negative staphylococci (CoNS), which are usually resistant to narrower spectrum antibiotics. Though CoNS is one of the most common causes of LOS, it is unlikely to lead to near term mortality compared to other LOS pathogens.<sup>1,2</sup> Empiric treatment vs. delayed treatment of CoNS (initiation of vancomycin when the blood culture is reported positive) has not been associated with a detectable mortality benefit in a large neonatal cohort study.<sup>3</sup>

Given the adverse effects of vancomycin exposure, including selection for antibiotic resistance, modification of the neonatal microbiome, nephrotoxicity, and ototoxicity, Choosing Wisely guidelines have recommended avoidance of routine empiric

vancomycin use in neonatal intensive care patients.<sup>4</sup> Other institutions have implemented guidelines to reduce use of empiric vancomycin in LOS and reported reducing empiric vancomycin without identifiable detriment to LOS outcomes.<sup>1,5-7</sup>

Nafcillin is a narrow spectrum antibiotic with less impact on resistance and the neonatal microbiome, yet it covers major neonatal LOS pathogens including methicillin-susceptible *Staphylococcus aureus* (MSSA), group B streptococcus, and when combined with gentamicin has some activity against *Enterococcus faecalis*.<sup>8,9</sup> The combined regimen of nafcillin + gentamicin provides coverage against > 90% of sterile site microbiologic isolates in the UCSF Intensive Care Nursery (over Feb 2015-Aug 2018) and a majority of urine culture isolates. Nafcillin does not cover methicillin-resistant *Staphylococcus aureus* (MRSA); empiric vancomycin is indicated for infants who have a history of MRSA colonization or prior MRSA infection.

#### References:

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