Antibiotic Stewardship in the NICU
Learning Points

These Learning Points were collected and edited from those made available after each session in Year 1 of the Optimizing Antibiotic Stewardship in California NICUs (OASCN) collaborative (March 2021 - February 2022). For related references, please see OASCN's NICU Stewardship Reference List which is also sorted by topic. Please note, Learning Points were arbitrarily numbered for easy reference.

NICU Stewardship Topic Areas

Bacterial Sepsis Diagnosis/Biomarkers

#1 I:T ratio, procalcitonin, and CRP are of very limited use for EOS given low positive predictive value. Not a required part of sepsis evaluation; should only be used "with caution" for EOS evaluations.

- CRP continues to rise for at least 48 hours in healthy asymptomatic newborns.
- Consistently normal values of CRP and procalcitonin over the first 48 HOL are associated with the absence of EOS. Serial abnormal values alone should not be used to decide whether to administer antibiotics in the absence of culture-confirmed infection (low PPV).

#2 Adjusting CSF WBC count (per peripheral CBC ratio) to correct for blood in CSF is not validated. Use with caution.

#3 CSF PCR is underutilized. Consider using in all rule out meningitis cases. The BioFire platform detects 14 pathogens.

#4 CSF PCR sensitivity is higher than culture when done early in course, but less sensitive if obtained a few days into therapy (as with culture). Other CSF indices will remain positive for many days after therapy; eg, pleocytosis or high protein (glucose will more rapidly normalize).therapy; e.g. pleocytosis or high protein (glucose will more rapidly normalize).

Blood Culture Positivity, Timing and Contamination

#5 Blood cultures are very sensitive and have a high negative predictive value, if >1cc was sampled.

- Understanding individual prescriber perceptions of blood culture sensitivity may identify important opportunities for improving stewardship.

#6 Blood cultures should not be drawn from a UAC/UVC (risk of contamination) unless at insertion when still under sterile conditions.

#7 S. epidermidis is a very rare cause of EOS; if two cultures are positive, make sure the antibiograms are the same. If antibiograms do not match, do not treat.

#8 Timing, duration, and dose of maternal antibiotics is very important to help assess sepsis risk.

Diagnostic Efficiency of Antibiotic Use in CPQCC NICUs

#9 There is wide variation in the diagnostic efficiency among CPQCC NICUs (number of babies empirically treated per proven EOS-associated bloodstream infection). It ranges from 11 to 336 babies. This can't be computed for ~1/3 of NICUs because they reported zero EOS cases (despite treating many babies for it). Each unit should consider which range of rates is "right".

Early-Onset Sepsis (EOS) Management

#10 The AAP suggests no empiric antibiotics for infants <35 wks gestation delivered by C-section if indicated because of certain maternal indications (e.g. non-infectious illness, placental insufficiency in the absence of labor, attempts to induce labor, or ROM before delivery). Many prescribers are withholding antibiotics in these low-risk preterm infants.

#11 The AAP recommends that when blood cultures are sterile, antibiotic therapy should be discontinued by 36-48 hours unless there is clear evidence of site-specific infection for any gestational age.

- If started, stopping antibiotics in <32 weekers can be done safely (acknowledging that in the SCOUT stewardship study, only 11% were <28 weeks).
- For ELBW babies only, think about stopping rule out sepsis antibiotics at 24 hours of life instead of 36-48 hours. This is appropriate due to delayed clearance/prolonged antibiotic effect (eg, ampicillin, cefepime).
- 50 mg/kg/dose of ampicillin is appropriate for bacteremia (vs. 100 mg/kg/dose for meningitis).

#12 Viridans streptococcus is often a contaminant that may not require treatment.

#13 Emerging robust data suggest prolonged early antibiotic use may lead to unanticipated negative outcomes (related to systemic inflammation).

#14 The ACOG approach to “intraamniotic infection” (formerly chorioamnionitis) is worth fully understanding.

Fungal Sepsis Prophylaxis, Diagnosis and Management

#15 True “asymptomatic” candidemia is very rare and only if workup is completely negative, there are no clinical concerns, and repeat culture off antibiotics is also negative.

#16 Modern systems will identify C. albicans in a mean of 25-36 hours. “Fungal culture” is not needed. Discontinue antibacterials if fungal diagnosis is clear.

#17 Fluconazole and amphotericin are first line therapies; micafungin is acceptable if no renal/CNS disease. Double coverage is not necessary. Fluconazole resistance to C. glabrata and C. krusei is a problem so check the species result.

- Ampho B is well tolerated in babies and provides broader coverage than fluconazole. Its use with pre-existing thrombocytopenia is OK.
- Treatment for 2 weeks from last positive culture is sufficient for non-meningitic disease.
- Larger doses of micafungin are needed for newborns due to enhanced clearance. Anidulafungin is fine if that is the echinocandin on your formulary.

Herpes Simplex Virus

#18 TThe CSF multiplex (e.g. BioFire) PCR test for HSV is generally sensitive and specific. False negatives are rare. Some ID specialists believe a PCR test (separate from the BioFire) has higher sensitivity.

#19 HSV blood PCR increases the diagnostic yield for this infection.

Infection Prevention and Stewardship

#20 The likelihood of CLABSI (when comparing UVCs v PICCs) is not clearly different. If duration of use expected to be relatively short, UVC is the preferred option.

Neonatal Sepsis Calculator

#21 The calculator is an effective tool and reduces unnecessary antibiotic use. However, it does not identify all cases of sepsis. Additional monitoring for sepsis cases is requiired when it's used.

#22 The post-partum clinical portion of the calculator contributes the most weight to the risk estimate.

