# 2010–2011 Nelson's Pocket Book of Pediatric Antimicrobial Therapy

EIGHTEENTH EDITION

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American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

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**EIGHTEENTH EDITION**

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## Introduction

Medical information constantly evolves and practitioners require readily accessible, current, relevant, and accurate information. The *2010–2011 Nelson's Pocket Book of Pediatric Antimicrobial Therapy* is available as a quick reference book and in digital format, providing updated information to anyone who cares for children. For those who use handheld mobile devices, *Nelson's Pocket Book* is now available in an easy-to-use, quick, searchable version for a wide variety of PDA and smartphone platforms, including Palm, Windows Mobile, Blackberry, and iPhone.

New for this edition of *Nelson's Pocket Book* we provide the strength of recommendation and level of evidence for our treatment recommendations for major infections. We know that informed clinical decision-making is best supported when the clinician has access to the level and strength of evidence on which the recommendations are based. In the absence of published guidelines, we use our best judgment from the published medical literature, abstract presentations from scientific meetings, consensus statements, and our collective clinical experience. We provide 3 categories to rank each recommendation, along with 3 levels of evidence. Our grading system, outlined below, is based largely on those proposed by many professional organizations, including the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, the Centers for Disease Control and Prevention, and the Public Health Service.

| Strength of recommendation | Description |
|---|---|
| A | Strongly recommended |
| B | Recommended as a good choice |
| C | One option for therapy that is adequate, perhaps among many other adequate therapies |
| **Level of Evidence** | **Description** |
| I | Based on well-designed, prospective, randomized, and controlled studies in an appropriate population of children |
| II | Based on data derived from prospectively collected, small comparative trials, or noncomparative prospective trials, or reasonable retrospective data from clinical trials in children, or data from other populations (eg, adults) |
| III | Based on case reports, case series, consensus statements, or expert opinion for situations in which sound data do not exist |

In response to many requests, we have also included new information on maximal adult dosages and higher dosages of some antimicrobials commonly used in children (mostly grade III information), which is now incorporated into Chapter 9. New for the mobile version is the inclusion of references, which are designed to provide either the primary clinical data, a review article, or a professional society statement (American Academy of Pediatrics [AAP] policy statement, Centers for Disease Control and Prevention *Morbidity and Mortality Weekly Report*, Infectious Diseases Society of America clinical practice guideline). The Web site, www.nelsonspocketbook.com, provides an Internet-accessible site for posting new references, errata, and new recommendations as well as other AAP materials on infectious diseases.

As has been the case since the first edition, many recommendations in *Nelson's Pocket Book* fall outside of the FDA-approved indications for children, because many infections may be caused by pathogens not evaluated during the antimicrobial approval process, infections may occur at tissue sites not evaluated by the FDA, or studies in children may not have been performed. Clearly, the medical literature most often provides us with clinical data, frequently requiring careful interpretation, but ultimately providing us with valuable insight. With any drug at any dose, we believe that the potential risks of treatment need to be justified by the potential benefits.

We are extremely grateful to have worked with our collaborators for this new edition. Drs John Leake, Paul Palumbo, Pablo Sanchez, and Jason Sauberan have again graciously provided us with their in-depth clinical knowledge and their expertise.

As we have stated with all previous editions, we look to you, our colleagues, for your thoughts and suggestions on how to improve the book. Thank you for your support of *Nelson's Pocket Book of Pediatric Antimicrobial Therapy* as we continue to evolve with the AAP in this new era of medical information and technology, 38 years after John Nelson packed and mailed the first edition from his garage in Dallas!

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## 1. Choosing Among Antibiotics Within a Class: Beta-Lactams, Macrolides, Aminoglycosides, and Fluoroquinolones

New drugs should be compared with others in the same class regarding (1) antimicrobial spectrum; (2) degree of free, nonprotein-bound antibiotic exposure achieved at the site of infection (a function of the in vitro activity for a particular pathogen within the spectrum, the pharmacokinetics at the site of infection, and the pharmacodynamic properties of the drug); (3) demonstrated efficacy in adequate and well-controlled clinical trials; (4) tolerance, toxicity, and side effects; and (5) cost. If there is no substantial benefit in any of those areas, one should opt for using an older, more familiar, and less expensive drug.

**Oral Cephalosporins** (cephalexin, cefadroxil, cefaclor, cefprozil, cefuroxime, cefixime, cefdinir, cefpodoxime, cefditoren, and ceftibuten). As a class, the oral cephalosporins have the advantages over oral penicillins of somewhat greater safety and greater palatability of the suspension formulations (penicillins have a bitter taste). Cefuroxime and cefpodoxime, which are esters, are the least palatable. The serum half-lives of cefpodoxime, ceftibuten, and cefixime are greater than 2 hours. This pharmacokinetic feature accounts for the fact that they may be given in 1 or 2 doses per day for certain indications. Cefaclor, cefprozil, cefuroxime, cefdinir, cefixime, cefpodoxime, and ceftibuten have the advantage of adding coverage (to a greater or lesser extent depending on the particular drug) for *Haemophilus influenzae* (including beta-lactamase–producing strains) to the activity of cephalexin; however, ceftibuten and cefixime have the disadvantage of less activity against *Streptococcus pneumoniae* than the others, particularly against the penicillin (beta-lactam) non-susceptible strains. The most palatable oral cephalosporin suspensions are cephalexin, cefaclor, cefadroxil, cefdinir, and cefixime as marketed by the original manufacturers. Generic versions of these products may not have the same characteristics as the original products.

**Parenteral Cephalosporins.** First-generation cephalosporins, such as cefazolin, have been used mainly for treatment of gram-positive infections (excluding methicillin-resistant *Staphylococcus aureus* [MRSA]); the gram-negative spectrum is limited. Cefazolin is well tolerated on intramuscular or intravenous injection.

A second-generation cephalosporin (cefuroxime) and the cephamycins (cefoxitin and cefotetan) provide increased activity against many gram-negative organisms. Cefoxitin has, in addition, activity against approximately 80% of strains of *Bacteroides fragilis* and can be considered for use in place of metronidazole, clindamycin, and carbapenems when that organism is implicated in non–life-threatening disease. In many countries of the world, cefuroxime has utility as single drug therapy for infants and young children with pneumonia, bone and joint infections, or other conditions in which gram-positive cocci (excluding MRSA) and *Haemophilus* are the usual pathogens. Because of the substantial decrease of *H influenzae* type b disease in countries with routine Hib immunization of infants, this advantage in gram-negative spectrum is less important than in the past. However, cefuroxime does retain significant activity against many penicillin non-susceptible strains of pneumococcus.

Third-generation cephalosporins (cefotaxime, ceftriaxone, ceftizoxime, and ceftazidime) all have enhanced potency against many gram-negative bacilli. They are inactive against enterococci and *Listeria* and have variable activity against *Pseudomonas* and *Bacteroides*. Cefotaxime and ceftriaxone have been used successfully to treat meningitis caused by pneumococcus (mostly penicillin-susceptible strains), *H influenzae* type b, meningococcus, and small numbers of infants with *Escherichia coli* meningitis. These drugs have the greatest usefulness for treating gram-negative bacillary infections due to their safety. Because ceftriaxone is excreted to a large extent via the liver, it can be used with little dosage adjustment in patients with renal

failure. Ceftazidime has the unique property of activity against *Pseudomonas aeruginosa* that is comparable to that of the aminoglycosides. Ceftriaxone has a serum half-life of 4 to 7 hours and can be given once a day for all infections, including meningitis, caused by susceptible organisms.

Cefepime, a fourth-generation cephalosporin approved for use in children, exhibits the antipseudomonal activity of ceftazidime, the gram-positive activity of second-generation cephalosporins, and better activity against gram-negative enteric bacilli such as *Enterobacter* and *Serratia* than is documented with cefotaxime and ceftriaxone.

Ceftobiprole and ceftaroline are fifth-generation cephalosporins, the first cephalosporins with activity against MRSA. Ceftobiprole has successfully completed phase 3 trials in adults and is pending approval for use in adults by US regulatory agencies as of September 2009. Studies are planned for children.

**Penicillinase-Resistant Penicillins** (dicloxacillin, nafcillin, and oxacillin). In this sense, penicillinase refers to the beta-lactamase produced by *S aureus,* not those produced by gram-negative bacteria. These antibiotics are active against penicillin-resistant *S aureus,* but not against MRSA. Nafcillin differs pharmacologically from the others in being excreted primarily by the liver rather than by the kidneys. This may be the reason for its lack of nephrotoxicity. Nafcillin pharmacokinetics are erratic in persons with liver disease. For oral use, dicloxacillin has excellent antistaphylococcal activity in vitro, but is virtually unpalatable.

**Antipseudomonal Beta-Lactams** (ticarcillin/clavulanate, piperacillin, piperacillin/tazobactam, aztreonam, ceftazidime, cefepime, meropenem, imipenem, and doripenem). Timentin (ticarcillin/clavulanate) and Zosyn (piperacillin/tazobactam) represent combinations of 2 beta-lactam drugs. One beta-lactam drug in the combination, clavulanic acid or tazobactam (known as beta-lactamase inhibitors) binds irreversibly to and neutralizes specific beta-lactamase enzymes produced by the organism, allowing the second beta-lactam drug as the active antibiotic (ticarcillin or piperacillin) to bind effectively to the intracellular target site, resulting in death of the organism. Thus the combination only adds to the spectrum of the original antibiotic when the mechanism of resistance is a beta-lactamase enzyme, and only when the beta-lactamase inhibitor is capable of binding to and inhibiting that particular organism's beta-lactamase. Timentin and Zosyn have no significant activity against *Pseudomonas* beyond that of ticarcillin or piperacillin, because their beta-lactamase inhibitors do not effectively inhibit all of the relevant beta-lactamases of *Pseudomonas.* However, the combination does extend the spectrum of activity to include many other beta-lactamase–positive bacteria, including *S aureus* and *B fragilis.*

*Pseudomonas* has an intrinsic capacity to develop resistance following exposure to any beta-lactam, based on inducible chromosomal beta-lactamases, upregulated efflux pumps, and changes in the cell wall. Because development of resistance is not uncommon during single drug therapy with these agents, an aminoglycoside such as tobramycin is often used in combination. Cefepime, meropenem, and imipenem are relatively stable to the beta-lactamases induced while on therapy and can be used as single agent therapy for most *Pseudomonas* infections, but resistance may still develop to these agents based on other mechanisms of resistance. For *Pseudomonas* infections in compromised hosts or in life-threatening infections, these drugs, too, should be used in combination with an aminoglycoside or a second active agent.

**Aminopenicillins** (amoxicillin, amoxicillin/clavulanate, ampicillin, and ampicillin/sulbactam). Ampicillin is more likely than the others to cause diarrhea, to disturb colonic coliform

flora, and to cause overgrowth of *Candida.* Amoxicillin is very well absorbed, good tasting, and associated with very few side effects. Augmentin is a combination of amoxicillin and clavulanate (see previous text regarding beta-lactam/beta-lactamase inhibitor combinations) that is available in several fixed proportions that permit amoxicillin to remain active against many beta-lactamase–producing bacteria, including *H influenzae* and *S aureus* (but not community-associated MRSA). Amoxicillin/clavulanate has undergone many changes in formulation since its introduction. It is available only in oral form in the United States, but is available for parenteral use in many other countries. The ratio of amoxicillin to clavulanate was originally 4:1, based on susceptibility data of pneumococcus and *Haemophilus* during the 1970s. With the emergence of penicillin-resistant pneumococcus, recommendations for increasing the dosage of amoxicillin, particularly for upper respiratory tract infections, were made. However, if one increases the dosage of clavulanate even slightly, the incidence of diarrhea increases. If one can keep the dosage of clavulanate constant while increasing the dosage of amoxicillin, one can treat the relatively resistant pneumococci while not increasing the gastrointestinal side effects. Although Augmentin suspensions containing 125-mg and 250-mg amoxicillin/5 mL, and the 125-mg and 250-mg chewable tablets contain the original 4:1 ratio, Augmentin suspensions containing 200-mg and 400-mg amoxicillin/5 mL, and the 200-mg and 400-mg chewable tablets, contain a higher 7:1 ratio. Augmentin ES-60, a suspension formulation of amoxicillin/clavulanate, contains amoxicillin:clavulanate in a ratio of 14:1. This preparation is designed to deliver 90 mg/kg/day of amoxicillin, divided twice daily, for the treatment of ear infections. The high serum and middle ear fluid concentrations achieved with 45 mg/kg/dose, combined with the long middle ear fluid half-life of amoxicillin, allow for a therapeutic antibiotic exposure to pathogens in the middle ear with a twice-daily regimen. However, the prolonged half-life in the middle ear fluid is not necessarily found in other infection sites (eg, skin, lung tissue, joint tissue), for which dosing of amoxicillin and Augmentin should continue to be 3 times daily for most susceptible pathogens.

For older children who can swallow tablets, the amoxicillin:clavulanate ratios are as follows: 500-mg tab (4:1); 875-mg tab (7:1); 1,000-mg tab (16:1).

Sulbactam, another beta-lactamase inhibitor like clavulanate, is combined with ampicillin in the parenteral formulation, Unasyn. The cautions regarding spectrum of activity for Timentin and Zosyn (see Antipseudomonal Beta-Lactams) also apply to Unasyn.

**Carbapenems.** Meropenem, imipenem, doripenem and ertapenem are carbapenems with a broader spectrum of activity than any other class of beta-lactam currently available. Meropenem, imipenem, and ertapenem are approved by the US Food and Drug Administration (FDA) for use in children. At present, we recommend them for treatment of infections caused by bacteria resistant to standard therapy, or for mixed infections involving aerobes and anaerobes. While imipenem has the potential for greater central nervous system irritability compared with other carbapenems, leading to an increased risk of seizures in children with meningitis, meropenem was not associated with an increased rate of seizures when compared with cefotaxime in children with meningitis. Both imipenem and meropenem are active against virtually all coliform bacilli, including cefotaxime-resistant (ESBL–producing or ampC-producing) strains, against *P aeruginosa* (including most ceftazidime-resistant strains), and against anaerobes, including *B fragilis.* While ertapenem lacks the excellent activity against *P aeruginosa* of the other carbapenems, it has the advantage of a prolonged serum half-life, which allows for once-daily dosing in adults and children 13 years of age and older; and twice-daily dosing in younger children. Newly emergent strains of *Klebsiella pneumoniae* contain *K pneumoniae* carbapenemase (KPC) enzymes, active against the carbapenems, reinforcing the need to keep track of your local antibiotic susceptibility patterns. While the current strains are seen predominantly

in the Northeast United States, it is not known how quickly or how far these strains will ultimately spread.

**Macrolides.** Erythromycin is the prototype of macrolide antibiotics. Almost 30 macrolides have been produced, but only 3 are FDA approved in the United States: erythromycin, azithromycin (also called an azalide), and clarithromycin, while a fourth, telithromycin (also called a ketolide) is approved for adults. As a class, these drugs achieve greater concentrations in tissues than in serum, particularly with azithromycin and clarithromycin. As a result, measuring serum concentrations is usually not clinically useful. Gastrointestinal intolerance to erythromycin is caused by the breakdown products of the macrolide ring structure. This is much less of a problem with azithromycin and clarithromycin. Azithromycin, clarithromycin, and telithromycin extend the activity of erythromycin to include *Haemophilus;* azithromycin and clarithromycin also have substantial activity against certain mycobacteria.

**Aminoglycosides.** Although 5 aminoglycoside antibiotics are available in the United States, only 3 are widely used for systemic therapy of aerobic gram-negative infections and for synergy in the treatment of certain gram-positive infections: amikacin, gentamicin, and tobramycin. Streptomycin and kanamycin have more limited utility. Resistance in gram-negative bacilli to aminoglycosides is caused by bacterial enzyme adenylation, acetylation, or phosphorylation. The specific activities of each enzyme in each pathogen are highly variable. As a result, antibiotic susceptibility tests must be done for each aminoglycoside drug separately. There are small differences in comparative toxicities of these aminoglycosides to the kidneys and eighth cranial nerve, although it is uncertain whether these small differences are clinically significant. For all children receiving a full treatment course, it is advisable to monitor peak and trough serum concentrations early in the course of therapy as the degree of drug exposure correlates with toxicity and elevated trough concentrations predict impending drug accumulation. With amikacin, desired peak concentrations are 20 to 35 μg/mL, and trough drug concentrations are less than 10 μg/mL; for gentamicin and tobramycin, depending on the frequency of dosing, peak concentrations should be 5 to 10 μg/mL and trough concentrations less than 2 μg/mL. Children with cystic fibrosis require greater dosages to achieve therapeutic serum concentrations. Inhaled tobramycin has been very successful in children with cystic fibrosis as an adjunctive therapy of gram-negative bacillary infections. The role of inhaled aminoglycosides in other gram-negative pneumonias has not been well studied.

**Once-Daily Dosing of Aminoglycosides.** Once-daily dosing of 5 to 7.5 mg/kg gentamicin or tobramycin has been used in adults and in some children; peak serum concentrations are greater than those achieved with dosing 3 times daily. Aminoglycosides demonstrate concentration-dependent killing of organisms, suggesting a potential benefit to higher serum concentrations achieved with once-daily dosing. Regimens giving the daily dosage as a single infusion, rather than as traditionally split doses every 8 hours are safe and effective in adults and may be less toxic. Experience with once-daily dosing in children is still limited, but increasing. In normal children with urinary tract infections, it seems likely that once-daily dosing will become the standard of care; however, for immune-compromised children and for those with other sites of infection, more prospectively collected data are needed before once-daily dosing can be recommended routinely.

**Fluoroquinolones (FQs).** Based on toxicity to cartilage in weight-bearing joints in juvenile animals investigated more than 30 years ago, pediatric studies were not undertaken with ciprofloxacin or other FQs. However, with increasing antibiotic resistance in pediatric pathogens, and an accumulating database in pediatrics suggesting that joint toxicity may be uncommon

in humans, the FDA allowed prospective studies to proceed in 1998. As of September 2009, no cases of documented FQ-attributable joint toxicity have occurred in children with FQs that are approved for use in the United States. However, no published data are available from prospective, blinded studies to accurately assess this risk. Unblinded studies with levofloxacin[1] and unpublished randomized studies comparing with ciprofloxacin versus other agents for complicated urinary tract infection[2] suggest the possibility of uncommon, reversible, FQ-attributable tendon/joint/muscle inflammation, but these data should be interpreted with caution. The use of FQs in situations of antibiotic resistance where no other agent is available is reasonable, weighing the benefits of treatment against the low risk of toxicity of this class of antibiotics. The use of an oral FQ in situations in which the only alternative is parenteral therapy also represents a reasonable use of this class of antibiotic.[3]

Ciprofloxacin usually has very good gram-negative activity (with great regional variation in susceptibility) against enteric bacilli *(E coli, Klebsiella, Enterobacter, Salmonella,* and *Shigella)* and against *P aeruginosa.* However, it lacks substantial gram-positive coverage, and should not be used to treat streptococcal, staphylococcal, or pneumococcal infections. Newer-generation FQs are more active against these pathogens; levofloxacin has published, documented efficacy and short-term safety in pediatric clinical trials for respiratory tract infections (acute otitis media and community-acquired pneumonia). No prospective pediatric clinical data exist for moxifloxacin, currently approved for use in adults, although pediatric studies are planned. None of the newer-generation FQs are more active against gram-negative pathogens than ciprofloxacin. Quinolone antibiotics are bitter tasting. Ciprofloxacin and levofloxacin are currently available in a suspension form; ciprofloxacin is FDA approved in pediatrics (for complicated urinary tract infections). For reasons of safety, and to prevent the emergence of widespread resistance, FQs should not be used for primary therapy of pediatric infections, and should be limited to situations in which safe and effective oral therapy with other classes of antibiotics does not exist.

## 2. Choosing Among Antifungal Agents: Amphotericins B, Azoles, and Echinocandins

**Amphotericins B.** Amphotericin is a polyene antifungal antibiotic that has been available since 1960 for the treatment of invasive fungal infections. It remains the most broad-spectrum antifungal available for clinical use, with a mechanism of action against the fungal cell membrane in which pores are created, compromising the integrity of the membrane and creating a fungicidal effect. The toxicity of the original formulation, amphotericin B deoxycholate (AmB-D), is substantial from the standpoints of both systemic reactions ("shake and bake") and renal toxicity. Premedication with acetaminophen, diphenhydramine, and meperidine is often required to prevent systemic reactions during infusion. Renal dysfunction manifests primarily as decreased glomerular filtration with a rising serum creatinine concentration, but substantial tubular nephropathy is associated with potassium wasting, requiring supplemental potassium for virtually all neonates and children, regardless of clinical symptoms associated with infusion. Fluid loading with saline pre- and post-AmB-D infusions seems to mitigate renal toxicity. These clinical and renal toxicities have limited the dosage used. Newer lipid preparations decrease toxicity with no apparent decrease in clinical efficacy. Decisions on which AmB preparation to use should therefore focus on side effects and costs. Two lipid formulations exist: one in which lipid complexes of amphotericin are created (AmB-LC), Abelcet; and one in which amphotericin is incorporated into liposomes (AmB-LP), AmBisome. The dosages used of these preparations are 3 to 5 mg/kg/day, in contrast to the 1 mg/kg/day of standard amphotericin. In most studies, the side effects of AmB-LP were somewhat less than those of AmB-LC, but both have significantly fewer side effects than AmB-D. The cost of standard AmB-D is substantially less than either lipid formulation. A colloidal "dispersion" of amphotericin in cholesteryl sulfate (AmB-CD), Amphotec, is also available, with decreased nephrotoxicity but infusion-related side effects closer to AmB-D than to the lipid formulations. The advantage of the lipid preparations is the ability to increase the dosages beyond what is approved by the US Food and Drug Administration (FDA) up to 10 to 15 mg/kg/day to maximize the chances of a successful outcome in life-threatening infections. The actual tissue concentrations of amphotericin at the molecular sites of infection are not known for any of the preparations, despite publication of liver or brain whole organ concentrations. If one needs to use amphotericin, the lipid formulations should be used as they are far better tolerated than AmB-D (CII).

**Azoles.** A new class of systemic agents for the treatment of fungal infections was approved first in 1981: an imidazole, ketoconazole. All of the azoles work by inhibition of ergosterol synthesis (fungal cytochrome P450 sterol 14-demethylation), required for fungal cell membrane integrity. In general, the azoles are fungistatic in vitro, in contrast to polyenes like AmB, that are fungicidal. Primarily active against *Candida* sp, ketoconazole is available in an oral formulation. The spectrum of activity is less than the newer triazoles, fluconazole, itraconazole, voriconazole, and posaconazole.

