C.S. MOTT CHILDREN'S HOSPITAL
MICHIGAN MEDICINE

EMPIRIC ANTIBIOTIC GUIDELINES FOR UNDIFFERENTIATED OR SEVERE SEPSIS IN PATIENTS ON PEDIATRIC SERVICES (EXCLUDING NICU)

Clinicians should prescribe antibiotics promptly when sepsis is suspected, ideally after obtaining appropriate cultures. Severe sepsis should be suspected in patients with respiratory failure, hemodynamic instability, or derangements of two or more other organ systems, especially in the absence of an alternative etiology. For patients with non-severe sepsis secondary to a specific infectious etiology (e.g., pneumonia), condition-specific guidelines may be followed instead. Empiric therapy for Neonatal Intensive Care Unit (NICU) patients, except for febrile young infants admitted from home, should be guided by NICU early/late-onset sepsis pathways.

Setting	Empiric Therapy	Comments
Healthy infant 0 – 59 days, admitted from home within last 72 hrs	See Febrile Young Infant guideline	Follow febrile young infant guideline, even if NICU patient
Patients 60 days or older WITHOUT Increased multi-drug resistant gram-negative (MDR-GN) risk Must meet the following: • Immunocompetent • No at risk[1] implanted or indwelling devices • No more than 72 hours of hospitalization in past 90 days (including current hospitalization)	****Empiric regimen may require adjustment for patients with infection or colonization with multidrug-resistant organisms in past 6 months**** 1st line therapy: **Vancomycin** IV* + **Ceftriaxone** 100 mg/kg IV once, then 50 mg/kg/DOSE IV q12h (max: 2 g/DOSE) Alternative for low/medium-risk[2] allergy to cephalosporins, OR high-risk allergy[3]/contraindication[4] to beta-lactams: **Vancomycin** IV* + **Aztreonam*** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) Suspected intra-abdominal or oropharyngeal source (anaerobic coverage): ADD **metronidazole** 30 mg/kg/DOSE IV q24h (max: 1.5 g/DOSE) Concern for toxic shock syndrome: ADD **clindamycin** 13 mg/kg/DOSE IV q8h (max: 900 mg/DOSE)	**Order all sepsis antibiotics STAT** For most patients, if antibiotics cannot be administered simultaneously, the cephalosporin or aztreonam should be given first. However, if there is strong suspicion for *Staphylococcus aureus* as the cause of sepsis, and in particular, methicillin-resistant *S. aureus* (MRSA), administer vancomycin first. Antibiotics should be de-escalated if cultures are negative at 36-48 hours and no bacterial infection is identified, or if results indicate that narrower therapy is sufficient. Consider Infectious Diseases consult, especially if: • significant prior antibiotic exposure • positive blood or CSF cultures • complicated infection (see separate condition-specific guidelines when available) • need for extensive infectious evaluation • unusual exposure history
Patient of any age, excluding those in NICU AND Increased MDR-GN risk: • Immunocompromised • At risk[1] implanted or indwelling device • Greater than 72 hours hospitalization in past 90 days (including current hospitalization)	****Empiric regimen may require adjustment for patients with infection or colonization with multidrug-resistant organisms in past 6 months**** 1st line therapy: **Vancomycin** IV* + **Cefepime** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) Alternative for low/medium-risk[2] allergy to cephalosporins, OR high-risk allergy[3]/contraindication[4] to beta-lactams: **Vancomycin** IV* + **Aztreonam*** 50 mg/kg/DOSE IV q8h (max: 2 g/DOSE) *If hemodynamically unstable or immunocompromised:* ADD **tobramycin** 7.5 mg/kg/DOSE IV q24h (max initial: 300 mg/DOSE) Suspected intra-abdominal or oropharyngeal source (anaerobic coverage): ADD **metronidazole** 30 mg/kg/DOSE IV q24h (max: 1.5 g/DOSE) Concern for toxic shock syndrome: ADD **clindamycin** 13 mg/kg/DOSE IV q8h (max: 900 mg/DOSE) High risk for Candida infection[5]: ADD **micafungin** 5 mg/kg/DOSE IV q24h (max: 150 mg/DOSE)	

*Renal adjustment may be necessary. See Pediatric Renal Dosing Guidelines.

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Footnotes:

[1] At risk implanted or indwelling devices are those deemed by the clinician to have a high risk of colonization or infection with resistant gram-negative organisms, including but not limited to Pseudomonas aeruginosa (e.g., central venous catheter, tracheostomy, nephrostomy/suprapubic catheter, percutaneous biliary catheter)

[2] Low-risk allergies include: pruritus without rash, remote (>10 years) unknown reaction, patient denies allergy but is on record, mild rash with no other symptoms (mild rash: non-urticarial rash that resolves without medical intervention). Medium-risk allergies include: urticaria/hives with no other symptoms, severe rash with no other symptoms (severe rash: requires medical intervention [corticosteroids, anti-histamines] and/or ER visit or hospitalization). See β-lactam allergy evaluation and empiric guidance for further information.

[3] High-risk allergies include: respiratory symptoms (chest tightness, bronchospasm, wheezing, cough), angioedema (swelling, throat tightness), cardiovascular symptoms (hypotension, dizzy/lightheadedness, syncope/passing out, arrhythmia), anaphylaxis. If a patient has a high-risk allergy to penicillins, cephalosporins, or carbapenems, the only beta-lactam antibiotic that can be safely used without Allergy consult is aztreonam (**if the allergy is to ceftazidime or aztreonam, aztreonam should be avoided as well**). See β-lactam allergy evaluation and empiric guidance for further information.

[4] Previous reactions that are contraindications to further beta-lactam use (**except aztreonam, which can be used unless the reaction was to ceftazidime or aztreonam**) unless approved by Allergy: organ damage (kidney, liver), drug-induced immune-mediated anemia/thrombocytopenia/leukopenia, rash with mucosal lesions (Stevens Johnson Syndrome/Toxic Epidermal Necrosis), rash with pustules (acute generalized exanthematous pustulosis), rash with eosinophils and organ injury (DRESS – drug rash eosinophilia and systemic symptoms), rash with joint pain, fever, and myalgia (Serum Sickness). See β-lactam allergy evaluation and empiric guidance for further information.

[5] High risk for Candida infection:

1. Invasive Candida infection in the past 6 months or
2. ICU-level patient with one of the following AND not receiving systemic antifungal prophylaxis:
   a. short bowel syndrome and TPN-dependence
   b. liver transplantation in the past 30 days
   c. prolonged (>7 days) neutropenia due to chemotherapy
   d. immunosuppression for GVHD

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References:

1. Timsit JF, et al. Empirical Micafungin Treatment and Survival Without Invasive Fungal Infection in Adults With ICU-Acquired Sepsis, Candida Colonization, and Multiple Organ Failure. JAMA. 2016 Oct 18;316(15):1555-1564.
2. Schuster MG et al. Empirical fluconazole versus placebo for intensive care unit patients: a randomized trial. Ann Intern Med. 2008 Jul 15;149(2):83-90.

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