Improving Pediatric Sepsis Outcomes (IPSO)
Recommendations for Empiric Antimicrobial Treatment by Site of Suspected/Identified Infection

For patients with sepsis, please refer first to the **"Recommendations for Empiric Antimicrobial Treatment of Sepsis with No Suspected/Identified Site of Infection".** The recommendations in this document augment the recommendations for empiric treatment of sepsis in situations where a specific site of infection has been identified, such as severe skin/soft tissue infection/necrotizing fasciitis. The recommendations in this document may also be used for patients who have a specific site of infection identified and do not have sepsis or have been treated for sepsis and have responded to treatment adequately.

Condition	Recommendation	Rationale	Examples of antibiotics that could be used
Community-acquired pneumonia, uncomplicated	Empiric treatment regimens should provide coverage for encapsulated bacteria Consider adding azithromycin if concern for atypical pneumonia Consider antiviral therapy if concern for influenza/SARS-CoV-2	Common pathogens can be treated with narrow coverage	Ampicillin
Community-acquired pneumonia, complicated (e.g. necrotizing pneumonia, empyema)	Empiric treatment regimens with coverage for encapsulated bacteria and *S. aureus* including methicillin/oxacillin resistant *Staph. Aureus* (MRSA) Consider adding azithromycin if concern for atypical pneumonia Consider antiviral therapy if concern for influenza/SARS-CoV-2	Complicated pneumonia may be caused by *S. aureus* including MRSA, sometimes with influenza co-infection	Ceftriaxone and vancomycin (or other antibiotic which provides reliable MRSA coverage based on local antibiogram e.g., clindamycin)[1]
Aspiration pneumonia, community-acquired	Empiric treatment regimens with coverage for normal oral flora	Aspiration pneumonia may be caused by common oral flora	Ampicillin/sulbactam or ceftriaxone plus clindamycin
Aspiration pneumonia, hospital-acquired	Empiric treatment regimens with coverage for GNR (Gram negative rods), including *Pseudomonas*, and anaerobic coverage	Aspiration pneumonia may be caused by GNR, including *Pseudomonas*, and anaerobic bacteria	Cefepime +/- metronidazole, or piperacillin/tazobactam, or meropenem if colonized with

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CHILDREN'S HOSPITAL ASSOCIATION

June 2022

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Condition	Recommendation	Rationale	Examples of antibiotics that could be used
			multidrug resistant-Gram negative rods (MDR-GNR)
Ventilator-associated pneumonia (VAP)	Empiric treatment regimens with coverage for encapsulated organisms, *S. aureus* and GNR including *Pseudomonas*	VAP may be caused by encapsulated organisms, *S. aureus* and GNR including *Pseudomonas* MRSA coverage if suspected MRSA	Cefepime or piperacillin/tazobactam, or meropenem if colonized with multidrug resistant-Gram negative rods (MDR-GNR) plus vancomycin if suspected MRSA[2]
CNS infection, meningitis, encephalitis, ≥1 month old	Empiric treatment regimens with good CNS penetration	Bactericidal activity in CSF is necessary for optimal treatment	Ceftriaxone, ceftazidime or cefepime and vancomycin Consider acyclovir if suspected HSV Consider adding ampicillin if immunocompromised or concern for *Listeria* infection
CNS infection, meningitis, encephalitis, <1 month old	Empiric treatment regimens with good CNS penetration	Bactericidal activity in CSF is necessary for optimal treatment	Ampicillin and gentamicin plus acyclovir Consider replacing gentamicin with ceftazidime or cefepime if GNR suspected
CNS infection, brain abscess or subdural empyema	Empiric treatment regimens with good CNS penetration and with coverage for penicillin-resistant streptococci, MRSA and anaerobes	Bactericidal activity in CSF is necessary for optimal treatment Infections may be polymicrobial including penicillin-resistant streptococci, MRSA and anaerobes	Ceftriaxone, ceftazidime or cefepime and vancomycin and metronidazole

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Condition	Recommendation	Rationale	Examples of antibiotics that could be used
CNS infection, CSF shunt infection	Empiric treatment regimens with good CNS penetration with *S. aureus*, including MRSA, coagulase negative staphylococcus and GNR	Bactericidal activity in CSF is necessary for optimal treatment CSF infection may be caused by *S. aureus*, including MRSA, coagulase negative staphylococcus and GNR	Ceftazidime or cefepime and vancomycin
Skin/soft tissue infection, not severe	Empiric treatment regimens effective against *S. aureus*, including MRSA, and streptococci	Common pathogens can be treated with narrow coverage	Cefazolin and/or vancomycin (or other antibiotic which provides reliable MRSA coverage based on local antibiogram e.g. clindamycin)
Severe skin/soft tissue infection/necrotizing fasciitis	Empiric treatment regimens with coverage for Gram-positive bacteria, GNR, and anaerobic bacteria, including toxin-producing bacteria	Infections may be polymicrobial, including anaerobes Clindamycin is a protein synthesis inhibitor, which may reduce toxin production	Piperacillin/tazobactam and vancomycin[2], or cefepime metronidazole and vancomycin, Add clindamycin for either regimen
Toxic shock syndrome (e.g., fever, rash, shock, organ dysfunction)* * see recommendations for severe skin/soft tissue infection/ necrotizing fasciitis	Empiric treatment regimens for no identified source plus coverage for MRSA, including toxin-producing bacteria	Clindamycin is a protein synthesis inhibitor, which may reduce toxin production	Ceftriaxone, ceftazidime, or cefepime and vancomycin Add clindamycin
Bone and joint infection	Empiric treatment regimens effective against *S. aureus* (including MRSA), *Kingella*, and streptococci	Common pathogens can be treated with narrow coverage	Cefazolin and/or vancomycin (or other antibiotic which provides reliable MRSA coverage based on local antibiogram e.g., clindamycin)