Fluconazole is active against a broader range of fungi than ketoconazole, and includes clinically relevant activity against *Cryptococcus, Coccidioides,* and *Histoplasma.* Fluconazole achieves relatively high concentrations in urine and cerebrospinal fluid compared with AmB. Fluconazole remains one of the most active, and so far the safest, systemic antifungal agent for the treatment of most *Candida* infections, although some resistance is present in many non-*albicans Candida* species as well as in *C albicans* in children repeatedly exposed to fluconazole. Available in both oral and parenteral formulations, clinical data have been generated in pediatrics down to premature neonates. Toxicity is unusual, and primarily hepatic.

Itraconazole, another triazole, is active against an even broader range of fungi and molds, including *Aspergillus.* It is available in capsule, solution, and intravenous forms; the solution provides higher, more consistent serum concentrations than capsules, and should be used preferentially. Itraconazole is indicated in adults for therapy of blastomycosis, histoplasmosis, and aspergillosis (although voriconazole is now a better option for *Aspergillus).* Limited pharmacokinetic data are available in children; itraconazole has not been approved by the FDA for pediatric indications. Toxicity in adults is primarily hepatic.

Voriconazole was approved in 2002, but is not yet FDA approved for children younger than 12 years; published data suggest superior efficacy, compared with amphotericin, in the empiric treatment of fever and neutropenia and in the treatment of invasive *Aspergillus* infections in adults. Given the poor clinical and microbiologic response of *Aspergillus* infections to amphotericin, and voriconazole's relative lack of side effects and toxicities compared with amphotericin, it is now the treatment of choice for *Aspergillus* infections. With in vitro activity against many fungi (including molds) that is better than itraconazole and similar to posaconazole, the ultimate role of voriconazole in deep fungal infections will depend on the side effect profile. Voriconazole retains activity against most *Candida* species, including some that are fluconazole-resistant, but it is unlikely to replace fluconazole for treatment of fluconazole-susceptible *Candida* infections. Voriconazole produces some unique visual field abnormalities that seem to be transient and resolve while still on therapy in about 10% of adults and children. Hepatotoxicity is uncommon, occurring only in 2% to 5% of patients. Voriconazole is cytochrome P450 metabolized and interacts with many similarly metabolized drugs to produce some profound changes in serum concentrations of many concurrently administered drugs.

Posaconazole is the most recently FDA-approved triazole for adults (2006) and is also not approved for children younger than 13 years; it is currently only available in an oral suspension formulation. The in vitro activity of posaconazole against *Candida* sp is better than that of fluconazole and similar to voriconazole. Overall activity against *Aspergillus* sp is also equivalent to voriconazole, but it is the first triazole with substantial activity against some zygomycetes, including *Rhizopus* sp and *Mucor* sp, as well as *Coccidioides, Histoplasma,* and *Blastomyces* and the pathogens of phaeohyphomycosis. In small case series of salvage therapy in zygomycosis, posaconazole was associated with clinical improvement in a substantial percentage (up to 60%) of patients. Posaconazole is eliminated by hepatic glucuronidation but does demonstrate inhibition of the cytochrome P450 3A4 enzyme system, leading to many drug interactions with other P450 metabolized drugs. It is currently approved for prophylaxis of *Candida* and *Aspergillus* infections in high-risk adults, and for treatment of *Candida* esophagitis in adults. Ongoing trials will allow a better assessment of posaconazole's role compared with other triazoles, and echinocandins.

**Echinocandins.** Another new class of systemic agents was approved in 2001, the echinocandins, which prevent cell wall formation (in contrast to the cell membrane site of action of amphotericin and the azoles) by inhibiting glucan synthesis. Caspofungin was the first of this class to be approved. Active in vitro against most *Candida* sp and *Aspergillus,* published data in adults suggest that the echinocandins produce equivalent clinical outcomes in the therapy of invasive *Candida* infections compared with AmB, but with far fewer side effects and toxicities. The echinocandins do not penetrate into cerebrospinal fluid, and therefore should be used very cautiously in children with disseminated fungal infections that may involve the central nervous system.

Caspofungin received FDA approval for children 3 months to 17 years of age in 2008 for empiric therapy of presumed fungal infections in febrile, neutropenic children: treatment of candidemia as well as *Candida* esophagitis, peritonitis, and empyema: and for salvage therapy

of invasive *Aspergillus*. Given a site of activity in the fungi distinct from amphotericin and the azoles, combination therapy of infections is being actively investigated. For children with invasive candidiasis who fail to respond to amphotericin, the addition of caspofungin has produced promising results. The combination of caspofungin and voriconazole for *Aspergillus* infections that failed treatment with AmB seemed to provide improved outcomes, compared with voriconazole alone. The combination has not been prospectively studied. Preliminary data suggest little toxicity at currently recommended dosages, certainly far less than treatment with AmB. Caspofungin is hepatically metabolized but not by the P450 system; however, significant drug interactions have been documented to occur with other hepatically metabolized drugs such as rifampin and phenobarbital.

Micafungin was approved in adults in 2005 and has been evaluated and approved for adults by the FDA for treatment of candidemia, *Candida* esophagitis, and peritonitis and prophylaxis of *Candida* infections in stem cell transplant recipients. The drug is also under active study in children, and like other echinocandins demonstrates a safety and tolerability profile that is far better than that of AmB, and similar to fluconazole. Micafungin is also metabolized in the liver, but not significantly by the P450 enzyme system. Fewer observed drug interactions occur when compared with caspofungin.

Anidulafungin was approved for adults for candidemia and *Candida* esophagitis in 2006. Like the other echinocandins, anidulafungin is not P450 metabolized and has not demonstrated significant drug interactions. Limited clinical efficacy data are available in children; however, some pediatric pharmacokinetic data have been presented and are present on the package label, demonstrating characteristics similar to other echinocandins.

## 3. How Antibiotic Dosages Are Determined Using Susceptibility Data, Pharmacodynamics, and Treatment Outcomes

**Factors Involved in Dosing Recommendations.** Our view of how to use antimicrobials is continually changing. As the published literature and our experience with each drug increases, our recommendations evolve as we compare the efficacy, safety, and cost of each drug in the context of current and previous data. Every new antibiotic must demonstrate some degree of efficacy and safety before we attempt to treat children. Occasionally, unanticipated toxicities and unanticipated clinical failures modify our initial recommendations.

Important considerations in any new recommendations we make include (1) the susceptibilities of pathogens to antibiotics, which are constantly changing, are different from region to region, and are hospital- and unit-specific; (2) the antibiotic concentrations achieved at the site of infection over a 24-hour dosing interval; (3) the mechanism of how antibiotics kill bacteria; (4) how often the dose we select produces a clinical and microbiological cure; (5) how often we encounter toxicity; and (6) how likely the antibiotic exposure leads to antibiotic resistance in the treated child, and in the population in general.

**Susceptibility.** Susceptibility data for each bacterial pathogen against a wide range of antibiotics are available from the microbiology laboratory of virtually every hospital. This antibiogram can help guide you in antibiotic selection. Many hospitals can separate the inpatient culture results from outpatient results, and many can give you the data by ward of the hospital (eg, pediatric ward vs neonatal intensive care unit vs adult intensive care unit). Susceptibility data are also available by region and by country. The recommendations made in this pocket book reflect overall susceptibility patterns present in the United States. Wide variations may exist for certain pathogens in different regions of the United States and the world.

**Drug Concentrations at the Site of Infection.** With every antibiotic, we can measure the concentration of antibiotic present in the serum. We also attempt to directly measure the concentrations in other infected tissues such as spinal fluid or middle ear fluid. Since free, unbound drug is required to kill pathogens, it is also important to calculate the amount of free drug available at the site of infection. While traditional methods of measuring antibiotics focused on the peak concentrations in serum and how rapidly the drugs were excreted, complex models of drug distribution and elimination now exist, not only for the serum, but for other tissue compartments as well. Antibiotic exposure to pathogens can be described in many ways: (1) the percentage of time in a 24-hour dosing interval that the antibiotic concentrations are above the minimum inhibitory concentration (MIC, the antibiotic concentration required for inhibition of growth of an organism) at the site of infection; (2) the mathematically calculated area below the serum-concentration-versus-time curve (area under the curve, AUC); and (3) the maximal concentration of drug achieved at the tissue site. For each of these 3 values, a ratio of that value to the MIC of the pathogen in question can be calculated and provides more useful information than simply looking at the MIC, as it allows us to compare the exposure of different antibiotics to each pathogen, and to compare the activity of the same antibiotic to many different pathogens.

**Pharmacodynamics.**[1] Pharmacodynamic data provide the clinician with information on how the bacterial pathogens are killed. Beta-lactam antibiotics tend to eradicate bacteria following prolonged exposure of the antibiotic to the pathogen at the site of infection, usually expressed as the percent of time over a dosing interval that the antibiotic is present at the site of infection in concentrations greater than the MIC. For example, amoxicillin needs to be present at the site of pneumococcal infection at a concentration above the MIC for that strain of pneumococ-

cus for only 40% of a 24-hour dosing interval. Remarkably, neither higher concentrations of amoxicillin nor a more prolonged exposure will substantially increase the cure rate. On the other hand, gentamicin's activity against *Escherichia coli* is based primarily on the absolute concentration of free antibiotic at the site of infection. The more antibiotic you can deliver to the site of infection, the more rapidly you can sterilize the tissue; we are only limited by the toxicities of gentamicin. For fluoroquinolones like ciprofloxacin, antibiotic exposure is best predicted by the ratio of AUC.

**Assessment of Clinical and Microbiological Outcomes.** In clinical trials of antiinfective agents, most children will be cured, but a few will fail therapy. For those few, we may note inadequate drug exposure (eg, more rapid drug elimination in a particular child) or infection caused by a pathogen with a particularly high MIC. By calculating the appropriate exposure parameters outlined above, we can often observe a particular value of exposure, above which we observe a very high rate of cure and below which the cure rate drops quickly. Knowing this target value (the exposure breakpoint) allows us to calculate the dosage that will create treatment success in most children. It is this dosage that we subsequently offer to you (if we have it) as one likely to cure your patient.

## 4. Community-Associated Methicillin-Resistant *Staphylococcus aureus*

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is a new pathogen in children that first appeared in the United States in the mid-1990s and currently represents 30% to 80% of all community isolates in various regions of the United States (check your hospital microbiology laboratory for your local rate); it is increasingly present in many areas of the world. This new CA-MRSA, like the hospital-associated MRSA that has been prevalent for the past 40 years, is resistant to methicillin and to all other beta-lactam antibiotics (that are US Food and Drug Administration [FDA]-approved as of September 2009). In contrast to the old strains, CA-MRSA usually does *not* have multiple antibiotic resistance genes. However, there are an undetermined number of pathogenicity factors that seem to make CA-MRSA more aggressive than its predecessor in the community, methicillin-susceptible *S aureus* (MSSA). Although published descriptions of clinical disease and treatment of the old *S aureus* found in textbooks, the medical literature, and *Nelson's Pocket Book* remain accurate for MSSA, CA-MRSA seems to cause greater tissue necrosis, an increased host inflammatory response, an increased rate of complications, and an increased rate of recurrent infections compared with MSSA. Response to therapy with non–beta-lactam antibiotics seems to be delayed, and it is unknown whether higher dosages and longer courses of alternative agents that seem to be needed for clinical cure are due to a hardier, better-adapted pathogen, or whether alternative agents are not as effective as beta-lactam agents against MSSA.

### Therapy for CA-MRSA

**Vancomycin (intravenous [IV])** has been the mainstay of parenteral therapy of MRSA infections for the past 4 decades and continues to have activity against more than 98% of strains isolated from children. A few cases of intermediate resistance and heteroresistance have been reported, most commonly in adults who are receiving long-term therapy or who have received multiple exposures to vancomycin. Unfortunately, the response to therapy using standard vancomycin dosing of 40 mg/kg/day in the treatment of the new CA-MRSA strains has not been as predictably good as in the past. Retrospective data in adults suggest that the meningitis dosage of 60 mg/kg/day is more effective, particularly for CA-MRSA strains with in vitro minimum inhibitory concentration (MIC) values of 1 or 2 mcg/mL. Serum trough concentrations of CA-MRSA should be kept in the range of 15 to 20 mcg/mL. Strains with MIC values of 4 mcg/mL or greater should generally be considered resistant to vancomycin. At the higher meningitis treatment dosage, one needs to follow renal function for the development of toxicity. Fortunately, children seem to tolerate this higher dosage much better than adults.

**Clindamycin (oral [PO] or IV)** is active against approximately 90% of strains, with great geographic variability (again, check with your hospital laboratory). The dosage for moderate to severe infections is 30 to 40 mg/kg/day, in 3 divided doses, using the same mg/kg dose PO or IV. Clindamycin is not as bactericidal as vancomycin, but gets into abscesses better than vancomycin. Some CA-MRSA strains are susceptible to clindamycin on initial testing, but have inducible clindamycin resistance that is usually assessed by the D-test. For infections that have a relatively low organism load (cellulitis, small abscesses), clindamycin should be effective therapy. Infections with a high organism load (empyema) may have a greater risk of failure against strains positive on a D-test, and clindamycin should not be used as the preferred agent. Clindamycin is used to treat most CA-MRSA infections that are not life-threatening, and if the child responds, therapy can be switched from IV to PO (although the oral solution is not very well-tolerated). *Clostridium difficile* enterocolitis is a concern as a clindamycin-associated complication; however, despite a great increase in the use of clindamycin in children during

the past decade, there are no recent published reports on any clinically significant increase in the rate of this complication in children.

**Trimethoprim-sulfamethoxazole (PO, IV),** Bactrim/Septra is active against CA-MRSA in vitro and has been used successfully to treat CA-MRSA skin infections by the oral route. There are no prospective comparative data on treatment of skin or skin structure infections, although some retrospective data in children suggest efficacy. Given our lack of information, this antibiotic should not be used to treat more serious infections.

**Linezolid, Zyvox (PO, IV),** active against virtually 100% of CA-MRSA strains, is another reasonable alternative but is considered bacteriostatic, and has relatively frequent hematologic toxicity (neutropenia, thrombocytopenia) and some infrequent neurologic toxicity (peripheral neuropathy, optic neuritis), particularly when used for courses of 2 weeks or longer (a complete blood count should be checked every week or two in children receiving prolonged linezolid therapy).

**Daptomycin (IV),** FDA approved for adults for skin infections and bacteremia/endocarditis, is a new class of antibiotic, a lipopeptide, and is highly bactericidal against MRSA by causing bacterial cell membrane depolarization. Daptomycin should be considered for treatment in failures with other better studied antibiotics, and may not be effective in the treatment of pneumonia due to binding of the drug to surfactant in the lung. Pediatric studies for skin infections are underway.

**Tigecycline and fluoroquinolones,** both of which may show in vitro activity, are not generally recommended for children if other agents are available and are tolerated, due to potential toxicity issues for children with tetracyclines and fluoroquinolones.

**Combination therapy** for serious infections, with vancomycin and rifampin (for deep abscesses), or vancomycin and gentamicin (for bacteremia) is often used, but no data exist on improved efficacy over single antibiotic therapy. Some experts use vancomycin and clindamycin in combination, particularly for children with a "toxic-shock" clinical presentation, but no data are currently available to compare one antibiotic against another for CA-MRSA, let alone one combination against another.

In Chapter 6, recommendations for treatment of staphylococcal infections are given for 2 situations, standard (eg, MSSA) and CA-MRSA. Cultures should be obtained whenever possible. If cultures demonstrate MSSA, then CA-MRSA antibiotics can be discontinued, continuing with the preferred beta-lactam agents. Rapid tests are becoming available to allow for identification of CA-MRSA within a few hours of obtaining a sample, rather than taking 1 to 3 days for the culture report.

**Life-threatening and Serious Infections.** If any CA-MRSA is present in your community, empiric therapy for presumed staphylococcal infections that are either life-threatening or infections for which any risk of failure is unacceptable (eg, bacterial arthritis), should follow the recommendations for CA-MRSA and include high-dose vancomycin, clindamycin, or linezolid. As beta-lactam antibiotics are considered better antibiotics for *S aureus* infections, nafcillin/oxacillin/methicillin or cefazolin should be used in combination with a CA-MRSA–active antibiotic until culture results are available.

**Moderate Infections.** If you live in a location with greater than 10% methicillin resistance, consider using the CA-MRSA recommendations for hospitalized children with presumed staphylococcal infections of any severity, and start empiric therapy with clindamycin (usually

active against >90% of CA-MRSA) or vancomycin IV. Standard empiric therapy can still be used for less severe infections in these regions, realizing that a certain low percentage of children who are actually infected by CA-MRSA may fail standard therapy.

In skin and skin structure abscesses, drainage of the abscess seems to be completely curative in some children, and antibiotics may not be necessary following incision and drainage.

**Mild Infections.** For nonserious, presumed staphylococcal infections in regions with significant CA-MRSA, empiric topical therapy with either mupirocin (Bactroban) or retapamulin (Altabax) ointment, or oral therapy with trimethoprim/sulfamethoxazole, clindamycin, or linezolid are preferred. For older children, doxycycline and minocycline are also options based on limited data in adults. Again, using standard empiric therapy with erythromycins, oral cephalosporins, or amoxicillin/clavulanate may be acceptable in areas with a low prevalence of CA-MRSA.

**Recurrent Infections.** For children with problematic, recurrent infections, no well-studied prospectively collected data provide a solution. Bleach baths (one-half cup of bleach in one-quarter filled bathtub) (Huang et al, *Pediatrics,* May 2009;123:e808–e814) seem to be able to transiently decrease the numbers of colonizing organisms. Bathing with chlorhexidine (Hibiclens, a preoperative antibacterial skin disinfectant) daily or a few times each week should provide topical anti-MRSA activity for several hours following a bath. Nasal mupirocin ointment (Bactroban) designed to eradicate colonization may also be used. All of these measures have advantages and disadvantages and need to be used together with environment measures (eg, washing towels frequently, using hand sanitizers, not sharing items of clothing). They can be found on the Centers for Disease Control and Prevention Web site at http://www.cdc.gov/mrsa/.

**The Future.** A number of new antibiotics are in clinical trials for adults, including 2 new cephalosporins that have been redesigned to regain activity against CA-MRSA (ceftobiprole and ceftaroline), as well as a number of improved glycopeptides and lipopeptides. It will be important to see how these drugs perform in adults before recommending them for children. Vaccines against staphylococcal infections have not been successful to date. Immune globulin and antibody products with activity against CA-MRSA are also under investigation.

## 5. Antimicrobial Therapy for Newborns

### A. Recommended Therapy for Selected Newborn Conditions

*NOTES*

- Prospectively collected data in newborns are slowly becoming available. In situations of inadequate data, suggested doses are based on efficacy, safety, and pharmacologic data from older children or adults. These may not account for the effect of developmental changes (effect of ontogeny) on drug metabolism that occur during early infancy and among premature and full-term infants.[1] These values may vary widely, particularly for the unstable premature infant. Oral convalescent therapy for neonatal infections has not been well studied, but may be used cautiously in non–life-threatening infections, in compliant families with easy access to medical care.
- The recommended antibiotic dosages and intervals of administration are given in the tables at the end of this chapter.
- *Adverse drug reaction:* Neonates should not receive ceftriaxone (IV or IM) while receiving IV calcium in any form (including hyperalimentation). Only neonatal cases have been reported to date. Neither milk nor oral calcium supplementation are likely to create the same conditions within the bloodstream as parenteral calcium. Current information is available on the FDA Web site.[2] Cefotaxime is usually preferred over ceftriaxone for neonates with hyperbilirubinemia.[3]
- *Abbreviations:* AOM, acute otitis media; CBC, complete blood count; CNS, central nervous system; CSF, cerebrospinal fluid; ESBL, extended spectrum beta-lactamase; FDA, US Food and Drug Administration; GI, gastrointestinal; G-CSF, granulocyte colony stimulating factor; HSV, herpes simplex virus; ID, infectious diseases; IM, intramuscular; IV, intravenous; IVIG, intravenous immune globulin; MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-susceptible *S aureus;* NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; NVP, nevirapine; oxacillin/nafcillin, oxacillin IV or nafcillin IV; PCR, polymerase chain reaction; PO, orally; RPR, rapid plasma reagin; RSV, respiratory syncytial virus; TIG, tetanus immune globulin; VDRL, Venereal Disease Research Laboratories; ZDV, zidovudine.

