

Duke University Hospital and Duke Regional Hospital Neonatal Antimicrobial Guidance for Select Infections

These antimicrobial recommendations are provided as general guidance for therapy with a goal of assisting with empiric agent selection based on the most common pathogens and local resistance patterns while minimizing unintended consequences for the patient. Antibiotic administration in neonates has been associated with alterations in the gut microbiome and increased risk of childhood diseases (i.e. wheezing, obesity, food allergy, and inflammatory bowel diseases). Cultures should be obtained from the appropriate sources prior to initiation of antimicrobial therapy, *EXCEPT* when this will cause a delay in treatment that will harm the patient. Previous culture results and the patient's antimicrobial history should be reviewed prior to initiation of therapy.

Culture and other laboratory test results should be used to guide definitive therapy. Always consider antimicrobials may *NOT* be necessary or medication selections may need to be modified, depending on the particular medical situations. Patient specific factors *should* influence selection decisions.

Pediatric infectious diseases consultation should be considered in complicated or unusual cases or cases with growth of multidrug resistant organisms.

The following document is organized by organ system and site of infection. All of these recommendations have been updated in CustomID (customID.org) with dosing and duration recommendations.

Questions? Page the Pediatric Infectious Diseases Team 970-7420 or the Antimicrobial Stewardship Evaluation Team (ASET) Pediatric Pharmacist at 206-9309.

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Diagnosis or Clinical Scenario	Common Pathogens	Preferred Empiric Agent(s)	Duration of Therapy	Comments
Bloodstream Infections				
Early-onset sepsis (EOS, 0-7 days of life)	Group B streptococcus Enteric Gram negatives <i>L. monocytogenes</i> HSV	Ampicillin PLUS gentamicin Consider acyclovir based on risk factors and acuity of illness	36-48 hours for rule out 7-14 days organism-specific therapy if culture positive	36 hours is the equivalent of 4 doses of ampicillin. The therapeutic window of ampicillin extends past the last dose. 97% of blood cultures with pathogenic organisms show growth by 36 hours. If acyclovir started, please collect surface cultures of the conjunctivae, mouth, nasopharynx, and rectum for HSV as well as PCR on blood, CSF, and vesicle fluid Empiric vancomycin PLUS gentamicin should be avoided due to nephrotoxicity Risk factors for resistant Gram positive infection include indwelling lines and prior history of resistant Gram positive infection Pediatric ID consult recommended for bloodstream infections caused by organisms exhibiting antimicrobial resistance (i.e. ESBL, CRE, etc.) Pediatric ID consult required for <i>S. aureus</i> and <i>S. lugdunensis</i> bacteremia and recommended for meningitis.
EOS with preliminary CSF results concerning for potential meningitis	Group B streptococcus Enteric Gram negatives <i>L. monocytogenes</i> HSV	Ampicillin PLUS cefotaxime Consider acyclovir based on risk factors and acuity of illness	36-48 hour rule out Organism-specific duration for meningitis	
Late-onset sepsis (LOS, >7 days of life)	Group B streptococcus <i>L. monocytogenes</i> MSSA or MRSA Coagulase-negative staphylococci	Ampicillin PLUS gentamicin Consider acyclovir based on risk factors and acuity of illness	48 hour rule out 7-14 days organism-specific therapy if culture positive	<i>Consider</i> vancomycin based on risk factors and acuity of illness
LOS with preliminary CSF results concerning for potential meningitis	Group B streptococcus <i>L. monocytogenes</i> MSSA or MRSA Coagulase-negative staphylococci	Ampicillin PLUS cefotaxime Consider acyclovir based on risk factors and acuity of illness	48 hour rule out Organism-specific duration for meningitis	<i>Consider</i> vancomycin based on risk factors and acuity of illness

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Fungal sepsis	Candida sp. Mucormycosis	Fluconazole	Based on extent of dissemination, minimum of 14 days for candidemia without obvious metastatic complications	Pediatric ID consult required for candidemia If candidemia is present: obtain LP, ophthalmologic exam, and imaging (Renal bladder US, Liver and spleen US) If candiduria is noted, neonates should receive a renal US to rule out a mycetoma
Central Nervous System				
Meningitis , age 0-14 days	Group B streptococcus Enteric Gram negatives <i>L. monocytogenes</i> HSV	Ampicillin PLUS cefotaxime	Organism-specific duration for meningitis	Consider adding acyclovir unless bacterial etiology strongly suspected <u>Consider Pediatric ID consult</u>
Meningitis , age 15-28 days	Group B streptococcus Enteric Gram negatives <i>L. monocytogenes</i> <i>S. pneumoniae</i> HSV	Vancomycin PLUS cefotaxime	Organism-specific duration for meningitis	Add ampicillin if <i>L. monocytogenes</i> suspected Consider adding acyclovir unless bacterial etiology strongly suspected <u>Consider Pediatric ID consult</u>
Lower Respiratory Tract				
Pneumonia	Group B streptococcus Enteric Gram negatives <i>L. monocytogenes</i> <i>P. aeruginosa</i> MSSA or MRSA	Ampicillin PLUS gentamicin OR Ampicillin PLUS cefotaxime (if ventilator-associated)	7 days	Colonization history should be reviewed. If history of MRSA, can consider vancomycin
Atypical	<i>M. pneumoniae</i> <i>Ureaplasma sp.</i>	Azithromycin	7 days	Data from the AZTEC trial suggest azithromycin does not improve pulmonary outcomes in preterm infants; testing and treatment for atypical organisms may not be warranted
	<i>C. trachomatis</i> <i>B. pertussis</i>	Azithromycin (high dose)	5 days	Treat only if symptomatic, consider PO Can present at 4-8 weeks of life
Viral	Influenza virus	Oseltamivir	5 days	
	SARS-CoV-2	Remdesivir	5 days	<u>Remdesivir requires Pediatric ID approval</u>