#23 Integrating a multidisciplinary serial clinical examination workflow within routine care is important to ensure that monitoring occurs systematically, especially within the first 24 hours of life.

#24 Several strategies can be used to successfully implement the calculator and serial clinical examinations, e.g., QI project, immediate adoption with education, or phased approaches.

#25 The AAP guideline for ≥35 GA babies endorses the serial clinical exam approach alone, either with or without an estimation of neonatal or maternal risk factors for EOS.

Late-Onset & Culture-Negative Sepsis

#26 Differentiating "sepsis" caused by infection from the physiologic changes associated with extreme prematurity is challenging, but strongly considering the latter is very important.

- Persistent cardiorespiratory instability is NOT an indication for prolonged empiric antibiotics.
- Clinical evaluation should occur each day without a definitive "treatment course" determined on day 1 necessarily.

#27 Strongly consider doing a respiratory nasal PCR test in rule out LOS babies. Blood PCR for enterovirus also may help identify cause eof clinical signs, especially if in the summer/fall season.

#28 Double gram negative coverage for sepsis is unnecessary. Data from older children and adults do not support this practice (some recommend only for pseudomonas sepsis/VAP in adults).

Necrotizing Enterocolitis (NEC)

#29 Vancomycin is unnecessary as empiric therapy for NEC, and most cases of LOS; it can be safely eliminated. If a CLABSI is being considered AND MRSA is a big problem in your NICU then empiric vancomycin might be reasonable.

#30 Anaerobic coverage for NEC not required; consider for known perforation or severe disease.

#31 Treatment duration for mild-moderate NEC can be 5-7 days. For more severe cases 10 days may be reasonable.

#32 Piperacillin-tazobactam (Zosyn) may be overkill for empiric (medical) NEC coverage and doesn't get into CSF well. Non-Zosyn-containing regimens are not inferior.

Neonatal Pneumonia

#33 Diagnosis of neonatal pneumonia can be challenging. No robust data in newborns, but in older children X-ray findings will persist well beyond 1 day if true pneumonia.

#34 If treated, optimal duration of therapy pneumonia is not known. One large and high-quality stewardship study showed no harm in treating for 5 days, assuming the clinical course is acceptable.

Quality Improvement in the NICU

#35 Gradually gaining momentum with small scale changes can organically address resistance to change.

#36 Distinguishing tasks from tests can optimize your time and resources during PDSA cycles. Education is usually a required task; it typically swon't need to be tested with a PDSA cycle.

#37 Linking QI data and QI tools (e.g. packaging your story and data in an A3 report) optimizes individual and group problem solving, engagement, and dissemination.

- One way to "herd the chaos" is to visualize your data in meaningful ways.

#38 Meticulous documentation of PDSA cycles can optimize efficient collaboration among team members and stakeholders.

- Intended output of the PDSA cycle may only be "learning"... not necessarily improvement.
- RAPID cycles can effectively accelerate your improvement.

Stewardship in the NICU

#39 Antibiotics are recommended for preterm deliveries (<35 weeks) when due to cervical incompetence, preterm labor, PROM, intra-amniotic infection, or acute onset of unexplained nonreassuring fetal status; clinical judgement plays a role in this decision otherwise.

#40 Every attempt should be made to perform an LP when clinically indicated.

#41 Work to become comfortable using the most narrow spectrum antimicrobials on your antibiogram, if susceptible.

#42 Immediate reporting of positive Gram stain/culture results should be done by the lab or by review of pending cultures at least once/day by unit staff if the lab cannot accommodate.

#43 Hard antibiotic stops at 36 or 48 hours after blood culture have been shown consistently to safely lower antibiotic use.

#44 Vignette research methods on antibiotic decisions and rationale guiding these decisions can help inform ideal stewardship strategies, process changes, and guideline development.

Stewardship Principles, Team Building

#45 Thinking systematically and objectively about differential diagnoses can minimize unwarranted use of empiric antibiotic therapy. Eg, maternal SIRS may manifest as SIRS in the baby potentially obviating the need for empiric antibiotics.

#46 One can't interpret a test result without considering pre-test probability.

#47 We need different ways of thinking to mitigate and address how antibiotic overuse continues in some centers, here and nationally. Ongoing engagement of nursing and others (e.g. L&D team) and building confidence is key.

Syphilis

#48 Always call your health dept to get (perhaps) more accurate/complete data on mom's RPR & treatment. May find out that mom got too much PCN for her disease stage (1 dose v 3 doses). This might move the conclusion from "possible" to "less likely/unlikely" in the baby.

#49 Think hard if mom might be serofast which may allow for NOT starting antibiotic (moves from "less likely" to "unlikely"). Serofast means resolution of infection, but with a demonstrable low yet persistent RPR titer (typically <1:8).

#50 Baby allergic to PCN? Desensitize (to avoid use of ceftriaxone alternative).

Urinary Tract Infection (UTI)

#51 There is no guideline on the management of UTI in the NICU.

#52 A negative urinalysis does not rule out UTI; a colony count >1000 on SPA and >50,000 for catheterization (or >10,000 with pyuria) is considered a probable UTI.

#53 A urine culture should be sent to lab ASAP, or at least refrigerated ASAP. If more than 1-2hrs in room temperature transport, the results may be falsely positive.

#54 Empiric therapy for UTI can be what is usually used in your NICU for rule out sepsis (including ampicillin and gentamicin alone) with de-escalation once susceptibility results are back.

#55 Antibiotic prophylaxis is not indicated for a first time UTI, except possibly in the case of severe GU anomalies.