| Condition | Therapy *(evidence grade) See Table 5B for Neonatal Dosages* | Comments |
|---|---|---|
| **Conjunctivitis** | | |
| – Chlamydial[4–7] | Azithromycin PO x 5 d (AII) or erythromycin ethylsuccinate PO x 14 d (AII) | Macrolides PO preferred to prevent development of pneumonia; topical therapy unnecessary; association of erythromycin and pyloric stenosis in young infants[8]<br>Alternatives: oral sulfonamides may be used after the immediate neonatal period for infants who do not tolerate erythromycin |
| – Gonococcal[9–13] | Ceftriaxone 25–50 mg/kg (max 125 mg) IV, IM x 1 (AI) (longer treatment may be used for severe cases) | Saline irrigation of eyes<br>Alternative: cefotaxime may be used in infants with hyperbilirubinemia<br>Evaluate for chlamydial infection<br>All infants born to mothers with gonococcal infection (regardless of symptoms) require therapy |

| | | |
|---|---|---|
| – *S aureus*[14–16] | Topical or oral therapy may be sufficient for mild *S aureus* cases (BIII)<br>MSSA: oxacillin/nafcillin IV or cefazolin (for non-CNS infections) IM, IV x 7 d<br>MRSA: vancomycin IV or clindamycin IV, PO | Neomycin or erythromycin (BIII) ophthalmic drops or ointment<br>No prospective data for MRSA conjunctivitis (BIII)<br>Cephalexin PO for mild-moderate disease caused by MSSA<br>Increasing *S aureus* resistance with ciprofloxacin/levofloxacin ophthalmic formulations (AII) |
| – *Pseudomonas aeruginosa*[17–19] | Ceftazidime IM, IV AND tobramycin IM, IV x 7–10 d (Alternatives: piperacillin/tazobactam, cefepime, or meropenem) (BIII) | Aminoglycoside or polymyxin B-containing ophthalmic drops or ointment as adjunctive therapy |
| **Cytomegalovirus** | | |
| – Congenital[20–23] | Ganciclovir 12 mg/kg/day IV div q12h for 6 wks (AII) | Minimal benefit, only for hearing loss (AII)<br>Neutropenia in up to 20% of infants on long-term therapy (responds to G-CSF)<br>Oral valganciclovir at 16 mg/kg/dose PO BID provides similar drug exposure as ganciclovir IV at 6 mg/kg/dose, but prospective clinical data do not yet exist. (BIII) |
| – Acquired[22,24,25] | Ganciclovir IV for 10 to 14 d (AIII) | Only recommended for acute disease with pneumonia, hepatitis, encephalitis, or persistent thrombocytopenia (AIII) |
| **Fungal infections** *(see Chapter 8)* | | |
| – Candidiasis[26–36] | Amphotericin B deoxycholate (AmB-D) 1 mg/kg/day IV as a single infusion over 2 to 6 h x 10 d to 3–6 wks (AII)<br>Alternatives: AmB-LC (lipid complex) or AmB-LP (liposomal) (AII) or micafungin/caspofungin IV (AII)<br>For susceptible strains, fluconazole is usually effective in non–life-threatening infections, and in meningitis (AII) | Prompt removal of all catheters essential (AII)<br>Addition of micafungin/caspofungin or fluconazole to amphotericin if cultures persistently positive (*Candida krusei* usually resistant to fluconazole) (BIII)<br>Length of therapy dependent on disease (BIII)<br>Echinocandins not effective for meningitis as virtually no entry into CSF |
| – Aspergillosis (usually cutaneous infection with systemic dissemination)[37–39] | Voriconazole AND AmB-LP AND micafungin/caspofungin (BIII) | Aggressive antifungal therapy, early debridement of skin lesions (AIII)<br>Amphotericin B is least active agent; can be discontinued once infection controlled (BIII) |

| Condition | Therapy *(evidence grade) See Table 5B for Neonatal Dosages* | Comments |
|---|---|---|
| **Gastrointestinal infections** | | |
| – NEC or peritonitis secondary to bowel rupture. As initial rupture may be related to vascular insult, not infection, therapy is directed at the GI flora (and presumed bowel wall inflammation) present at the time of onset of NEC[40–43] | Vancomycin IV AND gentamicin IM, IV x 10 d or longer (BII)<br>Alternatives: ceftazidime/cefotaxime AND gentamicin ± clindamycin/metronidazole (BIII); OR piperacillin/tazobactam AND gentamicin (BIII); OR meropenem (BIII) | Surgical drainage (AII)<br>Definitive antibiotic therapy based on culture results; meropenem or cefepime if ceftazidime-resistant gram-negative bacilli isolated. Vancomycin rather than ampicillin if MRSA prevalent. Bacteroides not common until several weeks of age (AIII)<br>Duration of therapy dependent on clinical response and risk of persisting intraabdominal abscess (AIII)<br>Probiotics may prevent NEC in infants born <1,500 g. |
| – *Salmonella*[44] | Ampicillin IM, IV (if susceptible) OR cefotaxime IM, IV OR ceftriaxone IV, IM x 7–10 d (AII) | Observe for focal complications (meningitis, arthritis, etc) (AIII) |
| **Herpes simplex infection** | | |
| CNS and disseminated disease[45–47] | Acyclovir 60 mg/kg/day IV div q8h x 21 d (AII) | For CNS disease, perform CSF HSV PCR at 21 days of therapy and continue acyclovir until PCR negative<br>Foscarnet for acyclovir-resistant disease<br>Acyclovir PO suppression x 6 mos to prevent recurrent disease not routinely recommended; consultation with ID specialist suggested (AIII) |
| Skin, eye, or mouth disease[45–47] | Acyclovir 30 mg/kg/day IV div q8h x 14 d (AII) (if eye disease present, ADD topical trifluridine ophthalmic solution OR topical 0.1% iododeoxyuridine) | |

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|---|---|---|
| **Human immunodeficiency virus infection**[48,49] | Peripartum presumptive therapy and management: ZDV for the first 6 wks of life (AI)<br>Gestational age (GA) ≥35 wks: ZDV 8 mg/kg/day PO div q6h OR 6 mg/kg/day IV div q6h for 6 wks<br>GA <35 wks but >30 wks: ZDV 3 mg/kg/day IV (OR 4 mg/kg/day PO) div q12h. Increase at 2 wks of age to 6 mg/kg/day PO (4.5 mg/kg/d IV) div q8h.<br>GA <30 wks: ZDV 3 mg/kg/day IV (OR 4 mg/kg/day PO) div q12h. Increase at 4 wks of age to 6 mg/kg/day PO (OR 4.5 mg/kg/day IV) div q8h.<br>Consider (in consultation with a pediatric HIV specialist)<br>(1) Nevirapine 2 mg/kg PO (single dose) at 0–72 hrs of age if mother received this antiviral intrapartum (BIII)<br>(2) Lamivudine (3TC) 2 mg/kg PO q12h for 1 wk if mother received this intrapartum (BIII) | For detailed information: http://aidsinfo.nih.gov/Guidelines<br>Start therapy at 6 to 8 hrs of age if possible (AII)<br>Monitor CBC (AII)<br>Some experts consider the use of ZDV in combination with other antiretroviral drugs in certain situations (eg, mothers with minimal intervention before delivery or with known resistant virus). Since optimal prophylactic regimens have not been formally established, consultation with a pediatric HIV specialist is recommended. (BIII)<br>Perform HIV-1 DNA PCR at birth to 14 days, 1–2 mo, and 3–6 mo (AII)<br>Initiate prophylaxis for pneumocystis pneumonia at 6 wks of age if HIV infection not yet excluded (AII) |
| **Omphalitis and funisitis** | | |
| – Empiric therapy for omphalitis and necrotizing funisitis: direct therapy against coliform bacilli, *S aureus* (consider MRSA), and anaerobes. Need to culture to direct therapy[50–52] | Cefotaxime OR gentamicin, AND clindamycin x 10 d or longer (AII) | Alternatives for coliform coverage: cefepime, meropenem<br>For suspect MRSA: add vancomycin<br>Alternatives for combined MSSA and anaerobic coverage: piperacillin/tazobactam, or ticarcillin/clavulanate<br>Appropriate wound management for infected cord and necrotic tissue (AIII) |
| – Group A or B streptococci[53] | Penicillin G IV x 7–14 d or longer (shorter course for superficial funisitis without invasive infection) (AII) | Group A streptococcus usually causes "wet cord" without pus and with minimal erythema<br>Consultation with pediatric ID specialist is recommended for necrotizing fasciitis (AII) |
| – *S aureus*[52] | MSSA: oxacillin/nafcillin IV, IM x 5–7 d or longer (shorter course for superficial funisitis without invasive infection) (AIII)<br>MSSA: vancomycin (AIII) | Assess for bacteremia and other focus of infection<br>Alternatives for MRSA: linezolid, clindamycin (if susceptible) |

| Condition | Therapy *(evidence grade) See Table 5B for Neonatal Dosages* | Comments |
|---|---|---|
| – *Clostridium* species[54] | Clindamycin OR penicillin G IV x 10 d or longer, with additional agents based on culture results (AII) | Crepitance and rapidly spreading cellulitis around umbilicus<br>Mixed infection with other gram-positive and gram-negative bacteria common |
| **Osteomyelitis, suppurative arthritis[55–59]** | Duration of therapy dependent on causative organism and normalization of erythrocyte sedimentation rate and C-reactive protein; minimum for osteomyelitis 3–4 wks; arthritis therapy 2–3 wks (AIII) | Surgical drainage of pus (AIII); physical therapy may be needed (BIII)<br>Obtain cultures (aerobic; fungal if NICU) of bone or joint<br>Neonatal osteoarticular infections have not been prospectively studied in sufficiently powered trials |
| – Empiric therapy[58,59] | Vancomycin IV AND cefotaxime or gentamicin IV, IM (AIII) | Can use nafcillin/oxacillin instead of vancomycin if MRSA is not a concern |
| – Coliform bacteria *(Escherichia coli, Klebsiella* sp, *Enterobacter* sp)[59] | For *E coli* and *Klebsiella:* cefotaxime OR ceftriaxone, OR ampicillin (if susceptible) (AIII)<br>For *Enterobacter, Serratia,* or *Citrobacter:* ADD gentamicin IV, IM to cefotaxime or ceftriaxone, OR use cefepime or meropenem alone (AIII) | If pus drained, gentamicin is also an appropriate alternative (BIII)<br>Meropenem for ESBL-producing *E coli* and *Klebsiella* (AIII)<br>Piperacillin-tazobactam is an alternative for susceptible bacilli (BIII) |
| – Gonococcal arthritis and tenosynovitis[10–13,59] | Ceftriaxone 25–50 mg/kg IV, IM q24h OR cefotaxime x 7–10 d (AII) | Cefotaxime is preferred for infants with hyperbilirubinemia (>10 mg/dL) |
| – *S aureus*[59] | MSSA: oxacillin/nafcillin IV (AII)<br>MRSA: vancomycin IV (AIII) | Alternative for MSSA: cefazolin (AIII)<br>Alternatives for MRSA: linezolid, clindamycin (if susceptible) (BIII)<br>Addition of rifampin if persistently positive cultures |
| – Group B streptococcus[59] | Ampicillin or penicillin G IV (AII) | |
| **Otitis media[60]** | No controlled treatment trials in newborns; if no response, obtain middle ear fluid for culture. For otitis in NICU infants, culture for nosocomial pathogens. (AIII) | In addition to *Pneumococcus* and *Haemophilus,* coliforms and *S aureus* may also cause AOM in the newborn (AIII) |
| – Empiric therapy[61] | Amoxicillin/clavulanate (AIII) | If parenteral therapy needed: oxacillin/nafcillin AND cefotaxime or gentamicin |

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|---|---|---|
| – *E coli* (therapy of other coliforms based on susceptibility testing)[62] | Amoxicillin/clavulanate (AIII) | Cefotaxime if parenteral therapy needed |
| – *S aureus*[62] | MSSA: cephalexin PO x 10 d or cloxacillin PO (AIII)<br>MRSA: linezolid PO or clindamycin PO (BIII) | Oxacillin/nafcillin IV or vancomycin IV if unable to treat PO |
| – Group A or B streptococcus[62] | Amoxicillin 30–40 mg/kg/day PO div q8h x 10 d | May treat IV with penicillin G, ampicillin or cefotaxime, OR ceftriaxone IV, IM |
| – *Haemophilus*[62] | Amoxicillin/clavulanate PO OR amoxicillin PO if susceptible (AIII) | |
| **Parotitis, suppurative**[63] | Oxacillin/nafcillin IV AND gentamicin IV, IM x 10 d; consider vancomycin if MRSA suspected (AIII) | Usually staphylococcal but occasionally coliform<br>Antimicrobial regimen without incision/drainage is adequate in more than 75% of cases. |
| **Pulmonary infections** | | |
| – Aspiration pneumonia[64] | Clindamycin IV, IM AND gentamicin IV, IM x 7–10 d (AIII) | Mild aspiration episodes may not require antibiotic therapy |
| – *Chlamydia trachomatis*[65] | Azithromycin PO x 5 d or erythromycin ethylsuccinate PO x 14 d (AII) | Association of erythromycin and pyloric stenosis in young infants |
| – *Mycoplasma hominis*[66–69] | Clindamycin 20–30 mg/kg/day PO, IV x 10 d (organisms are resistant to macrolides) | Pathogenic role in pneumonia not well-defined and clinical efficacy unknown; no association with bronchopulmonary dysplasia (BIII) |
| – Pertussis[70] | Azithromycin 10 mg/kg PO, IV q24h x 5 d, or erythromycin ethylsuccinate PO x 14 d (AII) | Association of erythromycin and pyloric stenosis in young infants; may also occur with azithromycin<br>Alternatives for >1 month of age, clarithromycin for 7 days, and for >2 months of age, trimethoprim-sulfamethoxazole for 14 days |
| – *P aeruginosa*[71] | Ceftazidime IV, IM AND tobramycin IV, IM x 10–14 d or longer (AIII) | Alternatives: cefepime or meropenem, OR piperacillin/tazobactam AND tobramycin |
| – *S aureus*[16,72–74] | MSSA: oxacillin/nafcillin IV x 21 d minimum (AIII)<br>MRSA: vancomycin IV OR clindamycin IV if susceptible (AIII) | Alternative for MSSA: cefazolin IV<br>Addition of rifampin or linezolid if persistently positive cultures (AIII)<br>Thoracostomy drainage of empyema |

| Condition | Therapy *(evidence grade) See Table 5B for Neonatal Dosages* | Comments |
|---|---|---|
| – Group B streptococcus[75,76] | Penicillin G IV OR ampicillin IV, IM x 10–14 d (AIII) | For serious infections, ADD gentamicin for synergy until clinically improved<br>No prospective, randomized data on the efficacy of a 7-day treatment course |
| – *Ureaplasma* species *(urealyticum* or *parvum)*[77]<br>Pathogenic role of Ureaplasma not well defined, particularly for CNS | Azithromycin PO x 5 d, or erythromycin ethylsuccinate PO x 10 d (BIII) | Association of erythromycin and pyloric stenosis in young infants; *Ureaplasma* spp may be resistant to macrolides |
| **RSV**[78] | Prevention of infection with palivizumab (Synagis®) at 15 mg/kg IM, monthly during the RSV season in high-risk infants (AII):<br>1. Infants <24 mo of age with chronic lung disease and requiring medical therapy (max 5 doses)<br>2. Infants <24 mo of age with hemodynamically significant congenital heart disease (max 5 doses)<br>3. Premature infants: a) gestational age (GA) ≤28 wks, and chronologic age (CA) <12 mos at the start of the season; b) GA 29 to <32 wks, and CA <6 mos at the start of the season; c) GA from 32 wks to <35 wks, and CA <3 mos before or during RSV season AND 1 of 2 risk factors (child care attendance, sibling <5 yr of age) (max 3 doses)<br>4. Infants <35 wk GA and <12 mo of age with congenital abnormalities of airway or neuromuscular disorder | Aerosol ribavirin provides little, if any, benefit and should only be used for life-threatening infection with RSV.<br>Difficulties in administration, complications with airway reactivity, and potential toxicities to health care workers preclude routine use<br>Palivizumab will not treat an active infection<br>Palivizumab may benefit immunocompromised children and those with cystic fibrosis, but not routinely recommended as benefits not well defined<br>The entire American Academy of Pediatrics policy statement is available at: http://pediatrics.aappublications.org/cgi/reprint/peds.2009-2345v1. |
| **Sepsis and meningitis**[75,79,80] | *NOTE:* Duration of therapy: 10 d for sepsis without a focus (AIII); 21 d for gram-negative meningitis (or at least 14 d after CSF is shown to be sterile); 14–21 d for group B streptococcal meningitis (AIII) | There are no prospective, controlled studies on 5- or 7-day courses for mild or presumed sepsis |
| – Initial therapy, organism unknown | Ampicillin IV AND cefotaxime IV (AII), OR ampicillin IV AND gentamicin IV, IM (AII) | Cefotaxime preferred if meningitis suspected or cannot be excluded (AIII)<br>Initial empiric therapy of nosocomial infection should be based on each hospital's pathogens and susceptibilities |

| | | |
|---|---|---|
| – *Bacteroides fragilis* | Metronidazole, clindamycin, or meropenem IV, IM (AIII) | Metronidazole or meropenem preferred for CNS infection<br>Increasing resistance to clindamycin |
| – *Enterococcus* spp | Ampicillin IV, IM AND gentamicin IV, IM (AIII); for ampicillin-resistant organisms: vancomycin AND gentamicin (AIII) | Gentamicin needed with either ampicillin or vancomycin for bactericidal activity (AIII)<br>For vancomycin-resistant enterococci that are also ampicillin resistant: linezolid (AIII) |
| – *E coli* (check susceptibility for other coliform bacteria)[79,80] | Cefotaxime IV, IM. (AII) Gentamicin IV, IM is an alternative for most non-CNS infections. For bacteremic infections, it is prudent to use antibiotics that also treat neonatal meningitis. | Meropenem or cefepime for most gentamicin/cefotaxime-resistant coliforms (eg, *Enterobacter, Serratia)* (AIII)<br>Meropenem for ESBL-producing *E coli* and *Klebsiella* spp (AIII) |
| – Gonococcal[10–13] | Ceftriaxone 25–50 mg/kg IV, IM q24h OR cefotaxime 100 mg/kg/day IV, IM div q12h (AII) | Duration of therapy not well defined, consider 5 d |
| – *Listeria monocytogenes*[81] | Ampicillin IV, IM AND gentamicin IV, IM (AIII) | Gentamicin is synergistic in vitro with ampicillin. Continue until clinical and microbiologic response documented. (AIII) |
| – *P aeruginosa* | Ceftazidime IV, IM AND tobramycin IV, IM (AIII) | Meropenem, cefepime, OR piperacillin/tazobactam AND tobramycin are suitable alternatives (AIII) |
| – *S aureus*[16,73,74,82–84] | MSSA: oxacillin/nafcillin IV, IM, or cefazolin IV, IM (AII)<br>MRSA: vancomycin IV (AIII) | Clindamycin and linezolid not well studied for invasive MRSA in the neonate |
| – *Staphylococcus epidermidis* (or any coagulase-negative staphylococci) | Vancomycin IV or, if organisms susceptible, oxacillin/nafcillin or cefazolin are preferred (AIII) | Add rifampin if cultures persistently positive<br>Alternative: linezolid |
| – Group A streptococcus | Penicillin G or ampicillin IV (AII) | |
| – Group B streptococcus[75] | Ampicillin or penicillin G IV AND gentamicin IV, IM (AI) | Continue gentamicin until clinical and microbiologic response documented (AIII)<br>Duration of therapy: 10–14 d for sepsis (AII); 21 d for meningitis (AII) |

| Condition | Therapy *(evidence grade) See Table 5B for Neonatal Dosages* | Comments |
|---|---|---|
| **Skin and soft tissues** | | |
| – Breast abscess[85] | Vancomycin IV (for MRSA) or oxacillin/nafcillin IV, IM (MSSA) OR cefotaxime AND gentamicin if gram-negative rods seen on Gram stain (AIII) | Gram stain of expressed pus guides empiric therapy; vancomycin if MRSA prevalent in community; alternative to vancomycin: clindamycin, linezolid; may need surgical drainage to minimize damage to breast tissue<br>Treatment duration individualized, until clinical findings have completely resolved (AIII) |
| – Erysipelas (and other group A streptococcal infections) | Penicillin G IV x 5–7 d, followed by oral therapy (if bacteremia not present) to complete a 10 d course (AIII) | Group B streptococcus may produce similar cellulitis or nodular lesions |
| – Impetigo neonatorum | MSSA: oxacillin/nafcillin IV, IM OR cephalexin (AIII)<br>MRSA: vancomycin IV; x 5 d (AIII) | Systemic antibiotic therapy usually not required for superficial impetigo; local chlorhexidine cleansing may help with or without topical mupirocin (MRSA) or bacitracin (MSSA)<br>Alternatives for MRSA: clindamycin IV, PO, or linezolid IV, PO |
| – *S aureus*[16,74,82,86] | MSSA: oxacillin/nafcillin IV, IM (AII)<br>MRSA: vancomycin IV (AIII) | Surgical drainage may be required<br>MRSA may cause necrotizing fasciitis<br>Alternatives for MRSA: clindamycin IV or linezolid IV<br>Convalescent oral therapy if infection responds quickly to IV therapy |
| – Group B streptococcus[75] | Penicillin G IV OR ampicillin IV, IM | Usually no pus formed<br>Treatment course dependent on extent of infection, 7–14 d |
| **Syphilis, congenital** (AIII) **(<1 month of age)[87]** | During periods when the availability of penicillin is compromised, see http://www.cdc.gov/nchstp/dstd/penicillinG.htm. | Evaluation and treatment do not depend on mother's HIV status<br>Obtain follow-up serology every 2–3 mos until non-treponemal test nonreactive or decreased 4-fold<br>If CSF positive, repeat spinal tap with CSF VDRL at 6 mos, and if abnormal, re-treat |

| | | |
|---|---|---|
| – Proven or highly probable disease (see comments for definitions) | Aqueous penicillin G 50,000 U/kg/dose q12h (day of life 1–7), q8h (>7 d) IV OR procaine penicillin G 50,000 U/kg IM q24h; x 10 d | Evaluation to determine type and duration of therapy: CSF analysis (VDRL, cell count, protein) CBC and platelet count. Other tests as clinically indicated, including long-bone radiographs, chest radiograph, liver function tests, cranial ultrasound, ophthalmologic exam, and hearing test (auditory brainstem response)<br>Proven or highly probable disease: (1) abnormal physical exam; (2) serum quantitative non treponemal serologic titer that is 4-fold higher than the mother's titer; or (3) a positive darkfield or fluorescent antibody test of body fluid(s).<br>If more than 1 day of therapy is missed, the entire course is restarted.<br>Reliable follow-up important if only a single dose of benzathine penicillin given |
| – Normal physical exam and risk factors (see comments for risk factors) | Laboratory and radiograph evaluation abnormal: Aqueous penicillin G 50,000 U/kg/dose q12h (day of life 1–7), q8h (>7 d) IV OR procaine penicillin G 50,000 U/kg IM q24h x 10 d<br>Laboratory and radiograph evaluation normal: Aqueous penicillin G 50,000 U/kg/dose q12h (day of life 1–7), q8h (>7 d) IV OR procaine penicillin G 50,000 U/kg IM q24h x 10 d; OR benzathine penicillin G 50,000 units/kg/dose IM in a single dose | Risk factors: a serum quantitative nontreponemal serologic titer ≤maternal titer and (1) mother was not treated, inadequately treated, or has no documentation of having received treatment; (2) mother was treated with erythromycin or other non-penicillin regimen; or (3) mother received treatment <4 weeks before delivery.<br>If more than 1 day of therapy is missed, the entire course is restarted.<br>Reliable follow-up important if only a single dose of benzathine penicillin given |