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	Cytomegalovirus (CMV)	Ganciclovir/Valganciclovir	Postnatal CMV: 2-4 weeks	See CMV Protocol. Very low birth weight infants (VLBW, < 1500 g) are at risk for symptomatic disease, which can include pneumonitis , enteritis, hepatitis and/or a sepsis-like illness. <u>Consult to Pediatric ID required for ganciclovir/valganciclovir approval</u>
Aspiration pneumonia	Oral flora	Ampicillin <u>Alternative:</u> ampicillin/sulbactam	5 days	Most aspiration events do NOT require antimicrobial therapy. Consider antibiotics if fever or lobar pneumonia present and/or patient requires escalating respiratory support Aspiration of gastric contents is often sterile due to high acidity. Enteric anaerobes cannot survive in the aerophilic environment of the lungs unless it creates a walled-off abscess; additionally oral anaerobes are typically implicated in patients with severe periodontal disease. For that reason, even for true aspiration pneumonia, coverage of enteric anaerobes is not indicated unless a patient has necrotizing pneumonia. [Chest, 2024 ; J Hosp Med, 2020]
Tracheitis	<i>S. pneumoniae</i> <i>M. catarrhalis</i> <i>H. influenzae</i> MSSA or MRSA Group A streptococcus	Cefazolin	3-5 days	ETS cultures are not required as part of rule out sepsis work up and do not needed to be repeated more than once a week. Initiate treatment only when increased secretions and one of the following: fever, moderate white cells on tracheal aspirate, or need for increase ventilator support
<i>Skin, Soft Tissue, & Musculoskeletal</i>				
Omphalitis	MSSA or MRSA Group A streptococcus Enteric Gram negatives	Vancomycin PLUS cefepime <u>Alternative:</u> clindamycin	10 days	Consider pediatric surgery consult Culture umbilical drainage if present

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Anaerobes				
Osteomyelitis	MSSA or MRSA Group B streptococcus Enteric Gram negatives	Vancomycin PLUS cefotaxime	Minimum of 28 days	Narrow based on culture data <u>Recommend Pediatric ID consult</u>
Periumbilical cellulitis	MSSA or MRSA Group A streptococcus Enteric Gram negatives Anaerobes	Clindamycin PLUS cefotaxime	7 days	If infant is toxic-appearing broaden coverage to treat for omphalitis as listed above
Cellulitis (non-periumbilical) and Imetigo	MSSA or MRSA Group A streptococcus	Cefazolin <u>Alternative:</u> clindamycin	5 days	Can consider PO (cephalexin, clindamycin)
Pustulosis	MSSA or MRSA	Topical mupirocin	7 days	Consider blood culture and systemic antibiotics for premature or VLBW infants with localized disease or full-term neonates with multiple sites of involvement
Surgical site infection	MSSA or MRSA Site-dependent organisms	Cefazolin OR vancomycin based on patient risk factors	7 days (minimum, dependent on extent of infection)	Consider piperacillin-tazobactam for abdominal surgery-related infection Can consider PO (cephalexin, clindamycin)
Genitourinary Tract				
Cystitis/Pyelonephritis	Enteric Gram negatives Enterococci	Ampicillin PLUS gentamicin	7 days Longer duration of therapy may be appropriate for infants without response to therapy or infants with complicated infections – consider consult to ID and/or urology	Recommend obtaining urine culture and UA from straight catheter; if unable to obtain enough volume via cath, place urine bag to collect UA Recommend the following cut offs for diagnosis and treatment of UTI in neonates: • Cath specimen: $\geq 50,000$ CFU/mL or 10,000 – 50,000 CFU/mL with pyuria, leukocyte esterase, or nitrates on UA • Clean catch (not recommended in neonates): $\geq 100,000$ CFU/mL Repeat UA and urine culture for tests of cure are <u>not</u> recommended.

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				Can consider PO based on patient and microbiological characteristics once organism is identified on urine culture
<i>Gastrointestinal / Abdominal</i>				
Medical necrotizing enterocolitis (NEC) without evidence of pneumatosis	Enteric Gram negatives Enterococci	Ampicillin PLUS gentamicin	7 days	
Medical NEC with evidence of pneumatosis	Enteric Gram negatives Enterococci	Ampicillin PLUS gentamicin; strongly consider addition of metronidazole based on clinical severity or DAAS score ≥ 8 <u>Alternative:</u> Piperacillin/tazobactam	7 days	Double coverage with piperacillin/tazobactam PLUS gentamicin is not recommended based on local epidemiology
Surgical NEC or spontaneous intestinal perforation	Enteric Gram negatives Enterococci <i>P. aeruginosa</i>	Piperacillin/tazobactam	10-14 days (pending source control)	Double coverage with piperacillin/tazobactam PLUS gentamicin is not recommended based on local epidemiology <u>Consider Pediatric ID consult</u> to assist with optimization and duration of therapy
Gastroschisis admission	Skin flora	Cefazolin	24 hours post-closure	See Gastroschisis protocol
Hirschsprung Disease with toxic megacolon	Enteric Gram negatives <i>P. aeruginosa</i> , anaerobes	Piperacillin/tazobactam	7 days	
Postnatal Cytomegalovirus	Cytomegalovirus (CMV)	Ganciclovir/Valganciclovir	Postnatal CMV: 2-4 weeks	See CMV Protocol. Very low birth weight infants (VLBW, < 1500 g) are at risk for symptomatic disease, which can include pneumonitis, enteritis , hepatitis and/or a sepsis-like illness. <u>Consult to Pediatric ID required for ganciclovir/valganciclovir approval</u>