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Fever and neutropenia, and other severely immunocompromised patients	Empiric treatment regimens with coverage for Gram-positive bacteria and GNR, including *Pseudomonas* Empiric treatment for penicillin-resistant streptococci, MRSA, or drug-resistant GNR should be added for patients who are clinically unstable, when a beta-lactam-resistant bacteria is suspected, or for centers or patient populations with a high rate of resistant pathogens Empiric treatment for anaerobic bacteria if symptoms suggest neutropenic colitis (e.g., typhlitis), other intestinal or intra-abdominal pathology, or perianal skin breakdown	Most infections are caused by beta-lactam susceptible Gram-positive cocci, enteric GNR or other beta-lactam susceptible bacteria; *Pseudomonas* is less common but may cause severe infection and should be covered empirically in all cases Penicillin-resistant streptococci, MRSA, and MDR-GNR may cause severe infection in specific situations Anaerobic bacteria are uncommon causes of infection, but should be treated in situations where infection with these bacteria is possible	Cefepime Add vancomycin in specific situations when infection with a beta-lactam resistant Gram-positive coccus is suspected Add a second agent effective against GNR (e.g., aminoglycoside, quinolone) or use meropenem in specific situations when infection with MDR-GNR is suspected Add metronidazole or use piperacillin/tazobactam[2] or meropenem when infection with anaerobic bacteria is suspected Add **treatment dose echinocandin** or liposomal amphotericin[4]
Prolonged fever (e.g., ≥5 days) and neutropenia, despite broad-spectrum antimicrobial therapy	Empiric **treatment regimens** as described for fever and neutropenia plus antifungal therapy[4]	*Candida*, in particular, but also mold infection may occur	Empiric treatment for fever and neutropenia plus **treatment dose echinocandin** or liposomal amphotericin or broad-spectrum azole if additional mold coverage is desired[4]
Intra-abdominal infection, uncomplicated, community acquired	Empiric **treatment regimens** with coverage for enteric GNR and anaerobes	GNR, *Bacteroides* and other anaerobes are often co-pathogens	Ceftriaxone and metronidazole or cefoxitin

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Condition	Recommendation	Rationale	Examples of antibiotics that could be used
Intra-abdominal infection, severe, hospital acquired or previously treated, compromised host, or inability to achieve adequate debridement or drainage	*Pseudomonas* and less than fully susceptible GNR may be co-pathogens Enterococcus and/or *Candida* may play a role in cases not responding to otherwise effective therapy	Enterococci and less than fully susceptible GNR may be co-pathogens	Ceftazidime or cefepime plus metronidazole or piperacillin/tazobactam[2] or meropenem Consider the need for fluconazole or echinocandin[4]
Urinary tract infection, uncomplicated[5]	Empiric treatment regimens with GNR coverage	GNR are the common pathogens, enterococci are occasional pathogens	Ceftriaxone, plus ampicillin if enterococci suspected
Urinary tract infection, complicated[5]	Empiric treatment regimens with GNR, including *Pseudomonas*, and possibly *Candida* coverage	GNR, including *Pseudomonas*, enterococcus and occasionally *Candida*	Ceftazidime, cefepime, piperacillin/tazobactam or meropenem (if colonized with MDR-GNR) Consider fluconazole if C*andida albicans*. Consult infectious diseases for non-*Candida albican*s or treatment failure with fluconazole
Infection with MDR-GNR (i.e., history of prior colonization/ infection, history of treatment with broad-spectrum agents, patient country of origin has high prevalence of MDR-GNR)	**Consult infectious diseases**	Mechanisms of resistance among MDR-GNR are complex and require individual, specific treatment approaches	--

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1. If concern for MRSA Influenza co-infection, add clindamycin or replace vancomycin with linezolid.
2. Use of vancomycin and piperacillin/tazobactam in combination should be avoided whenever possible, especially in children who have or are at high-risk for renal insufficiency. Use of this combination should be reassessed daily and, preferably, revised or discontinued within 2 days.
3. Consider replacing gentamicin with ceftazidime or cefepime if GNR identified.
4. Consider infectious diseases consult when adding antifungal therapy.
5. Review previous urine culture results and consider susceptibilities.

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