| Condition | Therapy *(evidence grade) See Table 5B for Neonatal Dosages* | Comments |
|---|---|---|
| **Syphilis, congenital** (AIII) **(<1 month of age)** *(continued)* | | |
| – Normal physical exam and risk factors (see comments for risk factors) | Benzathine penicillin G 50,000 units/kg/dose IM in a single dose | No evaluation required.<br>Some experts would not treat but provide close serologic follow-up.<br>Risk factors: a serum quantitative nontreponemal serologic titer ≤maternal titer and mother treated during pregnancy, treatment was appropriate for the stage of infection, and treatment was administered >4 weeks before delivery; and mother has no evidence of reinfection or relapse. |
| – Normal physical exam and risk factors (see comments for risk factors) | No treatment | No evaluation required.<br>Some experts would treat with benzathine penicillin G 50,000 units/kg as a single IM injection, particularly if follow-up is uncertain.<br>Risk factors: a serum quantitative nontreponemal serologic titer ≤maternal titer and the mother's treatment was adequate before pregnancy, and mother's nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (VDRL <1:2; RPR <1:4). |

| | | |
|---|---|---|
| **Syphilis, congenital (>1 month of age)[87]** | Aqueous crystalline penicillin G 200,000–300,000 units/kg/day IV div q4–6 hr for 10 d | Evaluation to determine type and duration of therapy: CSF analysis (VDRL, cell count, protein) CBC and platelet count. Other tests as clinically indicated, including long-bone radiographs, chest radiograph, liver function tests, cranial ultrasound, ophthalmologic exam, and hearing test (auditory brainstem response), If no clinical manifestations of disease, the CSF exam is normal, and the CSF VDRL test result is negative, some specialists would treat with up to 3 weekly doses of benzathine penicillin G, 50,000 U/kg IM. |
| **Tetanus neonatorum[88]** | Metronidazole IV/PO (alternative: penicillin G IV) x 10–14 d (AIII)<br>Human TIG 3,000–6,000 U IM x 1 (AIII) | Wound cleaning and debridement vital<br>IVIG (200–400 mg/kg) is an alternative if TIG not available; equine tetanus antitoxin not available in US but is alternative to TIG |
| **Toxoplasmosis, congenital[89,90]** | Sulfadiazine 100 mg/kg/day PO div q12h AND pyrimethamine 2 mg/kg PO daily x 2 (loading dose), then 1 mg/kg PO q24h for 2–6 months, then 3 times weekly (M-W-F) up to 1 yr (AIII)<br>Folinic acid (leukovorin) 10 mg 3 times weekly (AIII) | Corticosteroids (1 mg/kg/day div q12h) if active chorioretinitis or CSF protein >1 g/dL (AIII)<br>Start sulfa after neonatal jaundice has resolved.<br>Therapy is only effective against active trophozoites, not cysts. |
| **Urinary tract infection[91]** | Initial empiric therapy with ampicillin AND gentamicin; OR ampicillin AND cefotaxime pending culture and susceptibility test results x 7–10 days | Investigate for kidney disease and for abnormalities of urinary tract<br>Oral therapy for *E coli* acceptable once infant asymptomatic and culture sterile. |
| – Coliform bacteria (eg, *E coli, Klebsiella, Enterobacter, Serratia)* | Cefotaxime IV, IM OR, in the absence of renal or perinephric abscess, gentamicin IV, IM x 7–10 d (AII) | Ampicillin used for susceptible organisms |
| – *Enterococcus* | Ampicillin IV, IM X 7–10 days, add gentamicin until cultures are sterile (AIII); for ampicillin resistance, use vancomycin, add gentamicin until cultures are sterile | Aminoglycoside needed with ampicillin or vancomycin for bactericidal activity (assuming organisms susceptible to an aminoglycoside). |
| – *P aeruginosa* | Ceftazidime IV, IM OR, in the absence of renal or perinephric abscess, tobramycin IV, IM x 10 d (AIII) | Meropenem or cefepime are alternatives. |
| – *Candida* spp[33–36] | Amphotericin IV OR fluconazole (if susceptible) (AII) | Renal, bladder ultrasound for fungus ball. Other triazoles are alternatives; insufficient data on echinocandins for neonatal urinary tract infection. |

## B. Antimicrobial Dosages for Neonates

| | | Dosages (mg/kg/day) and Intervals of Administration | | | | |
|---|---|---|---|---|---|---|
| | | Chronologic Age ≤28 days | | | | Chronologic Age >28 days |
| | | Body Weight ≤2,000 g | | Body Weight >2,000 g | | |
| **Antibiotic** | **Route** | **0–7 d old** | **8–28 d old** | **0–7 d old** | **8–28 d old** | |
| Acyclovir[a] | IV | 40 div q12h | 60 div q8h | 60 div q8h | 60 div q8h | 60 div q8h |
| Amoxicillin/ clavulanate | PO | | | 30 div q12h | 30 div q12h | 30 div q12h |
| Amphotericins B | | | | | | |
| deoxycholate | IV | 1 q24h | 1 q24h | 1 q24h | 1 q24h | 1 q24h |
| lipid complex | IV | 5 q24h | 5 q24h | 5 q24h | 5 q24h | 5 q24h |
| liposomal | IV | 5 q24h | 5 q24h | 5 q24h | 5 q24h | 5 q24h |
| Ampicillin[b] | IV, IM | 100 div q12h | 150 div q8h | 150 div q8h | 200 div q6h | 200 div q6h |
| Azithromycin[c] | PO | 10 q24h | 10 q24h | 5 q24h[c] | 10 q24h[c] | 10 q24h[c] |
| | IV | 10 q24h | 10 q24h | 10 q24h | 10 q24h | 10 q24h |
| Aztreonam | IV, IM | 60 div q12h | 90 div q8h | 60 div q12h | 120 div q8h | 120 div q6h |
| Caspofungin[d] | IV | 2 q24h | 2 q24h | 2 q24h | 2 q24h | 2 q24h |
| Cefazolin | IV, IM | 50 div q12h | 50 div q12h | 50 div q12h | 75 div q8h | 75 div q8h |
| Cefepime[e] | IV, IM | 60 div q12h | 100 div q12h[e] | 60 div q12h | 100 div q12h[e] | 150 div q8h |
| Cefotaxime | IV, IM | 100 div q12h | 150 div q8h | 100 div q12h | 150 div q8h | 200 div q6h |
| Ceftazidime | IV, IM | 100 div q12h | 150 div q8h | 100 div q12h | 150 div q8h | 150 div q8h |
| Ceftriaxone[f] | IV, IM | 50 q24h | 50 q24h | 50 q24h | 75 q24h | 100 q24h |
| Cefuroxime | IV, IM | 100 div q12h | 150 div q8h | 150 div q8h | 150 div q8h | 150 div q8h |
| Clindamycin | IV, IM, PO | 10 div q12h | 15 div q8h | 15 div q8h | 20 div q6h | 30 div q6h |
| Daptomycin | IV | No systematically collected pharmacokinetic data available in the neonate | | | | |
| Erythromycin ethylsuccinate | PO | 20 div q12h | 30 div q8h | 20 div q12h | 40 div q8h | 40 div q6h |

| | | Dosages (mg/kg/day) and Intervals of Administration | | | | |
|---|---|---|---|---|---|---|
| | | Chronologic Age ≤28 days | | | | Chronologic Age >28 days |
| | | Body Weight ≤2,000 g | | Body Weight >2,000 g | | |
| **Antibiotic** | **Route** | **0–7 d old** | **8–28 d old** | **0–7 d old** | **8–28 d old** | |
| Fluconazole | | | | | | |
| – treatment | IV, PO | 12 q48h | 12 q24h | 12 q48h | 12 q24h | 12 q24h |
| – prophylaxis | IV, PO | 3 twice wkly | 3 twice wkly | 3 twice wkly | 3 twice wkly | 3 twice wkly |
| Flucytosine[g] | PO | 75 div q8h | 75 div q6h | 75 div q6h | 75 div q6h | 75 div q6h |
| Imipenem/ cilastin | IV | 50 div q12h | 50 div q12h | 50 div q12h | 50 div q12h | 50 div q12h |
| Lamivudine (3TC)[h] | PO | 4 div q12h | — | 4 div q12h | — | — |
| Linezolid | IV, PO | 20 div q12h | 30 div q8h | 30 div q8h | 30 div q8h | 30 div q8h |
| Meropenem | IV | | | | | |
| - sepsis | IV | 40 div q12h | 60 div q8h | 60 div q8h | 90 div q8h | 90 div q8h |
| - meningitis | IV | 120 div q8h | 120 div q8h | 120 div q8h | 120 div q8h | 120 div q8h |
| Metronidazole | IV, PO | 7.5 div q24h | 15 div q12h | 7.5 div q24h | 15 div q12h | 30 div q8h |
| Micafungin | IV | 10 q24h | 10 q24h | 10 q24h | 10 q24h | 10 q24h |
| Nafcillin,[i] oxacillin | IV, IM | 50 div q12h | 75 div q8h | 75 div q8h | 150 div q6h | 150 div q6h |
| Nevirapine[j] | PO | 2 once | — | 2 once | — | — |
| Nystatin | | | | | | |
| -treatment | PO | 4 cc div q6h | 4 cc div q6h | 8 cc div q6h | 8 cc div q6h | 8 cc div q6h |
| -prophylaxis | PO | 3 cc div q8h | 3 cc div q8h | 3 cc div q8h | 3 cc div q8h | 3 cc div q8h |
| Penicillin G, benzathine | IM | 50,000 U | 50,000 U | 50,000 U | 50,000 U | 50,000 U |
| Penicillin G, crystalline | IV | 300,000 U div q8h | 450,000 U div q8h | 300,000 U div q8h | 450,000 U div q6h | 450,000 U div q6h |

| | | Dosages (mg/kg/day) and Intervals of Administration | | | | |
|---|---|---|---|---|---|---|
| | | Chronologic Age ≤28 days | | | | Chronologic Age >28 days |
| | | Body Weight ≤2,000 g | | Body Weight >2,000 g | | |
| **Antibiotic** | **Route** | **0–7 d old** | **8–28 d old** | **0–7 d old** | **8–28 d old** | |
| Penicillin G, crystalline (congenital syphilis) | IV | 100,000 U div q12h | 150,000 U div q8h | 100,000 U div q12h | 150,000 U div q8h | 200,000 U div q6h |
| Penicillin G, procaine | IM | 50,000 U q24h | 50,000 U q24h | 50,000 U q24h | 50,000 U q24h | 50,000 U q24h |
| Piperacillin/ tazobactam | IV | 150 div q12h | 225 div q8h | 150 div q12h | 225 div q8h | 240 div q6h |
| Rifampin | IV, PO | 10 q24h | 10 q24h | 10 q24h | 10 q24h | 10 q24h |
| Ticarcillin/ clavulanate | IV | 150 div q12h | 225 div q8h | 150 div 12h | 225 div q8h | 300 div q6h |
| Voriconazole | IV, PO | 8–20 div q12h | 8–20 div q12h | 8–20 div q12h | 8–20 div q12h | 8–20 div q12h |

[a] Increase dosing interval for renal impairment, eg, from q8h to q12h or q12 to q18–24h dosing. For severe renal failure, reduce dose to 10 mg/kg/dose as well.

[b] For group B streptococcal meningitis, the recommended dosage for infants ≤7 days of age 200–300 mk/kg/day q8h, and for infants >7 days of age, 300 mg/kg/day q6h.

[c] Azithromycin oral dose for pertussis should be 10 mg/kg once daily for the entire 5-day treatment course, while for other upper respiratory tract infections, 10 mg/kg is given on the first day, followed by 5 mg/kg for 4 subsequent days. For CNS disease, 10 mg/k once daily is recommended for entire course.

[d] Higher dosage may be needed for aspergillus than for candida. May also be dosed as 25–50 mg/m$^2$ qd for all age groups.

[e] Cefepime should be given at 60 mg/kg/day div q12h for the first 2 weeks of age, after which the dosing increases to 100 mg/kg/day div q12h. For meningitis or *Pseudomonas* infections, dosage is 150 mg/kg/day div q8h.

[f] 25–50 mg/kg (maximum 125 mg) as single dose for gonococcal eye prophylaxis or treatment.

[g] Increase to 150/mg/kg/day to achieve serum concentration of 50–70 µg/mL.

[h] 3TC is provided from birth to 1 week of age. Use of antiretroviral drugs other than zidovudine cannot be recommended in premature infants due to lack of dosing and safety data.

[i] Nafcillin preferred for meningitis (increase to 50 mg/kg/dose)

[j] Single dose given once orally at 2–3 days of age if mother received intrapartum single-dose NVP, or given at birth if mother did not receive intrapartum single-dose NVP. If maternal dose is given <2 hours before delivery, infant dose should be administered as soon as possible following birth. Use of antiretroviral drugs other than zidovudine cannot be recommended in premature infants due to lack of dosing and safety data.

## C. Drugs for Neonates Dosed According Only to Age

| | | Dosage (mg/kg/DOSE) by Gestational Age Plus Weeks of Age | | | |
|---|---|---|---|---|---|
| **Drug** | **Routes of Administration** | **≤26 Wks** | **27–34 Wks** | **35–42 Wks** | **≥43 Wks** |
| Acyclovir | IV | 20 q12h | 20 q12h | 20 q8h | 20 q8h |
| Amikacin[a,b] | IV, IM | 7.5 q24h | 7.5 q18h | 15 q24h | 15 q24h |
| Ganciclovir | IV | 6 q24h | 6 q18h[c] | 6 q12h | 6 q12h |
| Valganciclovir | PO | 16 q24h | 16 q18h[c] | 16 q12h | 16 q12h |
| Gentamicin[b,c,d] | IV, IM | 2.5 q24h[e] | 2.5 q18h[e] | 4 q24h | 4 q8h |
| Tobramycin[b,c] | IV, IM | 2.5 q24h[e] | 2.5 q18h[e] | 4 q24h | 4 q24h |
| Vancomycin[f] | IV | 15 q18h | 15 q12h[g] | 15 q8h[g] | 15 q6h[g] |
| Zidovudine | IV | 1.5 q12[h] | 1.5 q12h[h] | 1.5 q6h | 1.5 q6h |
| | PO[i] | 2 q12h[h] | 2 q12h[h] | 2 q6h | 2 q6h |

[a] Desired serum concentrations: 20–30 µg/mL (peak), <10 µg/mL (trough).
[b] Once daily dosing regimen (amikacin, 15 mg/kg; gentamicin, tobramycin, 4 mg/kg) is used by some neonatologists
[c] At ≥32 wks gestation, q12h
[d] Desired serum concentrations: 5–12 µg/mL (peak), <2.0 µg/mL (trough).
[e] Alternative regimen: ≤29 wks: postnatal age 0–7 days, 5 mg/kg q48h; 8–28 days, 4 mg/kg q36h; ≥29 days, 4 mg/kg q24h
30–34 wks: postnatal age 0–7 days, 4.5 mg/kg q36h; ≥8 days, 4 mg/kg q24h.
[f] Desired serum concentrations: 20–40 µg/mL (peak), <10–15 µg/mL (trough); for MRSA infections, trough 15–20 µg/mL.
[g] At 28 days of age, vancomycin is dosed at 20 mg/kg/dose. The interval remains the same.
[h] Zidovudine dosing of 4 mg/kg per dose given PO q12 h has been used for infant prophylaxis in some international perinatal studies. Although there are no definitive data to show equivalent pharmacokinetic parameters or efficacy in preventing transmission, a regimen of ZDV 4 mg/kg per dose given PO twice daily instead of 2 mg/kg per dose given PO 4 times daily may be considered when there are concerns about adherence to drug administration to the infant.
[i] For infants with gestational age <30 wks, change dosing interval to every 8 hours at 4 wks of age. For infants with gestational age ≥30 wks, change dosing interval to every 8 hours at 2 wks of age.

(Table prepared by Pablo J. Sánchez, MD.)

## D. Use of Antimicrobials During Pregnancy or Breastfeeding

The use of antimicrobials during pregnancy should be balanced by the risk of fetal toxicity including anatomic anomalies. A number of factors determine the degree of transfer of antibiotics across the placenta: lipid solubility, degree of ionization, molecular weight, protein binding, placental maturation, and placental and fetal blood flow. The FDA provides 5 categories to indicate the level of risk to the fetus: (1) Category A: fetal harm seems remote since controlled studies have not demonstrated a risk to the fetus; (2) Category B: animal reproduction studies have not shown a fetal risk but no controlled studies in pregnant women have been done, or animal studies have shown an adverse effect that has not been confirmed in human studies (penicillin, amoxicillin, ampicillin, cephalexin/cefazolin, azithromycin, clindamycin, vancomycin, zanamivir); (3) Category C: studies in animals have shown an adverse effect on the fetus but there are no studies in women and no animal data are available; the potential benefit of the drug may justify the possible risk to the fetus (chloramphenicol, ciprofloxacin, gentamicin, levofloxacin, oseltamivir, rifampin); (4) Category D: evidence exists of human fetal risk but the benefits may outweigh such risk (doxycycline); (5) Category X: The drug is contraindicated since animal or human studies have shown fetal abnormalities or fetal risk (ribavirin). Drugs not listed should be used with caution for firm clinical indications.

Fetal serum concentrations of the following drugs are equal to, or only slightly less than, those in the mother: penicillin G, amoxicillin, ampicillin, sulfonamides, trimethoprim, tetracyclines, and nitrofurantoin. The aminoglycoside concentrations in fetal serum are 20% to 50% of those in maternal serum. Cephalosporins, nafcillin, oxacillin, and clindamycin penetrate poorly (10%–15%), and fetal concentrations of erythromycin and dicloxacillin are less than 10% of those in the mother.

The use of antimicrobials by the mother during breastfeeding should be balanced by the risk of clinical or laboratory toxicities in the infant. In general, the neonatal exposure is well-tolerated. While maternal treatment with sulfa-containing antibiotics should be approached with caution in the breastfed jaundiced or ill neonate, no symptoms have been associated with maternal treatment with amoxicillin, cefazolin, cefotaxime, ceftazidime, ceftriaxone, ciprofloxacin, clindamycin, erythromycin, ethambutol, fluconazole, gentamicin, isoniazid, rifampin, (used for <3 weeks). Metronidazole seems safe, but may impart a metallic taste to breast milk.

The most current, updated information can be found at the National Library of Medicine Web site (http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT). This Web site provides the Drugs and Lactation Database (LactMed), which contains a peer-reviewed and fully referenced database of drugs to which breastfeeding mothers may be exposed. Among the data included are maternal and infant levels of drugs, possible effects on breastfed infants and on lactation, and alternate drugs to consider. Just type in the drug for which you need information, and the full report on that drug is provided.[92]

## 6. Antimicrobial Therapy According to Clinical Syndromes

*NOTES*

- This chapter should be considered a rough guideline for a typical patient. Dosage recommendations are for patients with relatively normal hydration, renal function, and hepatic function. See Chapter 14 for information on patients with impaired renal function. Higher dosages may also be necessary if the antibiotic does not penetrate well into the infected tissue, or if the child is immune-compromised.
- Duration of treatment should be individualized. Those recommended are based on the literature, common practice, and general experience. Critical evaluations of duration of therapy have been carried out in very few diseases. In general, a longer duration of therapy should be used (1) for tissues in which antibiotic concentrations may be relatively low (eg, abscess, bone), (2) when the organisms are less susceptible, (3) when a relapse of infection is unacceptable (eg, CNS infections), or (4) when the host is immune-compromised in some way. An assessment after therapy will ensure that your selection of antibiotic, dose, and duration of therapy was appropriate.
- Diseases are arranged by body systems. Consult the index for the alphabetized listing of diseases and Chapters 7 through 10 for the alphabetized listing of pathogens and for uncommon organisms not included in this chapter.
- *Abbreviations:* ADH, antidiuretic hormone; AFB, acid-fast bacilli; amox/clav, amoxicillin/clavulanate; amp/sulbactam, ampicillin/sulbactam; bid, twice daily; AOM, acute otitis media; CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*; CMV, cytomegalovirus; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; div, divided; EBV, Epstein-Barr virus; ESBL, extended spectrum beta-lactamase; ESR, erythrocyte sedimentation rate; FDA, US Food and Drug Administration; HAP/VAP, hospital-acquired pneumonia/ventilator-acquired pneumonia; HIV, human immunodeficiency virus; HSV, herpes simplex virus; HUS, hemolytic uremic syndrome; I&D, incision and drainage; IM, intramuscular; inh, inhaled; IV, intravenous; IVIG, intravenous immune globulin; LP, lumbar puncture; MAC, *Mycobacterium avium* complex; MSSA, methicillin-susceptible *S aureus*; MSSE, methicillin-sensitive *Staphylococcus epidermidis;* MRSE, methicillin-resistant *S epidermidis;* ophth, ophthalmic; pen-R, penicillin-resistant; pen-S, penicillin-susceptible; pip/tazo, piperacillin/tazobactam; PO, orally; PPD, purified protein derivative; qd, once daily; qid, 4 times daily; RSV, respiratory syncytial virus; SPAG-2, small particle aerosol generator-2; STI, sexually transmitted infection; soln, solution; ticar/clav, ticarcillin/clavulanate; tid, 3 times daily; TB, tuberculosis; TMP/SMX, trimethoprim/sulfamethoxazole; VDRL, Venereal Disease Research Laboratories; WBC, white blood cell.

## A. SKIN AND SOFT TISSUE INFECTIONS

NOTE: CA-MRSA (see Chapter 4 on CA-MRSA) is now prevalent in many areas of the world. Recommendations below are given for 2 scenarios, CA-MRSA and standard. Antibiotic recommendations for CA-MRSA should be used for empiric therapy when CA-MRSA is suspected and for documented CA-MRSA infections, while standard recommendations refer to treatment of MSSA

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Adenitis, acute bacterial**[1–7] (*S aureus,* including CA-MRSA, or group A streptococcus) | Empiric IV therapy:<br>Standard: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (AI)<br>CA-MRSA: clindamycin 30 mg/kg/day IV div q8h or vancomycin 40 mg/kg/day IV q8h (BII) | May need surgical drainage<br>For oral therapy for MSSA: cephalexin OR cloxacillin; for CA-MRSA: clindamycin, TMP/SMX, or linezolid<br>For group A strep: amoxicillin<br>Total IV plus PO therapy x 7–10 d |
| **Adenitis, nontuberculous (atypical) mycobacterial**[8–11] | Excision usually curative (BII); azithromycin PO OR clarithromycin PO x 6–12 wks (with or without rifampin) if susceptible (BII) | Antibiotic susceptibility patterns are quite variable; cultures should guide therapy; medical therapy 60%–70% effective. |
| **Adenitis, tuberculous**[12,13] | Isoniazid 10–15 mg/kg/day (max 300 mg) PO qd, IV x 6 mos AND rifampin 10–20 mg/kg/day (max 600 mg) PO qd, IV x 6 mos AND pyrazinamide 20–40 mg/kg/day PO qd x first 2 mos therapy (BI); if suspected multidrug resistance, add ethambutol 20 mg/kg/day PO qd | Surgical excision usually not indicated<br>Adenitis caused by *Mycobacterium bovis* (unpasteurized dairy product ingestion) is uniformly resistant to pyrazinamide. Treat 9–12 mos with isoniazid and rifampin, if susceptible. (BII) |
| **Anthrax, cutaneous**[14] | Empiric therapy: ciprofloxacin 20–30 mg/kg/day PO div bid OR doxycycline 4 mg/kg/day (max 200 mg) PO div bid (regardless of age) (AIII) | If susceptible, amoxicillin, or clindamycin (BIII). Ciprofloxacin and levofloxacin are approved for inhalation anthrax. (BIII) |
| **Bites, animal and human1,**[15–17] *Pasteurella multocida* (animal), *Eikenella corrodens* (human), *Staphylococcus* spp and *Streptococcus* spp | Amox/clav 45 mg/kg/day PO div tid (amox/clav 7:1, see Chapter 1, Aminopenicillins) x 5–10 d (AII); for hospitalized children, use ticar/clav 200 mg ticarcillin/kg/day div q6h OR ampicillin and clindamycin (BII) | Consider rabies prophylaxis for animal bites (AI); consider tetanus prophylaxis<br>Human bites have a very high rate of infection (do not close open wounds)<br>*S aureus* coverage is only fair with amox/clav, ticar/clav, pip/tazo. For penicillin allergy, consider ciprofloxacin plus clindamycin. (BIII) |
| **Bullous impetigo**[1–3,5–7] (usually *S aureus,* including CA-MRSA) | Standard: cephalexin 50–75 mg/kg/day PO div tid OR cloxacillin 50 mg/kg/day PO div qid OR amox/clav 45 mg/kg/day PO div tid (CII)<br>CA-MRSA: clindamycin 30 mg/kg/day PO div tid OR TMP/SMX 8 mg/kg/day of TMP PO div bid; x 5–7 d (CIII) | For topical therapy if mild infection: mupirocin or retapamulin ointment |

| | | |
|---|---|---|
| **Cellulitis of unknown etiology** (usually *S aureus,* including CA-MRSA; or group A streptococcus[1–7,18] | Empiric IV therapy:<br>Standard: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (BII)<br>CA-MRSA: clindamycin 30 mg/kg/day IV div q8h OR vancomycin 40 mg/kg/day IV q8h (BII)<br>For oral therapy for MSSA: cephalexin OR cloxacillin (AII); for CA-MRSA: clindamycin (BII), TMP/SMX (CIII), or linezolid. (BII) | For periorbital or buccal cellulitis also consider *Streptococcus pneumoniae* or *Haemophilus influenzae* type b in unimmunized infants<br>Total IV plus PO therapy x 7–10 d |
| **Cellulitis, buccal** (*H influenzae*, type b)[19] | Cefotaxime 100–150 mg/kg/day IV div q8h OR ceftriaxone 50 mg/kg/day (AI) IV, IM q24h OR chloramphenicol 50–75 mg/kg/day IV div q6h; x 2–7 d parenteral therapy before switch to oral (BII) | Rule out meningitis (larger dosages may be needed)<br>Oral therapy: amoxicillin if beta-lactamase neg; amox/clav or oral 2nd or 3rd gen cephalosporin if beta-lactamase pos |
| **Cellulitis, erysipelas** (streptococcal)[1,2,7] | Penicillin G 100,000–200,000 U/kg/day IV div q4–6h (BII) initially then penicillin V 100 mg/kg/day PO div qid or tid OR amoxicillin 50 mg/kg/day PO div tid x 10 d | These dosages may be unnecessarily large, but there is little clinical experience with smaller dosages |
| **Gas gangrene** (clostridial)[1,20,21] | Penicillin G 250,000 U/kg/day IV div q4h (BI) x 10 d; for penicillin allergy, clindamycin or meropenem (CIII) | Aggressive, extensive debridement |
| **Impetigo** (*S aureus,* including CA-MRSA; occasionally group A streptococcus)[1,2,6,7,22,23] | Mupirocin OR retapamulin topically (BII) to lesions tid; OR for more extensive lesions, oral therapy:<br>Standard: cephalexin 50–75 mg/kg/day PO div tid OR cloxacillin 50 mg/kg/day PO div qid OR amox/clav 45 mg/kg/day PO div tid (AII)<br>CA-MRSA: clindamycin 30 mg/kg/day (CII) PO div tid OR TMP/SMX 8 mg/kg/day of TMP PO div bid (CIII); x 5–7 d | Cleanse infected area with soap and water; bathe daily |
| **Ludwig's angina**[24] | Penicillin G 200,000–250,000 U/kg/day IV div q6h AND clindamycin 40 mg/kg/day IV div q8h (CIII) | Alternatives: meropenem, imipenem, ticar/clav, pip/tazo if gram-negative aerobic bacilli also suspected (CIII); high risk of respiratory tract obstruction from inflammatory edema |
| **Lymphadenitis** (see Adenitis, acute bacterial) | | |
| **Lymphangitis, blistering dactylitis** (group A streptococcus)[1,2,7] | Penicillin G 200,000 U/kg/day IV div q6h (BII) initially then penicillin V 100 mg/kg/day PO div qid OR amoxicillin 50 mg/kg/day PO div tid x 10 d | For mild disease, penicillin V 50 mg/kg/day PO div qid OR erythromycin 40 mg/kg/day PO div tid x 10 d |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Myositis, suppurative**[25] (*S aureus*, including CA-MRSA; synonyms: tropical myositis, pyomyositis) | Standard: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (CII)<br>CA-MRSA: clindamycin 40 mg/kg/day IV div q8h OR vancomycin 40 mg/kg/day IV q8h (CIII) | Aggressive, emergent debridement; consider IVIG to bind bacterial toxins for life-threatening disease; use clindamycin to help decrease toxin production; abscesses may develop with CA-MRSA while on therapy |
| **Necrotizing fasciitis** (pathogens vary, depending on the age of the child and location of infection: Single pathogen: group A streptococcus; *Clostridia* spp, *S aureus* [including CA-MRSA], *Pseudomonas aeruginosa, Vibrio* spp, *Aeromonas;* multiple pathogen, mixed aerobic/anaerobic synergistic fasciitis: any organism(s) above, plus gram-negative bacilli, plus *Bacteroides* spp, and other anaerobes[1,21,26,27]) | Empiric therapy: Ceftazidime 150 mg/kg/day IV div q8h, or cefepime 150 mg/kg/day IV div q8h or cefotaxime 200 mg/kg/day IV div q6h AND clindamycin 40 mg/kg/day IV div q8h (BIII); OR meropenem 60 mg/kg/day IV div q8h or pip/tazo 400 mg/kg/day pip component IV div q6h AND clindamycin (AIII); ADD vancomycin for suspect CA-MRSA (AIII)<br>Group A streptococcal: Penicillin G 200,000–250,000 U/kg/day div q6h AND clindamycin 40 mg/kg/day div q8h (AIII)<br>Mixed aerobic/anaerobic/gram-negative: meropenem or pip/tazo AND clindamycin (AIII) | Aggressive emergent wound debridement (AII)<br>Clindamycin to inhibit synthesis of toxins at the ribosomal level (AIII)<br>Consider IVIG to bind bacterial toxins for life-threatening disease (BIII)<br>Value of hyperbaric oxygen is not established (CIII)<br>Focus definitive antimicrobial therapy based on culture results |
| **Pyoderma, cutaneous abscesses** (*S aureus*, including CA-MRSA; group A streptococcus)[2,5–7,28–30] | Standard: cephalexin 50–75 mg/kg/day PO div tid OR cloxacillin 50 mg/kg/day PO div qid OR amox/clav 45 mg/kg/day PO div tid (BII)<br>CA-MRSA: clindamycin 30 mg/kg/day PO div tid (BII) OR TMP/SMX 8 mg/kg/day of TMP PO div bid (CIII) | I&D when indicated; IV for serious infections.<br>For prevention of recurrent CA-MRSA infection, use bleach baths (1/2 cup of bleach per full bathtub) (BII), OR bathe with chlorhexidine soap. Decolonization with mupirocin may also be helpful. |
| **Rat-bite fever** (*Streptobacillus moniliformis, Spirillum minus*)[31] | Penicillin G 100,000–200,000 U/kg/day IV div q6h (BII) x 7–10 d; for endocarditis, ADD gentamicin x 4–6 wks (CIII)<br>For mild disease, oral therapy with amox/clav (CIII) | Organisms are normal oral flora for rodents<br>Alternatives: doxycycline; 2nd and 3rd generation cephalosporins (CIII) |
| **Staphylococcal scalded skin syndrome**[6,32] | Standard: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (CII)<br>CA-MRSA: clindamycin 30 mg/kg/day IV div q8h (CII) or vancomycin 40 mg/kg/day IV q8h (CIII) | Burow's or Zephiran compresses for oozing skin and intertriginous areas<br>Corticosteroids are contraindicated |

| B. SKELETAL INFECTIONS | See Chapter 4 for additional information on CA-MRSA. | |
|---|---|---|
| **Clinical Diagnosis** | **Therapy (evidence grade)** | **Comments** |
| **Arthritis, bacterial**[33–37] | Switch to appropriate high-dose oral therapy when clinically improved (See Chapter 13.)[38,39] | |
| – Newborns | See Chapter 5. | |
| – Infants *(S aureus,* including CA-MRSA; group A streptococcus; *Kingella kingae;* in unimmunized or immune-compromised children: pneumococcus, *H influenzae* type b) | Empiric therapy: clindamycin (to cover CA-MRSA). For serious infections, ADD cefazolin to provide better MSSA coverage and add *Kingella* coverage<br>For CA-MRSA: clindamycin 30 mg/kg/day IV div q8h or vancomycin 40 mg/kg/day IV q8h<br>For MSSA: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h | Oral therapy options:<br>For CA-MRSA: clindamycin OR linezolid[40]<br>For MSSA: cephalexin OR dicloxacillin<br>For *Kingella*, most penicillins or cephalosporins (but not clindamycin) |
| – Children *(S aureus,* including CA-MRSA; group A streptococcus); *K kingae* | For *Kingella*: cefazolin, ampicillin, or ceftriaxone 50 mg/kg/day IV, IM q24h<br>For pen-S pneumococci or group A streptococcus: penicillin G 200,000 U/kg/day IV div q6h<br>For pen-R pneumococci or *Haemophilus*: ceftriaxone 50–75 mg/kg/day IV, IM q24h, OR cefotaxime (BII) | Total therapy (IV plus PO) for 3 wks with normal ESR; low-risk, non-hip arthritis may respond to a 10-day course. [35,36] |
| – Gonococcal arthritis or tenosynovitis[41,42] | Ceftriaxone 50 mg/kg IV, IM q24h (BII); OR (if susceptible) penicillin G 100,000 U/kg/day IV div q6h (AII); x 7 d | PO cefixime 8 mg/kg/day (CII) as a single daily dose for penicillin-resistant strains. Quinolone resistance is increasing. |
| – Other bacteria | See Chapter 7 for preferred antibiotics. | |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Osteomyelitis**[33,34,37,43-45] | Switch to appropriate high-dose oral therapy when clinically improved (See Chapter 13.)[38,39] | |
| – Newborn | See Chapter 5. | |
| – Infants and children, acute infection (usually *S aureus*, including CA-MRSA; group A streptococcus; *K kingae)* | Empiric therapy: clindamycin. For serious infections, ADD cefazolin to provide better MSSA coverage and add *Kingella* coverage (CIII)<br>For CA-MRSA: clindamycin 30 mg/kg/day IV div q8h or vancomycin 40 mg/kg/day IV q8h (BII)<br>For MSSA: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (AII)<br>For *Kingella:* cefazolin, ampicillin or ceftriaxone 50 mg/kg/day IV, IM q24h (BIII)<br>Total therapy (IV plus PO) for 4–6 wks for MSSA. May need more extended therapy for CA-MRSA. (BII)<br>Follow closely for clinical response to empiric therapy | In children with open fractures secondary to trauma, add ceftazidime for extended aerobic gram-negative activity<br>*Kingella* is often resistant to clindamycin<br>For MSSA (BI) and *Kingella* (BIII), follow-up oral therapy with cephalexin 100 mg/kg/day PO div tid<br>Oral therapy alternatives for CA-MRSA include clindamycin and linezolid[40] |
| – Acute, other organisms | See Chapter 7 for preferred antibiotics. | |
| – Chronic (staphylococcal)[46] | For MSSA: dicloxacillin 75–100 mg/kg/day PO div qid OR cephalexin 100–150 mg/kg/day PO div tid x 3–6 mos or longer (CIII)<br>For CA-MRSA: clindamycin or linezolid (CIII) | Surgery to debride sequestrum is usually required for cure. For prosthetic joint infection caused by staphylococci, add rifampin. (CIII)<br>Watch for beta-lactam–associated neutropenia with high-dose, long-term therapy, and neutropenia/thrombocytopenia with long-term linezolid |
| **Osteomyelitis of the foot**[47] (osteochondritis after a puncture wound)<br>*P aeruginosa* (occasionally *S aureus,* including CA-MRSA) | Ceftazidime 150 mg/kg/day IV, IM div q8h AND tobramycin 6–7.5 mg/kg/day IM, IV div q8h (BIII); OR cefepime 150 mg/kg/day IV div q8h (BIII); OR meropenem 60 mg/kg/day IV div q8h (BIII); ADD vancomycin 40 mg/kg/day IV q8h for serious infection (for CA-MRSA), pending culture results | Thorough surgical debridement required (2nd drainage procedure needed in at least 20% of children); oral convalescent therapy with ciprofloxacin (BIII)[46]<br>Treatment course 7–10 d after surgery |

## C. EYE INFECTIONS

| | | |
|---|---|---|
| **Cellulitis, orbital**[48–50] usually secondary to sinus infection; caused by respiratory tract flora and *S aureus,* including CA-MRSA) | Cefotaxime 150 mg/kg/day div q8h or ceftriaxone 50 mg/kg/day q24h; AND antistaphylococcal therapy (BIII). If any CA-MRSA isolated locally, ADD clindamycin 30 mg/kg/day IV div q8h or vancomycin 40 mg/kg/day IV q8h. (AIII)<br>If *S aureus* isolated, and susceptible, use: oxacillin OR cefazolin | Surgical drainage of larger collections of pus, if present by CT scan in orbit or subperiosteal tissue. Try medical therapy alone for small abscess (BIII)<br>Treatment course x 10–14 d after surgical drainage, up to 21 d. CT scan to confirm cure. (BIII) |
| **Cellulitis, periorbital**[48] (preseptal infection) | | |
| – Associated with entry site lesion on skin (*S aureus,* including CA-MRSA, group A streptococcus) | Standard: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (BII)<br>CA-MRSA: clindamycin 30 mg/kg/day IV div q8h or vancomycin 40 mg/kg/day IV q8h (BIII) | Oral antistaphylococcal antibiotic for less severe infection. Treatment course x 7–10 d. |
| – Idiopathic (no entry site) in unimmunized infants: pneumococcal or *H influenzae* type b | Ceftriaxone 50 mg/kg/day q24h OR cefotaxime 100–150 mg/kg/day IV, IM div q8h OR cefuroxime 150 mg/kg/day IV div q8h (AII) | Treatment course x 7–10 d; rule out meningitis; alternative: other 2nd, 3rd, or 4th generation cephalosporins or chloramphenicol |
| – Periorbital swelling, non-tender (usually associated with sinusitis), sinus pathogens rarely may erode anteriorly causing cellulitis | Ceftriaxone 50 mg/kg/day q24h OR cefotaxime 100–150 mg/kg/day IV, IM div q8h OR cefuroxime 150 mg/kg/day IV div q8h (BIII)<br>ADD clindamycin 30 mg/kg/day IV div q8h for more severe infection with suspect *S aureus* including CA-MRSA or for chronic sinusitis (covers anaerobes) (AIII) | For oral convalescent antibiotic therapy see Sinusitis, acute; total treatment course of 21 d |
| **Conjunctivitis, acute** (*Haemophilus* and pneumococcus predominantly)[51–53] | Polymyxin/trimethoprim ophth soln OR polymyxin/bacitracin ophth ointment OR tobramycin ophth soln OR ciprofloxacin ophth soln (CII), x 7–10 days<br>For neonatal infection, see Chapter 5.<br>Steroid-containing therapy only if HSV ruled out | Other topical antibiotics (gentamicin, erythromycin, moxifloxacin, norfloxacin, ofloxacin, levofloxacin) may offer advantages for particular pathogens (CII)<br>High rates of resistance to sulfacetamide |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Conjunctivitis, herpetic**[54,55] | Trifluridine 1% ophth soln OR acyclovir 3% ophth ointment (BII)<br>Acyclovir PO (60–80 mg/kg/day div qid) has been effective in limited studies (BIII) | Refer to ophthalmologist. Recurrences common; corneal scars may form. Topical steroids for keratitis while using topical antiviral solution.<br>Long-term prophylaxis for suppression of recurrent infection with oral acyclovir 20–25 mg/kg/dose (max 400 mg) PO bid (little long-term safety data in children). Assess for neutropenia on long-term therapy; potential risks must balance potential benefits to vision. (BIII) |
| **Dacryocystitis** | No antibiotic usually needed; oral therapy for more symptomatic infection, based on Gram stain and culture of pus; topical therapy as for conjunctivitis may be helpful | Warm compresses; may require surgical probing of nasolacrimal duct |
| **Endophthalmitis**[56,57]<br>*NOTE:* Subconjunctival/subtenon antibiotics usually needed; steroids commonly used; requires anterior chamber or vitreous tap for microbiological diagnosis | | Refer to ophthalmologist; vitrectomy may be necessary for advanced endophthalmitis |
| – Empiric therapy following open globe injury | Vancomycin 40 mg/kg/day IV div q8h AND ceftazidime 150 mg/kg/day IV div q8h (AIII) | |
| – Staphylococcal | Vancomycin 40 mg/kg/day IV div q8h pending susceptibility testing; oxacillin 150 mg/kg/day IV div q6h if susceptible (AIII) | Treatment course x 10–14 d |
| – Pneumococcal, meningococcal, *Haemophilus* | Ceftriaxone 100 mg/kg/day IV q24h; penicillin G 250,000 U/kg/day IV div q4h if susceptible (AIII) | Rule out meningitis; treatment course x 10–14 d |
| – Gonococcal | Ceftriaxone 50 mg/kg q24h IV, IM (AIII) | Treatment course 7 d or longer |
| – *Pseudomonas* | Ceftazidime 150 mg/kg/day IV div q8h AND tobramycin 6–7.5 mg/kg/day IM, IV, or amikacin 15–20 mg/kg/day IM, IV div q8h x 10–14 d (AIII) | Cefepime IV, meropenem IV, or imipenem IV are alternatives (no clinical data). Very poor outcomes. |
| – *Candida* | Intravitreal amphotericin AND fluconazole 10 mg/kg/day IV (AIII) | |

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| **Hordeolum (sty) or chalazion** | None (topical antibiotic not necessary) | Warm compresses; I&D when necessary |
| **Retinitis** | | |
| – CMV[58–60]<br>For neonatal: See Chapter 5<br>For HIV-infected children: visit NIH Web site at http://aidsinfo.nih.gov/contentfiles/Pediatric_OI.pdf | Ganciclovir 10 mg/kg/day IV div q12h for 2 weeks (BIII); if needed, continue at 5 mg/kg/day q24h to complete 6 weeks total (BIII) | Neutropenia risk increases with duration of therapy<br>Foscarnet IV and cidofovir IV are alternatives, but demonstrate significant nephrotoxicity<br>Insufficient data available yet to recommend valganciclovir extemporaneous suspension<br>Intravitreal ganciclovir and combination therapy for non-responding, immune-compromised hosts |

## D. EAR AND SINUS INFECTIONS

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|---|---|---|
| **Bullous myringitis (see Otitis media, acute)** | Believed to be a clinical presentation of acute bacterial otitis media | |
| **Otitis externa** | | |
| – Bacterial (swimmer's ear) *(P aeruginosa, S aureus,* including CA-MRSA)[61,62] | Topical antibiotics: fluoroquinolone (ciprofloxacin or ofloxacin) with steroid, OR neomycin/polymyxin B/hydrocortisone (BII)<br>Irrigation and cleaning canal of detritus important | Wick moistened with Burow solution used for marked swelling of canal; to prevent swimmer's ear, 2% acetic acid to canal after water exposure will restore acid pH |
| – Bacterial (malignant otitis externa) *(P aeruginosa)*[63,64] | Ceftazidime 150 mg/kg/day IV div q8h AND tobramycin 6–7.5 mg/kg/day IM (AIII) | Other antipseudomonal antibiotics should also be effective: cefepime IV, meropenem IV or imipenem IV, pip/tazo |
| – Bacterial furuncle of canal *(S aureus,* including CA-MRSA) | Standard: oxacillin 150 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h (BIII)<br>CA-MRSA: clindamycin 30 mg/kg/day IV div q8h or vancomycin 40 mg/kg/day IV q8h (BIII) | I&D; antibiotics for cellulitis<br>Oral therapy for mild disease, convalescent therapy: for MSSA: cephalexin OR dicloxacillin; for CA-MRSA: clindamycin, TMP/SMX, OR linezolid (BIII) |
| – *Candida* | Fluconazole 5–10 mg/kg/day PO once daily x 5–7 d (CIII) | May occur following antibiotic therapy of bacterial external otitis; debride canal |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Otitis media, acute** | | |
| **A note on AOM:** The natural history of AOM in different age groups by specific pathogens is not well defined; therefore, the actual contribution of antibiotic therapy on resolution of disease is also poorly defined, which has lead to controversy regarding which antibiotic is best or whether therapy is even necessary. In the past, FDA approvals for antibiotics for AOM have almost uniformly been based on equivalence in efficacy to previously approved antibiotics (which were themselves approved based on comparison to previously approved antibiotics, etc).[65] The benefits and risks (including development of antibiotic resistance) of antibiotic therapy for AOM need to be better studied before the most accurate advice on the "best" antibiotic can be provided. However, based on available data, for most children, amoxicillin can be used initially and other antibiotics are used for amoxicillin failures, relapses, or recurrent AOM. Considerations include severity of disease, age of child, previous antibiotics, child care attendance, in vitro antibacterial spectrum of antibiotic, palatability of suspensions, and cost. The most current American Academy of Pediatrics guidelines[66] and meta-analyses[67] suggest the greatest benefit with therapy occurs in children with bilateral AOM who are younger than 2 years; for other children, close observation is also an option. Some experts advocate providing a prescription to parents, but waiting 1–2 days before treating mild cases. Although prophylaxis is only rarely indicated, amoxicillin or other antibiotics can be used in one-half the therapeutic dose once or twice daily to prevent infections if the benefits outweigh the risks of development of resistant organisms for that child.[68] | | |
| – Newborns | See Chapter 5. | |
| – Infants and children (pneumococcus, *H influenzae* non-type b, *Moraxella* most common)[69–71] | Usual therapy: amoxicillin 90 mg/kg/day PO div bid; failures will be caused by either beta-lactamase–producing *Haemophilus* (or *Moraxella*) or highly pen-R pneumococcus<br>a) For pen-R pneumococci: high-dosage amoxicillin achieves better middle ear activity than oral cephalosporins. Options include: ceftriaxone IM 50 mg/kg/day q24h x 1–3 doses; OR a macrolide-class antibiotic: azithromycin PO at 1 of 3 dosages: (1) 10 mg/kg on day 1, followed by 5 mg/kg once daily on days 2–5, or (2) 10 mg/kg once daily x 3 d; OR clarithromycin PO at 15 mg/kg/day div bid. Caution: up to 40% of pen-R pneumococci are also macrolide-resistant<br>b) For *Haemophilus* strains that are beta-lactamase–positive, the following oral antibiotics offer better in vitro activity than amoxicillin: amox/clav, cefdinir, cefpodoxime, cefuroxime, OR ceftriaxone IM | See Chapter 11 for dosages. High-dosage amoxicillin (90 mg/kg/day) should be used for empiric therapy in most areas, given the prevalence of pen-R pneumococci, and resurgence of non-Prevnar® vaccine strains that are pen-R. The high serum and middle ear fluid concentrations achieved with 45 mg/kg/dose of amoxicillin, combined with a long half life in middle ear fluid, allow for a therapeutic antibiotic exposure in the middle ear with only twice daily dosing; high-dose amoxicillin (90 mg/kg/day) with clavulanate (Augmentin-ES®) is also available.<br>Tympanocentesis should be performed in children who fail second-line therapy. |

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| **Otitis, chronic suppurative** (*P aeruginosa, S aureus,* including CA-MRSA, and other respiratory tract/skin flora)[72,73] | Topical antibiotics: fluoroquinolone (ciprofloxacin or ofloxacin) with or without steroid (BIII)<br>Cleaning of canal, view of tympanic membrane (TM), for patency; cultures important | Presumed middle ear drainage through open TM; possible aminoglycoside toxicity if neomycin-containing topical therapy used[74]<br>Other topical fluoroquinolones with/without steroids available |
| **Mastoiditis, acute** (pneumococcus, *S aureus,* including CA-MRSA; group A streptococcus; *Haemophilus* rare)[75–77] | Cefotaxime 150 mg/kg/day div q8h or ceftriaxone 50 mg/kg/day q24h AND clindamycin 40 mg/kg/day IV div q8h (BIII) | Rule out meningitis; surgery as needed for mastoid and middle ear drainage<br>Change to appropriate oral therapy after clinical improvement |
| **Mastoiditis, chronic** (see also Chronic suppurative otitis media) anaerobes, *Pseudomonas, S aureus* (including CA-MRSA)[76] | Antibiotics only for acute superinfections (according to culture of drainage); for *Pseudomonas:* meropenem 60 mg/kg/day IV div q8h, OR pip/tazo 240 mg/kg/day IV div q4–6h x one wk after drainage stops (BIII) | Daily cleansing of ear important; if no response to antibiotics, surgery<br>Alternative: ceftazidime IV (poor anaerobic coverage)<br>Be alert for CA-MRSA |
| **Sinusitis, acute** (*H influenzae* non–type b, pneumococcus, group A streptococcus, *Moraxella*)[78,79] | Same antibiotic therapy as for AOM (amoxicillin 90 mg/kg/day PO div bid) (BIII).<br>Therapy of 14 d may be necessary while mucosal swelling resolves and ventilation is restored | For more severe symptoms, use high-dosage amox/clav to increase the likelihood of cure by extending coverage for ampicillin-R *H influenzae* (BII)<br>Sinus irrigations for severe disease or failure to respond |

**E. OROPHARYNGEAL INFECTIONS**

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| **Dental abscess**[80,81] | Clindamycin 30 mg/kg/day PO, IV, IM div q6–8h OR penicillin G 100–200,000 U/kg/day IV div q6h (AIII) | Amox/clav PO; amoxicillin PO; ampicillin AND metronidazole IV are other options<br>Tooth extraction usually necessary. Erosion of abscess may occur into facial, sinusitis, deep head, and neck compartments. |
| **Diphtheria**[82] | Erythromycin 40–50 mg/kg/day PO div qid x 14 d OR penicillin G 150,000 U/kg/day IV div q6h; PLUS antitoxin (AIII) | Diphtheria antitoxin (DAT), a horse antisera, is investigational and only available from CDC's Emergency Operations Center at: 770/488-7100. The investigational protocol and dosages of DAT are provided on the CDC's Web site (protocol version 4/30/2009) at http://www.cdc.gov/ vaccines/vpd-vac/diphtheria/dat/downloads/protocol_032504.pdf |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
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| **Epiglottitis** (aryepiglottitis, supraglottitis; *H influenzae* type b in an unimmunized child); rarely pneumococcus, *S aureus*[83,84] | Ceftriaxone 50 mg/kg/day IV, IM q24h OR cefotaxime 150 mg/kg/day IV div q8h x 7–10 d | Emergency: provide airway<br>For *S aureus* (causes only 5% of epiglottitis), consider adding clindamycin 40 mg/kg/day IV div q8h |
| **Gingivostomatitis, herpetic**[85] | Acyclovir 80 mg/kg/day PO div qid x 7 d (for severe disease, use IV therapy at 30 mg/kg/day div q8h) (BIII); OR for infants ≥3 mos of age, valacyclovir 50 mg/kg/day PO div bid (crush tablets to create 25 or 50 mg/mL in Susp Structured Vehicle USNF)(CIII) | This is the safe and effective acyclovir dosage for varicella; 75 mg/kg/day div into 5 equal doses has been studied for HSV.[86] Valacyclovir pharmacokinetics have been determined in one pediatric study.[87]<br>Start treatment as soon as oral intake compromised. Consider adding amox/clav or clindamycin for severe disease with oral flora superinfection. |
| **Lemierre syndrome** *(Fusobacterium necrophorum)*[88] pharyngitis with internal jugular vein septic thrombosis, postanginal sepsis, necrobacillosis | Empiric: meropenem 60 mg/kg/day div q8h (or 120 mg/kg/day div q8h for CNS metastatic foci) (AIII) OR ceftriaxone 100 mg/kg/day q24h AND metronidazole 40 mg/kg/day div q8h or clindamycin 40 mg/kg/day div q6h (BIII) | Anecdotal reports suggest metronidazole may be effective for apparent failures with other agents.<br>Metastatic and recurrent abscesses often develop while on active, appropriate therapy, requiring multiple debridements and prolonged antibiotic therapy. |
| **Peritonsillar cellulitis or abscess** (group A streptococcus with mixed oral flora)[89,90] | Clindamycin 30 mg/kg/day PO, IV, IM div q8h AND cefotaxime 150 mg/kg/day IV div q8h (BIII) | Consider incision and drainage for abscess<br>Alternatives: meropenem or imipenem; PIP/TAZO; amox/clav for convalescent oral therapy (BIII)<br>No useful data on benefits of steroids |
| **Pharyngitis** (group A streptococcus) tonsillopharyngitis[7,91–93] | Amoxicillin 50–75 mg/kg/day PO, either once daily, bid or tid x 10 d OR penicillin V 50–75 mg/kg/day PO div bid or tid, OR benzathine penicillin 600,000 units IM for children <27 kg, 1.2 million units IM if >27 kg, as a single dose (AII)<br>For penicillin-allergic children: erythromycin (estolate at 20–40 mg/kg/day PO div bid to qid; or ethylsuccinate at 40 mg/kg/day PO div bid to qid) x 10 d; or azithromycin 12 mg/kg once daily x 5 d (AII) | Amoxicillin displays better gastrointestinal absorption than oral phenoxymethyl penicillin; the suspension is better tolerated. These advantages should be balanced by the increased spectrum of activity that is not needed.<br>Once daily amoxicillin dosage: for children >3 years of age and <40 kg: 750 mg once daily; for those >40 kg, 1,000 mg once daily.<br>Meta-analysis suggests that oral cephalosporins are more effective than penicillin for treatment of strep.[94] |

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| | | Clindamycin is also effective.<br>A 5-day treatment course is FDA approved for some oral cephalosporins (cefdinir, cefpodoxime), but longer follow-up for rheumatic fever is important before short-course therapy can be recommended for all streptococcal pharyngitis. (CIII) [95] |
| **Retropharyngeal, parapharyngeal, or lateral pharyngeal cellulitis or abscess** (mixed aerobic/anaerobic flora)[90,96,97] | Clindamycin 40 mg/kg/day IV div q8h AND cefotaxime 150 mg/kg/day IV div q8h or ceftriaxone 50 mg/kg/day IV q24h | Consider I&D; possible airway compromise, mediastinitis<br>Alternatives: meropenem or imipenem (BIII) |
| **Tracheitis, bacterial** (*S aureus,* including CA-MRSA; group A streptococcus; pneumococcus; *H influenzae* type b)[98,99] | Vancomycin 40 mg/kg/day IV div q8h or clindamycin 40 mg/kg/day IV div q8h AND ceftriaxone 50 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h | For susceptible *S aureus,* oxacillin or cefazolin<br>May represent bacterial superinfection of viral laryngotracheobronchitis |
| **F. LOWER RESPIRATORY TRACT INFECTIONS** | | |
| **Abscess, lung** | | |
| – Primary (severe, necrotizing community-acquired pneumonia caused by pneumococcus, *S aureus,* including CA-MRSA, group A streptococcus)[100] | Empiric therapy with ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h. For severe disease (presumed *S aureus*), ADD clindamycin 40 mg/kg/day div q8h; x 14–21 d or longer (AIII) | For severe CA-MRSA infections, see Chapter 4.<br>Bronchoscopy necessary if abscess fails to drain; surgical excision rarely necessary for pneumococcus, but more important for CA-MRSA and MSSA<br>For susceptible staph: oxacillin or cefazolin |
| – Primary, putrid (ie, foul-smelling; polymicrobial infection with oral aerobes and anaerobes)[101] | Clindamycin 40 mg/kg/day IV div q8h OR meropenem 60 mg/kg/day IV div q8h x 10 d or longer (AIII) | Alternatives: imipenem IV, or pip/tazo IV, or ticar/clav IV (BIII) |
| **Allergic bronchopulmonary aspergillosis** | Prednisone 0.5 mg/kg every other day | Larger dosages may lead to tissue invasion by *Aspergillus.* |
| **Aspiration pneumonia** (polymicrobial infection with oral aerobes and anaerobes)[101] | Clindamycin 40 mg/kg/day IV div q8h OR meropenem 60 mg/kg/day IV div q8h if additional gram-negative aerobic coverage is needed; x 10 d or longer (BIII) | Alternatives: imipenem IV or pip/tazo IV or ticar/clav IV (CIII) |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
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| **Atypical pneumonia (see *Mycoplasma*, Legionnaire's disease)** | | |
| **Bronchitis, acute** | No antibiotic needed for most cases, as disease is usually viral | If bacterial infection suspected, treat with antibiotics as for AOM or sinusitis |
| **Community-acquired pneumonia (see Pneumonia: community-acquired below)** | | |
| **Cystic fibrosis, acute exacerbation**<br>*(P aeruginosa* primarily; also *Burkholderia cepacia, S aureus,* including CA-MRSA)[102–105] | Ceftazidime 150–200 mg/kg/day div q6–8h or piperacillin 300–400 mg/kg/day IV div q4h, AND tobramycin 6–10 mg/kg/day IM, IV div q6–8h (BII). Alternatives: meropenem, imipenem, or cefepime AND aminoglycosides; OR ciprofloxacin 30 mg/kg/day PO, IV div tid; x 7–10 d (BIII) | Larger than normal dosages of antibiotics required in most patients with cystic fibrosis; monitor peak serum concentrations of aminoglycosides<br>Cultures with susceptibility testing and synergy testing may help select antibiotics[106,107]<br>Combination therapy may provide synergistic killing and delay the emergence of resistance (CIII)<br>Inhaled tobramycin 300 mg twice daily, cycling 28 days on therapy, 28 days off therapy, is effective adjunctive therapy between exacerbation[108] |
| **Pertussis[109,110]** | Azithromycin (10 mg/kg/day x 5 d) or clarithromycin (15 mg/kg/day div bid x 7 d) or erythromycin (estolate preferable) 40 mg/kg/day PO div qid; x 14 d (AII)<br>Alternative: TMP/SMX (8 mg/kg/day TMP) div bid x 14 d (BIII) | Azithromycin and clarithromycin are better tolerated than erythromycin (Chapter 5); azithromycin is preferred in young infants to reduce pyloric stenosis risk<br>The azithromycin dosage that is recommended for infants <1 month of age, but this dosage is well tolerated and safe for older children (12 mg/kg/day X 5 d is actually FDA approved for other indications). Alternatively, 10 mg/kg on day 1, followed by 5 mg/kg on days 2–5 should also be effective.[109]<br>Isolate for the first 5 days of therapy.<br>Provide prophylaxis to family members. |

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| **Pneumonia: Community-acquired, bronchopneumonia** | | |
| – Mild to moderate illness (overwhelmingly viral, especially in preschool children) | No antibiotic therapy unless epidemiologic, clinical, or laboratory reasons to suspect bacteria or *Mycoplasma* | Broad-spectrum antibiotics may increase risk of subsequent infection with antibiotic-resistant pathogens |
| – Moderate to severe illness (pneumococcus; group A streptococcus; *S aureus,* including CA-MRSA; or *Mycoplasma pneumoniae*)[100,111–114] | Empiric therapy: ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h (AI)<br>For suspected CA-MRSA, use vancomycin 40–60 mg/kg/day (AIII)<br>For suspect *Mycoplasma*/atypical pneumonia agents, particularly in school-aged children, ADD azithromycin 10 mg/kg IV, PO x 1, then decrease dose to 5 mg/kg once daily for days 2–5 of treatment (AII) | Tracheal aspirate or bronchoalveolar lavage for Gram stain/culture when indicated<br>Check vancomycin serum concentrations and renal function, particularly at the higher dosage for CA-MRSA.<br>Alternatives to azithromycin for atypical pneumonia include erythromycin IV, PO, or clarithromycin PO, or doxycycline IV, PO for children >7 years of age, or levofloxacin for post-pubertal older children. |
| **Pneumonia: Community-acquired, lobar consolidation** | | |
| Pneumococcus (even if immunized), *S aureus,* including CA-MRSA (can cause necrotizing pneumonia) and group A streptococcus.[100,111–114] Consider *H influenzae* type b in the unimmunized child. *M pneumoniae* may cause lobar pneumonia. | Empiric therapy: ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h (AI); for more severe disease ADD clindamycin 40 mg/kg/day div q8h or vancomycin 40–60 mg/kg/day div q8h for *S aureus* (AIII)<br>For suspect *Mycoplasma*/atypical pneumonia agents, particularly in school-aged children, ADD azithromycin 10 mg/kg IV, PO x 1, then decrease dose to 5 mg/kg once daily for days 2–5 of treatment (AII)<br>Empiric oral outpatient therapy for less severe illness: high dosage amoxicillin 80–100 mg/kg/day PO div q8h (NOTq12h); for *Mycoplasma*, ADD a macrolide as above (BIII) | Change to PO after improvement (decreased fever, no oxygen needed); treat until clinically asymptomatic and chest radiography significantly improved (7–21 days) (BIII)<br>No reported failures of ceftriaxone/cefotaxime for pen-R pneumococcus: no need to add empiric vancomycin for this reason (CIII)<br>Oral therapy for pneumococcus and *Haemophilus* may also be successful with: amox/clav, cefdinir, cefpodoxime or cefuroxime<br>Levofloxacin is an alternative (BI)[115] but due to cartilage toxicity concerns, should not be first-line therapy. |
| – Pneumococcal, pen-S | Penicillin G 250,000–400,000 U/kg/day IV div q4–6h x 10 d (BII) | After improvement, change to PO amoxicillin 50–75 mg/kg/day PO div tid, or penicillin V 50–75 mg/kg/day div qid–tid |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
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| – Pneumococcal, pen-R | Ceftriaxone 75 mg/kg/day q24h, or cefotaxime 150 mg/kg/day div q8h for 10–14 d (BIII) | Addition of vancomycin has not been required for eradication of pen-R strains<br>For oral convalescent therapy, clindamycin (30 mg/kg/day PO div tid), or linezolid (30 mg/kg/day PO div tid), or high-dosage amoxicillin (100–150 mg/kg/day PO div tid) |
| – *S aureus* (including CA-MRSA)[6,100,116,117] | For MSSA: oxacillin or cefazolin (AII)<br>For CA-MRSA: vancomycin 60 mg/kg/day; may need addition of rifampin, clindamycin or gentamicin (AIII) (see Chapter 4) | Check vancomycin serum concentrations and renal function, particularly at the higher dosage needed for invasive CA-MRSA disease<br>For life-threatening disease, optimal therapy of CA-MRSA is not defined: add gentamicin and/or rifampin 6<br>Linezolid 30 mg/kg/day IV, PO div q8h is another option (follow platelets and WBC weekly) |
| **Pneumonia: with empyema** (same pathogens as for community-associated bronchopneumonia) May benefit from video-assisted thoracoscopic/chest tube drainage[118–120] | Empiric therapy: ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h AND vancomycin 40–60 mg/kg/day IV div q8h (BIII) | Initial therapy based on Gram stain of empyema fluid; typically clinical improvement is slow, with persisting but decreasing "spiking" fever for 2–3 wks |
| – Group A streptococcal | Penicillin G 250,000 U/kg/day IV div q4–6h x 10 d (BII) | Change to PO amoxicillin 75 mg/kg/day div tid or penicillin V 50–75 mg/kg/day, div qid to tid after clinical improvement (BIII) |
| – Pneumococcal | (See above, Pneumonia: Community-acquired, lobar consolidation, *Pneumococcus)* | |
| – *S aureus* (including CA-MRSA)[6,100,116] | For MSSA: oxacillin or cefazolin (AII)<br>For CA-MRSA: use vancomycin 60 mg/kg/day (AIII) (follow serum concentrations and renal function); may need additional antibiotics (see Chapter 4) | For life-threatening disease, optimal therapy of CA-MRSA is not defined: add gentamicin and/or rifampin<br>Oral convalescent therapy for MSSA: cephalexin PO; for CA-MRSA: clindamycin PO<br>Total course x 21 d or longer (AIII)<br>Linezolid 30 mg/kg/day IV, PO div q8h is another option (follow platelets and WBC weekly) |

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| **Pneumonia: Immunosuppressed, neutropenic host**<br>*P aeruginosa,* other community-associated or nosocomial gram-negative bacilli, *S aureus,* fungi, AFB, *Pneumocystis,* viral (adenovirus, CMV, EBV, influenza, RSV, others) | Ceftazidime 150 mg/kg/day IV div q8h and tobramycin 6.0–7.5 mg/kg/day IM, IV div q8h (AII), OR cefepime 150 mg/kg/day div q8h, or meropenem 60 mg/kg/day div q8h (AII) ± tobramycin (BIII); AND if *S aureus* suspected clinically, ADD vancomycin 40–60 mg/kg/day IV div q8h (AIII)<br>Biopsy or bronchoalveolar lavage may be needed to determine need for antifungal, antiviral, antimycobacterial treatment | Amikacin 15–22.5 mg/kg/day is alternative aminoglycoside. Use 2 active agents for improved efficacy and decreased risk of emergence of resistance (BIII) |
| – **Pneumonia: Interstitial pneumonia syndrome of early infancy** | If *Chlamydia trachomatis* suspected, azithromycin 10 mg/kg on day 1, followed by 5 mg/kg/day once daily days 2–5 OR erythromycin 40 mg/kg/day PO div qid; x 14 d (BII) | Most often respiratory viral pathogens, CMV, or chlamydial; role of *Ureaplasma* uncertain |
| – **Pneumonia, Nosocomial (HAP/VAP)**<br>*P aeruginosa,* gram-negative enteric bacilli *(Enterobacter, Klebsiella, Serratia, Escherichia coli), Acinetobacter, Stenotrophomonas,* and gram-positive organisms including CA-MRSA and *Enterococcus*[121–124] | Commonly used regimens:<br>Meropenem 60 mg/kg/day div q8h, OR pip/tazo 240–300 mg/kg/day div q6–8h, OR cefepime 150 mg/kg/day div q8h; ± gentamicin 6.0–7.5 mg/kg/day div q8h (AIII); ADD vancomycin 40–60 mg/kg/day div q8h for suspect CA-MRSA (AIII) | For multidrug-resistant gram-negative bacilli, colistin may be required[125]<br>Should be institution-specific, based on your hospital's nosocomial pathogens and susceptibilities. Pathogens that cause nosocomial pneumonia often have multidrug resistance. Cultures are critical. Empiric therapy also based on child's prior colonization/infection. |
| **Pneumonias of other established etiologies**<br>(see Chapter 7 for treatment by pathogen) | | |
| – *Chlamydia* (now *Chlamydophila) pneumoniae, C psittaci or C trachomatis*[126] | Azithromycin 10 mg/kg on day 1, followed by 5 mg/kg/day once daily days 2–5 or erythromycin 40 mg/kg/day PO div qid; x 14 d | Doxycycline (patients >7 yrs) |
| – CMV (immune-compromised host)[127] | Ganciclovir IV 10 mg/kg/day IV div q12h for 2 weeks (BIII); if needed, continue at 5 mg/kg/day q24h to complete 4–6 weeks total. (BIII) | Add IVIG or CMV immune globulin to provide a small incremental benefit (BII)<br>For older children, oral valganciclovir may be used for convalescent therapy (BIII) |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
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| – *E coli* | Ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h (AII) | For resistant strains (ESBL-producers), use meropenem, imipenem, or ertapenem (AIII) |
| – *Enterobacter* spp | Cefepime 100 mg/kg/day div q12h or meropenem 60 mg/kg/day div q8h; OR ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h AND gentamicin 6.0–7.5 mg/kg/day IM, IV div q8h (AIII) | Addition of aminoglycoside to 3rd generation cephalosporins may retard the emergence of resistance; not needed with cefepime, meropenem, or imipenem |
| – *Francisella tularensis*[128,129] | Gentamicin 6.0–7.5 mg/kg/day IM, IV div q8h x 10 d or longer for more severe disease (AIII); for less severe disease, doxycycline PO (AIII) | Alternatives for oral therapy of mild disease: ciprofloxacin or levofloxacin (BIII)<br>The rate of relapse seems to be higher with tetracycline. |
| – Fungi (see Chapter 8)<br>– Community-associated pathogens vary by region (eg, coccidioides,[130,131] histoplasma[132,133])<br>– *Aspergillus*, mucor, others in immune-compromised hosts | For pathogen-specific recommendations, see Chapter 8.<br>For suspected deep fungi in immune-compromised host, treat empirically with a lipid amphotericin B AND voriconazole and/or an echinocandin; biopsy needed to guide therapy | For normal hosts, triazoles (fluconazole, itraconazole, voriconazole) are better tolerated than amphotericin and equally effective for many community-associated pathogens (see Chapter 2) |
| – Influenza virus[134]<br>For 2009–10, swine flu (pandemic H1N1, aka novel H1N1) is oseltamivir-S, adamantane-R, as are seasonal H3N2 and influenza B strains<br>Seasonal strains of H1N1 are oseltamivir-R, zanamivir-S, adamantane-S | Empiric therapy for flu A: 1 yr to ≤7 yrs old: oseltamivir AND an adamantane; for >7 yrs old: zanamivir inh alone OR oseltamivir AND an adamantane (AIII)<br>For flu B: 1 yr to ≤7 yrs old: oseltamivir; for >7 yrs old: oseltamivir or zanamivir inh (AII)<br>For swine flu: birth to ≤7 yrs old: oseltamivir; for >7 yrs old: oseltamivir or zanamivir inh (AIII) | Adamantanes are amantadine and rimantadine<br>For empiric therapy of infants younger than 1 year: if swine flu is a concern, use oseltamivir. NO safety or efficacy data for adamantanes in infants younger than 1 year of age.<br>For dosage, see Chapter 11. |
| – *Klebsiella pneumoniae*[135] | Ceftriaxone 50–75 mg/kg/day IV, IM q24h OR cefotaxime 150 mg/kg/day IV, IM div q8h (AIII); for ceftriaxone-resistant strains (ESBL strains), use meropenem 60 mg/kg/day IV div q8h (AIII) | For *K pneumoniae* carbapenemase-producing strains: alternatives include fluoroquinolones or colistin (BIII) |

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| – Legionnaire's disease *(Legionella pneumophila)*[136] | Azithromycin 10 mg/kg IV, PO q24h x 5 d (AIII) | Alternatives: clarithromycin, erythromycin, ciprofloxacin, levofloxacin, doxycycline |
| – *Mycobacteria*, nontuberculous (*M avium* complex most common)[9,137] | In a normal host: azithromycin PO or clarithromycin PO x 6–12 wks if susceptible.<br>For more extensive disease: a macrolide AND rifampin AND ethambutol; ± amikacin or streptomycin (AIII) | Highly variable susceptibilities of different nontuberculous mycobacterial species<br>Check for immune-compromise: HIV or gamma-interferon receptor deficiency |
| – *Mycobacterium tuberculosis* (see Tuberculosis) | | |
| – *M pneumoniae*[136,138] | Azithromycin 10 mg/kg on day 1, followed by 5 mg/kg/day once daily days 2–5, or clarithromycin 15 mg/kg/day div bid x 7–14 d, or erythromycin 40 mg/kg/day PO div qid x 14 d | *Mycoplasma* often cause self-limited infection and does not require treatment. (AIII)<br>For older children, doxycycline |
| – *Paragonimus westermani* | Praziquantel | For dosage, see Chapter 10. |
| – *Pneumocystis jiroveci* (previously *Pneumocystis carinii*)[139,140] | Mild-moderate disease: TMP/SMX 20 mg of TMP/kg/day PO div qid x 14–21 d (AII)<br>Moderate-severe disease: same dosage of TMP/SMX given IV, each dose over 1h (AI)<br>Use steroid adjunctive treatment for more severe disease (AII) | Alternatives: pentamidine 3–4 mg IV once daily, infused over 60–90 minutes (AII); TMP AND dapsone; OR primaquine AND clindamycin; OR atovaquone<br>Prophylaxis: TMP/SMX 5 mg TMP/kg/day PO daily or 3x/wk (AI); OR dapsone 1 mg/ kg PO once daily |
| – *P aeruginosa*[121,124,141] | Ceftazidime 150 mg/kg/day IV div q8h AND tobramycin 6.0–7.5 mg/kg/day IM, IV div q8h (AII). Alternatives: cefepime 150 mg/kg/day div q8h or meropenem 60 mg/kg/day div q8h (AII) ± tobramycin (BIII) | Ciprofloxacin for short-term oral convalescent therapy of a few weeks (less safety data in children for long-term therapy) |
| – RSV infection (bronchiolitis, pneumonia)[142] | For immune-compromised hosts: ribavirin aerosol: 6-g vial (20 mg/mL in sterile water), by SPAG-2 generator, over 18–20 h daily x 3–5 d | Treat only for severe disease, immune-compromise, severe underlying cardiopulmonary disease<br>Ribavirin may also be given systemically (no data on efficacy)<br>Palivizumab is not effective for treatment, only prevention |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
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| **Tuberculosis** | | |
| – Primary pulmonary disease[12,143] | Isoniazid (INH) 10–15 mg/kg/day (max 300 mg) PO qd x 6 mos AND rifampin 10–20 mg/kg/day (max 600 mg) PO qd x 6 mos AND pyrazinamide (PZA) 20–40 mg/kg/day PO qd x first 2 mos therapy only (AII)<br>If risk factors present for multidrug resistance, add ethambutol 20 mg/kg/day PO qd OR streptomycin 30 mg/kg/day IV, IM div q12h initially | Contact TB specialist for therapy of drug-resistant TB. Fluoroquinolones may play a role.<br>Directly observed therapy preferred; after 2 wks of daily therapy, can change to twice weekly dosing (double dosage of INH (max 900 mg), PZA (max 2 g) and ethambutol (max 2.5 g); rifampin remains same dosage (10–20 mg/kg/day, max 600 mg) (AII)<br>LP ± computed tomography of head for children ≤2 years old to rule out occult, concurrent CNS infection; consider test for HIV infection (AIII) |
| – Skin test conversion (latent TB infection) | INH 10–15 mg/kg/day (max 300 mg) PO daily x 9 mos (12 mos for immune-compromised patients) (AIII); treatment with INH at 20–30 mg twice weekly x 9 mos is also effective (AIII) | Single drug therapy if no clinical or radiographic evidence of active disease.<br>For exposure to known INH-R but rifampin-S strains, use rifampin 6 mos (AIII) |
| – Exposed infant <4 yrs, or immune-compromised patient (high risk of dissemination) | INH 10–15 mg/kg PO daily x 2–3 mos after last exposure with repeat skin test or interferon-gamma release assay test negative (AIII) | If PPD remains negative at 2–3 mos and child well, consider stopping empiric therapy. PPD may not be reliable in immune-compromised patients. |
| **G. CARDIOVASCULAR INFECTIONS** | | |
| **– Bacteremia** | | |
| – Occult bacteremia (fever without focus), infants <2 months old (group B streptococcus, *E coli, Listeria*, pneumococcus, meningococcus)[144–146] | In general, hospitalization with cultures of blood, urine, and CSF; start ampicillin 200 mg/kg/day IV div q6h AND cefotaxime 150 mg/kg/day IV div q8h (AII) | For a nontoxic, febrile infant with good access to medical care; cultures may be obtained of blood, urine and CSF, ceftriaxone 50 mg/kg IM given with outpatient follow-up the next day (BII) |
| – Occult bacteremia (fever without focus) in ages 2–3 mos to 36 mos (*H influenzae*, pneumococcus, meningococcus; increasingly *S aureus*)[147–149] | Empiric therapy: If unimmunized, febrile, mild-moderate toxic: after blood culture: ceftriaxone 50 mg/kg IM (BII)<br>If fully immunized (*Haemophilus* and *Pneumococcus*) and nontoxic, no routine antibiotic therapy recommended, but follow closely in case of vaccine failure or meningococcal bacteremia (BIII) | Oral convalescent therapy is selected by susceptibility of blood isolate, following response to IM/IV treatment, with CNS and other foci ruled out by exam ± lab tests ± imaging |

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| – *H influenzae*, type b, non-CNS infections | Ceftriaxone IM/IV OR if beta-lactamase neg, ampicillin IV, followed by oral convalescent therapy (see above) (AII) | If beta-lactamase neg: amoxicillin 75–100 mg/kg/day PO div tid (AII)<br>If pos: cefuroxime, cefixime, ceftibuten, cefdinir PO or chloramphenicol PO (CIII) |
| – Meningococcus | Ceftriaxone IM/IV or penicillin G IV, followed by oral convalescent therapy (AII) | Amoxicillin 75–100 mg/kg/day PO div tid (AIII) |
| – Pneumococcus | Ceftriaxone IM/IV or penicillin G IV (if pen-S), followed by oral convalescent therapy (AII) | If pen-S: amoxicillin 75–100 mg/kg/day PO div tid. (AII) If pen-R: continue ceftriaxone, or switch to clindamycin if susceptible. (CIII) Linezolid may also be effective. (CII) |
| – *S aureus*[6,150–152] | MSSA: nafcillin or oxacillin IV (150–200 mg/kg/day div q6h) ± gentamicin (6 mg/kg/day div q8h)<br>MRSA: vancomycin (40–60 mg/kg/day IV div q8h) ± gentamicin (6 mg/kg/day div q8h) ± rifampin (20 mg/kg/day div q12h) | For persisting bacteremia, consider daptomycin 6–8 mg/kg once daily<br>For toxic shock syndrome, clindamycin should be added for the initial 48–72 h of therapy to decrease toxin production; IVIG may be added to bind circulating toxin<br>Watch for the development of metastatic foci of infection, including endocarditis |
| **Endocarditis:** Surgical indications: intractable heart failure, persistent uncontrollable infection, large mobile vegetations, peripheral embolism, and valve dehiscence, perforation, rupture or fistula, or a large perivalvular abscess[153] | | |
| **– Native valve[153–155]** | | |
| – Empiric therapy for presumed endocarditis | Ceftriaxone IV (100 mg/kg q24h) AND gentamicin IV, IM (6 mg/kg/day div q8h) (AII)<br>For severe infection, ADD vancomycin (40–60 mg/kg/day IV div q8h) to cover *S aureus* (AIII) | Combination (ceftriaxone + gentamicin) provides bactericidal activity against most strains of viridans streptococci, the most common pathogens in infective endocarditis<br>May administer gentamicin with a once-daily regimen (CIII)<br>For beta-lactam allergy, use vancomycin 40 mg/kg/day IV div q8h AND gentamicin 6 mg/kg/day IV div q8h |
| – Viridans streptococci: Follow echocardiogram for resolution of vegetation (BIII); for beta-lactam allergy: vancomycin | | |
| – Fully susceptible to penicillin | Ceftriaxone 50 mg/kg IV, IM q24h x 4 wks OR penicillin G 200,000 U/kg/day IV div q4–6h x 4 wks (BII); OR penicillin G or ceftriaxone AND gentamicin 6 mg/kg/day IM, IV div q8h x 14 d (AII) | |
| – Relatively resistant to penicillin | Penicillin G 300,000 U/kg/day IV div q4–6h x 4 wks, or ceftriaxone 100 mg/kg IV q24h x 4 wks; AND gentamicin 6 mg/kg/day IM, IV div q8h x 2 wks (AIII) | Gentamicin is used for the first 2 wks of a total of 4 wks of therapy for relatively resistant strains |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| – Enterococcus (dosages for both native or prosthetic valve infections) | | |
| – ampicillin-susceptible (gentamicin-S) | Ampicillin 300 mg/kg/day IV, IM div q6h or penicillin G 300,000 U/kg/day IV div q4–6h; AND gentamicin 6.0 mg/kg/day IV div q8h; x 4–6 wks (AII) | Combined treatment with cell-wall active antibiotic plus aminoglycoside used to achieve bactericidal activity<br>For beta-lactam allergy: vancomycin |
| – ampicillin-resistant (gentamicin-S) | Vancomycin 40 mg/kg/day IV div q8h AND gentamicin 6.0 mg/kg/day IV div q8h; x 4–6 wks (AIII) | |
| – vancomycin-resistant (gentamicin-S) | Daptomycin 6–8 mg/kg/day q24h AND gentamicin 6.0 mg/kg/day IV div q8h; x 4–6 wks (AIII) | Little data exist in children. Linezolid and quinopristin/dalfopristin are alternatives.<br>For gentamicin-R strains, use streptomycin if susceptible |
| – Staphylococci: *S aureus*, including CA-MRSA; *S epidermidis*.[151] Consider continuing therapy at end of 6 wks if vegetations persist on echocardiogram | MSSA or MSSE: nafcillin or oxacillin 150–200 mg/kg/day IV div q6h x 6 wks AND gentamicin 6 mg/kg/day div q8h x 14 d<br>CA-MRSA or MRSE: vancomycin 40–60 mg/kg/day IV div q8h AND gentamicin;<br>ADD rifampin 20 mg/kg/day IV div q8–12h | Surgery may be necessary in acute phase; avoid cephalosporins (conflicting data on efficacy)<br>For failures on therapy, consider daptomycin 6–8 mg/kg/day q24h AND gentamicin 6 mg/kg/day div q8h |
| – Pneumococcus, gonococcus, group A streptococcus | Penicillin G 200,000 U/kg/day IV div q4–6h x 4 wks; alternatives: ceftriaxone or vancomycin | Ceftriaxone for gonococcus until susceptibilities known<br>For penicillin non-susceptible strains of pneumococcus, use high-dosage penicillin G 300,000 U/kg/day IV div q4–6h or high-dosage ceftriaxone 100 mg/kg IV q24h x 4 wks |
| **– Prosthetic valve/material**[153–155] | | |
| – Viridans streptococci | | Follow echocardiogram for resolution of vegetation<br>For beta-lactam allergy: vancomycin |
| – Fully susceptible to penicillin | Ceftriaxone 100 mg/kg IV, IM q24h x 6 wks OR penicillin G 300,000 U/kg/day IV div q4–6h x 6 wks (AII); OR penicillin G or ceftriaxone AND gentamicin 6.0 mg/kg/day IM, IV div q8h x 14 d (AII) | Gentamicin is used for the first 2 wks of a total of 6 wks of therapy for prosthetic valve/material endocarditis |
| – Relatively resistant to penicillin | Penicillin G 300,000 U/kg/day IV div q4–6h x 6 wks, or ceftriaxone 100 mg/kg IV q24h x 6 wks; AND gentamicin 6.0 mg/kg/day IM, IV div q8h x 6 wks (AIII) | Gentamicin is used for all 6 wks of therapy for prosthetic valve/material endocarditis caused by relatively resistant strains |

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|---|---|---|
| – Enterococcus (see dosages under Native valve) | | |
| – Staphylococci: *S aureus,* including CA-MRSA; *S epidermidis*. Consider continuing therapy at end of 6 wks if vegetations persist on echocardiogram | MSSA or MSSE: nafcillin or oxacillin 150–200 mg/kg/day IV div q6h AND gentamicin 6 mg/ kg/day div q8h AND rifampin 20 mg/kg/day IV div q8–12h IV (AIII)<br>CA-MRSA or MRSE: vancomycin 40–60 mg/kg/day IV div q8h AND gentamicin 6 mg/kg/day div q8h AND rifampin 20 mg/kg/day IV div q8–12h IV (AIII) | Surgery may be necessary in acute phase; avoid cephalosporins (conflicting data on efficacy)<br>For failure to respond in CA-MRSA, consider daptomycin 6–8 mg/kg/day q24h AND gentamicin 6 mg/kg/day div q8h (CIII) |

**Endocarditis Prophylaxis[156,157]:** Significant changes in recommendations *(Circulation* 2007;116:1736–1754) as (1) endocarditis rarely caused by procedures; (2) prophylaxis for procedures prevents an exceedingly small number of cases; (3) risks of antibiotics outweigh benefits. Highest risk conditions currently recommended for prophylaxis: (1) prosthetic heart valve (or prosthetic material used to repair a valve); (2) previous endocarditis; (3) cyanotic congenital heart disease that is unrepaired (or palliatively repaired with shunts and conduits); (4) congenital heart disease that is repaired but with defects at the site of repair adjacent to prosthetic material; (5) completely repaired congenital heart disease using prosthetic material, for the first 6 months after repair; or (6) cardiac transplant patients with valvulopathy. Routine prophylaxis no longer is required for children with native valve abnormalities.

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| – In highest risk patients: dental procedures that involve manipulation of the gingival or periodical region of teeth | Amoxicillin 50 mg/kg PO 1 h before procedure OR ampicillin or ceftriaxone or cefazolin, all at 50 mg/kg IM/IV 30 to 60 min before procedure | If penicillin allergy: clindamycin 20 mg/kg PO (60 min before) or IV (30 min before); OR azithromycin 15 mg/kg or clarithromycin 15 mg/kg, 1 h before |
| – Genitourinary and gastrointestinal procedures | None | No longer recommended |
| **Lemierre syndrome** (*Fusobacterium necrophorum*)[88,158,159] postanginal sepsis, pharyngitis with internal jugular vein septic thrombosis | Empiric: meropenem 60 mg/kg/day div q8h (or 120 mg/kg/day div q8h for CNS metastatic foci) (AIII) OR ceftriaxone 100 mg/kg/day q24h AND metronidazole 40 mg/kg/day div q8h or clindamycin 40 mg/kg/day div q6h (BIII) | Anecdotal reports suggest metronidazole may be effective for apparent failures with other agents.<br>Metastatic and recurrent abscesses often develop while on active, appropriate therapy, requiring multiple debridements and prolonged antibiotic therapy. |
| **Purulent pericarditis** | | |
| – Empiric (acute, bacterial: pneumococcus, meningococcus, *S aureus,* group A streptococcus, *H influenzae* type b)[160,161] | Vancomycin 40 mg/kg/day IV div q8h AND ceftriaxone 50–75 mg/kg/day q24h. (AIII) For presumed staphylococcal infection, ADD gentamicin. (AIII) | Pericardiocentesis is essential to establish diagnosis. Surgical drainage of pus with pericardial window or pericardiectomy is important to prevent tamponade. |
| – *S aureus* | For MSSA: oxacillin 150–200 mg/kg/day IV div q6h OR cefazolin 100 mg/kg/day IV div q8h<br>For CA-MRSA: continue vancomycin | Continue therapy with gentamicin and add rifampin in severe cases. Treatment for 3–4 weeks. |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| – *H influenzae* type b in unimmunized children | Ceftriaxone 50 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h; x 10–14 d (AIII) | Ampicillin for beta-lactamase–negative strains |
| – Pneumococcus, meningococcus, group A streptococcus | Penicillin G 200,000 U/kg/day IV, IM div q6h x 10–14 d OR ceftriaxone 50 mg/kg once daily x 10–14 d (AIII) | Ceftriaxone or cefotaxime for penicillin-nonsusceptible pneumococci |
| – Coliform bacilli | Ceftriaxone 50–75 mg/kg/day q24h or cefotaxime 150 mg/kg/day div q8h x 3 wks or longer (AIII) | Alternative drugs depending on susceptibilities; for *Enterobacter, Serratia*, or *Citrobacter* use cefepime or meropenem |
| – Tuberculous[12] | Isoniazid 10–15 mg/kg/day (max 300 mg) PO qd, IV x 6 mos AND rifampin 10–20 mg/kg/day (max 600 mg) PO qd, IV x 6 mos. ADD pyrazinamide 20–40 mg/kg/day PO qd x first 2 mos therapy; if suspected multidrug resistance, also add ethambutol 20 mg/kg/day PO qd (AIII) | Corticosteroids improve survival in adults: prednisone 1 mg/kg/day x 4 weeks, then 0.5 mg/kg/day x 4 weeks, then 0.25 mg/kg/day x 2 wks, then 0.1 mg/kg/day x 1 wk (AIII) [12] |

## H. GASTROINTESTINAL INFECTIONS (see Chapter 10 for parasitic infections)

### Diarrhea/Gastroenteritis

**Note on *E coli* and diarrheal disease:** Antibiotic susceptibility of *E coli* varies considerably from region to region. For mild to moderate disease, TMP/SMX may be started as initial therapy, but for more severe disease, and for locations with rates of TMP/SMX resistance greater than 10%–20%, oral 3rd generation cephalosporins (eg, cefixime, cefdinir, or ceftibuten), azithromycin, or ciprofloxacin should be used (AIII). Cultures and antibiotic susceptibility testing are recommended for significant disease (AIII).

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| – Empiric therapy of community-associated diarrhea *(E coli* (including O157:H7 strains), *Salmonella, Campylobacter*, and *Shigella* predominate; *Yersinia*, and parasites causing less than 5%; however, viral pathogens are far more common, especially for children <3 yrs of age)[162,163] | Cefixime 8 mg/kg/day PO qd (BII); OR azithromycin 10 mg/kg once daily x 3 d (BII) | Alternatives: other oral 3rd generation cephalosporins (eg, cefdinir, ceftibuten); or ciprofloxacin 30 mg/kg/day PO div bid; x 5 d ; or rifaximin 600 mg/day div tid x 3 d (for nonfebrile, nonbloody diarrhea for children >11 yrs). Controversy exists regarding treatment of 0157:H7 strains.[164–167] |

| | | |
|---|---|---|
| – Traveler's diarrhea: empiric therapy *(E coli, Campylobacter, Salmonella, Shigella,* plus many other pathogens including protozoa)[166,168–173] | Azithromycin 10 mg/kg once daily x 3 d (AII); OR rifaximin 600 mg/day div tid x 3 d (for nonfebrile, nonbloody diarrhea for children ≥12 years) (BII); OR cefixime 8–10 mg/kg once daily x 5 d (CII); OR ciprofloxacin 30 mg/kg/day div bid (CII) | Susceptibility patterns of *E coli* vary widely by country; azithromycin preferable to ciprofloxacin for travelers to SE Asia given high prevalence of quinolone-resistant *Campylobacter*<br>Rifaximin is less effective than ciprofloxacin for invasive bacterial enteritis; rifaximin may not be as efficacious for *Shigella* and other enterics in patients with dysentery<br>Adjunctive therapy with loperamide (antimotility) is not recommended for children <2 yrs of age, and should be used only in nonfebrile, non-bloody diarrhea.[174,175] May shorten symptomatic illness by about 24 h. |
| – Traveler's diarrhea: prophylaxis[168,169] | – Prophylaxis: Early self-treatment with agents listed above is preferred over long-term prophylaxis, but for a short-term (<14 days) visit to very high-risk region: rifaximin (for older children), azithromycin, or bismuth subsalicylate (BIII) | |
| – *Aeromonas hydrophila*[176] | TMP/SMX (8 mg/kg/day of TMP) PO div bid (BII); OR cefixime 8 mg/kg/day PO qd (BII); OR ciprofloxacin 30 mg/kg/day PO div bid; x 5 d (BII) | Not all strains produce enterotoxins and diarrhea<br>Resistance to TMP/SMX about 10%–15%. Choose most narrow spectrum agent based on in vitro susceptibilities. |
| – *Campylobacter jejuni*[177–179] | Azithromycin 10 mg/kg/day x 3 d (BII) or erythromycin 40 mg/kg/day PO div qid x 5 d (BII) | Alternatives: doxycycline or ciprofloxacin |
| – Cholera[172,180] | Doxycycline 4 mg/kg/day (max 200 mg/day) PO div bid, for all ages. Do not use repeated courses of doxycycline, use alternative agents based on susceptibilities | Ciprofloxacin or TMP/SMX (if susceptible) or azithromycin 10 mg/kg once daily x 3 d |
| – *Clostridium difficile* (antibiotic-associated colitis)[181,182] | Metronidazole 30 mg/kg/day PO div qid OR vancomycin 40 mg/kg/day PO div qid x 7 d | Many infants and children may have asymptomatic colonization with *C difficile*[163,181,183]<br>Higher risk of relapse in children with multiple comorbidities |
| – *E coli* | | |
| Enterotoxigenic (etiology of most traveler's diarrhea)[166,171] | Azithromycin 10 mg/kg once daily x 3 d; OR cefixime 8 mg/kg/day PO qd x 5 d | Most illnesses brief and self-limited<br>Alternatives: ciprofloxacin or TMP/SMX |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| Enterohemorrhagic (O157:H7; shiga toxin-producing *E coli*, etiology of HUS)[164–167] | Controversy on whether treatment results in more or less toxin-mediated renal damage. Withhold therapy, if possible; otherwise for severe infection, therapy as for enterotoxigenic strains above | Injury to colonic mucosa may lead to invasive bacterial colitis. |
| Enteropathogenic | Neomycin 100 mg/kg/day PO div q6–8h x 5 d | Most traditional "enteropathogenic" strains are not toxigenic or invasive. |
| – Gastritis, peptic ulcer disease *(Helicobacter pylori)*[184–187] | Clarithromycin 7.5 mg/kg/dose 2–3 times each day AND amoxicillin 40 mg/kg/dose (max 1 g) PO bid AND omeprazole 0.5 mg/kg/dose PO bid 2 wks | Most data from studies in adults; of effective regimens, no one combination has been shown superior: other regimens include bismuth, metronidazole instead of amoxicillin, and other proton pump inhibitors |
| – Salmonellosis | | |
| Non-typhoid strains[179,188] | Usually none for self-limited diarrhea<br>For persisting symptomatic infection: azithromycin 10 mg/kg once daily x 7 d; OR ceftriaxone 70 mg/kg/day IV, IM q24h x 7 d; OR for susceptible strains: TMP/SMX (8 mg/kg/day of TMP) PO div bid; OR | Alternatives: ciprofloxacin 30 mg/kg/day PO div bid x 5–7 d |
| Typhoid fever[189–192] | Azithromycin 10 mg/kg once daily x 7 d; OR ceftriaxone 75 mg/kg/day IV, IM q24h x 7 d; OR cefixime 20 mg/kg/day PO, div q12h; OR for susceptible strains: TMP/SMX (8 mg/kg/day of TMP) PO div bid | Watch for relapse if ceftriaxone used<br>Alternatives: ciprofloxacin 30 mg/kg/day PO div bid x 5–7 d |
| – Shigellosis[179,193–195] | Cefixime 8 mg/kg/day PO qd; OR azithromycin 12 mg/kg PO on day 1, followed by 6 mg/kg daily x 4 d; OR ciprofloxacin 30 mg/kg/day PO div bid; | Alternatives for susceptible strains: TMP/SMX (8 mg/kg/day of TMP) PO div bid; x 5 d or ampicillin (not amoxicillin)<br>Ceftriaxone effective IM, IV if parenteral therapy necessary<br>Avoid antiperistaltic drugs<br>Treat to decrease communicability, even if symptoms resolving |
| – *Yersinia enterocolitica*[196] | Antimicrobial therapy probably not of value for mild disease in normal hosts<br>TMP/SMX PO, IV, or ciprofloxacin PO, IV | Alternatives: ceftriaxone or gentamicin<br>May mimic appendicitis<br>Limited clinical data exist on oral therapy |

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| **Perirectal abscess** (*Bacteroides* spp other anaerobes, enteric bacilli, and *S aureus* predominate)[197] | Clindamycin 30–40 mg/kg/day IV div q8h AND cefotaxime or ceftriaxone or gentamicin | Surgical drainage alone may be curative |

## I. GENITAL AND SEXUALLY TRANSMITTED INFECTIONS

Consider testing for HIV and other STIs in a child with one documented STI; consider sexual abuse in prepubertal children. The most recent CDC STI treatment guidelines are posted online at http://www.cdc.gov/std/treatment/.

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|---|---|---|
| **Chancroid** *(Haemophilus ducreyi)*[41] | Azithromycin 1 g PO as single dose OR ceftriaxone 250 mg IM as single dose | Alternative: erythromycin 2 g/day PO div qid x 7 d OR ciprofloxacin |
| ***C trachomatis*** (cervicitis, urethritis)[41] | Azithromycin 20 mg/kg (max 1 g) PO x 1; OR doxycycline (patients >7 yrs) 40 mg/kg/day (max 200 mg/day) PO div bid x 7 d | Alternatives: erythromycin 2 g/day PO div qid x 7 d; OR levofloxacin 500 mg PO q24h x 7 d |
| **Epididymitis** (associated with positive urine cultures and STIs)[41,198,199] | Ceftriaxone 50 mg/kg/day q24h x 7–10 d AND (for older children) doxycycline 200 mg/day div bid | Microbiology not well studied in children; in infants, also associated with urogenital tract anomalies<br>Treat infants for *S aureus* and *E coli;* may resolve spontaneously |
| **Gonorrhea** | | |
| – Newborns | See Chapter 5. | |
| – Genital infections (uncomplicated vulvovaginitis, cervicitis, urethritis, or proctitis)[41,200–202] | Ceftriaxone 125 mg IM x 1 (regardless of weight); OR cefixime 400 mg PO x 1, or spectinomycin 40 mg/kg (max 2 g) IM as single dose; AND test/treat for chlamydia | Cephalosporins used due to the prevalence of pen-R strains. Fluoroquinolones no longer recommended due to resistance. |
| – Pharyngitis[41,201] | Ceftriaxone 125 mg IM x 1 | |
| – Disseminated gonococcal infection[41,201] | Ceftriaxone 50 mg/kg/day IM, IV q24h (max: 1 g); convalescent oral therapy with cefixime PO; total course x 7 d | No studies in children: increase dosage for meningitis |
| **Granuloma inguinale** (Donovanosis, *Klebsiella granulomatis,* formerly *Calymmatobacterium)*[41] | Doxycycline 4 mg/kg/day (max 200 mg/day) PO x 21 d until lesions completely healed | Primarily in tropical regions of India, Pacific, and Africa<br>Option: azithromycin 1 g PO once weekly x 3 |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Herpes simplex virus, genital infection**[41,203,204] | Acyclovir 20–25 mg/kg/dose (max 400 mg) PO tid x 7–10 d (first episode); for more severe infection: acyclovir 15 mg/kg/day IV div q8h as 1 h infusion<br>For recurrent episodes: treat as above, but only x 5 d<br>For suppression: acyclovir 20–25 mg/kg/dose (max 400 mg) PO bid (little long-term safety data in children) | Alternatives: valacyclovir 25 mg/kg/dose (max 1.0 g) PO bid x 7–10 d; famciclovir (adult dose) 250 mg PO tid x 7–10 d<br>For suppression: valacyclovir 1.0 g qd for adults |
| **Lymphogranuloma venereum** (*C trachomatis*)[41] | Doxycycline 4 mg/kg/day (max 200 mg/day) PO (patients >7 yrs) div bid OR erythromycin 2 g/day PO div qid; x 21 d | Azithromycin 1.0 g PO once weekly x 3 |
| **Pelvic inflammatory disease** (*Chlamydia*, gonococcus, plus anaerobes)[41,205] | Cefoxitin 2 g IV q6h; AND doxycycline 200 mg/day PO div bid; OR clindamycin 900 mg IV q8h and gentamicin 1.5 mg/kg IV, IM q8h x 14 d | Drugs given IV until clinical improvement for 24 h, followed by doxycycline PO AND clindamycin PO to complete 14 days of therapy |
| **Syphilis**[41,206] (test for HIV) | | |
| – Congenital | See Chapter 5. | |
| – Neurosyphilis (positive CSF VDRL or CSF pleocytosis with serologic diagnosis of syphilis) | Crystalline penicillin G 200–300,000 U/kg/day (max 24 mill U/day) div q6h x 10–14 d | |
| – Primary, secondary | Benzathine penicillin G 50,000 U/kg (max 2,400,000 U) IM as a single dose; do not use benzathine-procaine penicillin mixtures | Follow-up serologic tests at 3, 6, and 12 mos. If allergy to penicillin: doxycycline (patients >7 yrs) 4 mg/kg/day (max 200 mg) PO div bid x 14 d<br>CSF exam is not routinely required for children being treated for primary or secondary syphilis unless clinical signs or symptoms of neurologic or eye involvement are present |
| – Syphilis of <1 yr duration, without clinical symptoms (early latent syphilis) | Benzathine penicillin G 50,000 U/kg (max 2,400,000 U) IM as a single dose | Alternative if allergy to penicillin: doxycycline (patients >7 yrs) 4 mg/kg/day (max 200 mg/day) PO div bid x 14 d |

| | | |
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| – Syphilis of >1 yr duration, without clinical symptoms (late latent syphilis) or syphilis of unknown duration | Benzathine penicillin G 50,000 U/kg (max 2,400,000 U) IM weekly for 3 doses | Alternative if allergy to penicillin: doxycycline (patients >7 yrs) 4 mg/kg/day (max 200 mg/day) PO div bid x 28 d<br>Look for neurologic, eye, and aortic complications of tertiary syphilis |
| **Trichomoniasis**[41] | Metronidazole 2 g PO as a single dose, OR 500 mg PO twice daily x 7 d | Tinidazole 50 mg/kg (max 2 g) PO x 1 dose |
| **Urethritis, non-gonococcal** (see page 57 for gonorrhea therapy)[41] | Azithromycin 20 mg/kg (max 1 g) PO x 1, OR doxycycline (patients >7 yrs) 40 mg/kg/day (max 200 mg/day) PO div bid x 7 d | Erythromycin or ofloxacin |
| **Vaginitis**[41] | | |
| – Bacterial vaginosis[207] | Metronidazole 500 mg PO twice daily x 7 d or metronidazole vaginal gel x 5 d; OR metronidazole 0.75% intravaginal gel once daily x 5d | Alternative: tinidazole 1 gm PO once daily x 5 d, OR clindamycin 300 mg PO bid x 7 d or clindamycin vaginal cream x 7 d<br>Relapse common<br>Caused by synergy of *Gardnerella* with anaerobes |
| – Candidiasis, vulvovaginal[41,208] | Fluconazole 5 mg/kg PO (max 150 mg) x 1 | Many topical vaginal azole agents are approved, most are available without prescription (eg, butoconazole, clotrimazole, miconazole, tioconazole, terconazole) |
| – *Shigella*[209] | Cefixime 8 mg/kg/day PO qd; OR ciprofloxacin 30 mg/kg/day PO div bid x 5 d | 50% have bloody discharge; usually not associated with diarrhea |
| – *Streptococcus*, group A[210] | Penicillin V 50–75 mg/kg/day PO div tid x 10 d | Amoxicillin 50–75 mg/kg/day PO div tid; may need to add rifampin for eradication |

## J. CENTRAL NERVOUS SYSTEM INFECTIONS

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| **Abscess, brain** (respiratory tract flora, skin flora, or bowel flora, depending on the pathogenesis of infection based on underlying disease and origin of bacteremia)[211–213] | Until etiology established: meropenem 120 mg/kg/day div q8h (AIII); OR nafcillin 150–200 mg/kg/day IV div q6h AND cefotaxime 200–300 mg/kg/day IV div q6h or ceftriaxone 100 mg/kg/day IV q24h AND metronidazole 30 mg/kg/day IV div q8h (BIII); x 2–3 wks after successful drainage (depending on pathogen, size of abscess, and response to therapy); longer course if no surgery (3–6 wks) (BIII) | Surgery for abscesses ≥2 cm diameter<br>If CA-MRSA suspected, ADD vancomycin 60 mg/kg/day IV div q8h ± rifampin 20 mg/kg/day IV div q12h, pending culture results<br>If secondary to chronic otitis, use meropenem or cefepime for anti-*Pseudomonas* activity<br>Follow abscess size by computed tomography<br>For treatment of rare and unusual pathogens that present with symptoms of encephalitis, see IDSA Guidelines on Encephalitis 2008[214] |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Encephalitis[214,215]** | | |
| – CMV[214] | Not well studied in children. Consider ganciclovir (10–20 mg/kg/day IV div q12h); for severe immune-compromise, ADD foscarnet | Toxicity not well defined over 10 mg/kg/day |
| – Enterovirus[216] | Supportive therapy | Investigational therapy with pleconaril (Schering-Plough) is not currently available |
| – EBV[214] | Not well studied. Consider ganciclovir (10–20 mg/kg/day IV div q12h) or acyclovir (60 mg/kg/day IV div q8h) | Efficacy and toxicity of high-dose ganciclovir and acyclovir are not well defined; some experts recommend against antiviral treatment[214] |
| – Herpes simplex virus[214,217] | Acyclovir 60 mg/kg/day IV div q8h (1 h infusion time) x 21 d | (See Chapter 5 for neonatal infection.)<br>Toxicity not well defined at this high dosage; follow closely for hematologic toxicity; FDA has approved acyclovir at this dosage for encephalitis for children up to 12 years of age |
| – *Toxoplasma* | See Chapter 10. | |
| – Arbovirus (flavivirus—West Nile, St Louis encephalitis, tickborne encephalitis; togavirus—Western equine encephalitis, Eastern equine encephalitis; bunyavirus—LaCrosse encephalitis, California encephalitis)[202] | Supportive therapy | Investigational only (antiviral, interferon, immune globulins) |
| **Meningitis, bacterial, community-associated** | | |
| *NOTES* | | |
| – In areas where pen-R pneumococci exist, initial empiric therapy for suspect pneumococcal meningitis should be with vancomycin AND cefotaxime or ceftriaxone until susceptibility test results are available | | |
| – Dexamethasone (0.6 mg/kg/day IV div q6h x 2 d) as an adjunct to antibiotic therapy decreases hearing deficits and other neurologic sequelae in adults and children (for *Haemophilus* and pneumococcus; not studied for meningococcus or *E coli*). The first dose of dexamethasone is given before or concurrent with the first dose of antibiotic; probably little benefit if given ≥1 hour after the antibiotic.[218,219] In areas where pen-R pneumococci exist, initial empiric therapy for suspect pneumococcal meningitis should be with vancomycin AND cefotaxime or ceftriaxone until susceptibility test results are available | | |

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| – Preliminary data (we hope to see these confirmed) suggest that oral glycerol (85% solution, 1 mL to contain 1 g of glycerol) given at 1.5 g (1.5 mL) per kg (max 25 mL) every 6 h for 48 h, may decrease neurologic sequelae[220,221] | | |
| – Empiric therapy[222] | Cefotaxime 200–300 mg/kg/day IV div q6h, or ceftriaxone 100 mg/kg/day IV q24h; AND vancomycin 60 mg/kg/day IV div q8h (AII) | If Gram stain or cultures demonstrate a pathogen other than pneumococcus, vancomycin is not needed |
| – *H influenzae* type b[222] | Cefotaxime 200–300 mg/kg/day IV div q6h, or ceftriaxone 100 mg/kg/day IV q24h; x 10 d (AI) | Alternative: ampicillin 200–400 mg/kg/day IV div q6h (for beta-lactamase negative strains) OR chloramphenicol 100 mg/kg/day IV div q6h |
| – Meningococcus *(Neisseria meningitidis)*[222] | Penicillin G 250,000 U/kg/day IV div q4h; or ceftriaxone 100 mg/kg/day IV q24h, or cefotaxime 200 mg/kg/day IV div q6h; treatment course x 7 d (AI) | Meningococcal prophylaxis: rifampin 10 mg/kg PO q12h x 4 doses OR ceftriaxone 125–250 mg IM once OR ciprofloxacin 500 mg PO once (adults) |
| – Neonatal | See Chapter 5. | |
| – Pneumococcus *(S pneumoniae)*[222] | For penicillin- and cephalosporin-susceptible strains: penicillin G 250,000 U/kg/day IV div q4–6h, OR ceftriaxone 100 mg/kg/day IV q24h or cefotaxime 200–300 mg/kg/day IV div q6h; x 10 d (AI)<br>For pen-R pneumococci: continue the combination of vancomycin and cephalosporin IV for total course (AIII) | Some pneumococci may be resistant to penicillin but susceptible to cefotaxime and ceftriaxone and may be treated with the cephalosporin alone<br>Test-of-cure LP helpful in those with pen-R pneumococci |
| **Meningitis, TB** *(M tuberculosis; M bovis)*[12,143] | Isoniazid 15 mg/kg/day PO, IV div q12–24h AND rifampin 15 mg/kg/day PO, IV, div q12–24h x 12 mos AND pyrazinamide 30 mg/kg/day PO div q12–24h for first 2 mos of therapy AND streptomycin 30 mg/kg/day IV, IM div q12h for first 4–8 wks of therapy until susceptibility test results available | Hyponatremia from inappropriate ADH common; ventricular drainage may be necessary for obstructive hydrocephalus.<br>Corticosteroids (same dexamethasone dose as for bacterial meningitis, 0.6 mg/kg/day IV div q6h) x 2–4 weeks or until neurologically stable, then taper dose x 1–3 mos to decrease neurologic complications and improve prognosis by decreasing the incidence of infarction[223] |
| **Shunt infections:** The use of antibiotic-impregnated shunts has decreased the frequency of this infection.[224] | | |
| – Empiric therapy pending Gram stain and culture[222] | Vancomycin 60 mg/kg/day IV div q8h, AND ceftriaxone 100 mg/kg/day IV q24h (AII) | If Gram stain shows only gram-positive cocci, can use vancomycin alone<br>Ceftazidime should be used instead of ceftriaxone if *Pseudomonas* is suspected |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| – *S epidermidis* or *S aureus*[222] | Vancomycin (for *S epidermidis* and for CA-MRSA) 60 mg/kg/day IV div q8h; OR nafcillin (if organisms susceptible) 150–200 mg/kg/day AND (if severe infection, or slow response) gentamicin or rifampin; x 10–14 d (AIII) | Shunt removal usually necessary; may need to treat with ventriculostomy until ventricular CSF cultures negative; obtain CSF cultures at time of shunt replacement, continue therapy an additional 48–72 h pending cultures |
| – Gram-negative bacilli[222] | Empiric therapy with meropenem 120 mg/kg/day IV div q8h OR cefepime 150 mg/kg/day IV div q8h (AIII)<br>For *E coli:* ceftriaxone 100 mg/kg/day IV q12h OR cefotaxime 200–300 mg/kg/day IV div q6h; ADD gentamicin 6–7.5 mg/kg/day IV until CSF sterile; x 21 d or longer | Remove shunt. Select appropriate therapy based on in vitro susceptibilities<br>Intrathecal therapy with aminoglycosides not routinely necessary with highly active beta-lactam therapy |

## K. URINARY TRACT INFECTIONS

NOTE: Antibiotic susceptibility profiles of *E coli*, the most common cause of urinary tract infection, vary considerably. For mild disease, TMP/SMX may be started as initial therapy if local susceptibility ≥80% and a 20% failure rate is acceptable. For moderate to severe disease (possible pyelonephritis), obtain cultures and begin oral 2nd or 3rd generation cephalosporins (cefuroxime, cefaclor, cefprozil, cefixime, ceftibuten, cefdinir, cefpodoxime), ciprofloxacin PO, or ceftriaxone IM. Antibiotic susceptibility testing will help direct your therapy.

| | | |
|---|---|---|
| **Cystitis, acute**<br>*(E coli)*[225,226] | For mild disease: TMP/SMX (8 mg/kg/day of TMP) PO div bid x 3 d<br>For moderate to severe disease: cefixime 8 mg/kg/day PO qd; OR ceftriaxone 50 mg/kg IM q24h x 3–5 d (with normal anatomy) (BII); follow-up culture after 36–48 h treatment ONLY if still symptomatic | Alternative: amoxicillin 30 mg/kg/day PO div tid if susceptible (BII); ciprofloxacin 15–20 mg/kg/day PO div bid if susceptible |
| **Nephronia, lobar**<br>*E coli* and other enteric rods (also called focal bacterial nephritis)[227,228] | Ceftriaxone 50 mg/kg/day IM/IV q24h<br>Duration depends on resolution of cellulitis vs development of abscess (10–21 d) (AIII) | Invasive, consolidative parenchymal infection; complication of pyelonephritis, can evolve into renal abscess |
| **Pyelonephritis, acute**<br>*(E coli)*[225,229] | Ceftriaxone 50 mg/kg/day IV, IM q24h OR gentamicin 5–6 mg/kg/day IV, IM q24h; switch to oral therapy following clinical response (BII). If organisms resistant to amoxicillin and TMP/SMX, use an oral 2nd or 3rd generation cephalosporin (BII); if cephalosporin-R, can use ciprofloxacin PO 30 mg/kg/day div q12h (BIII); x 10 d total. | If bacteremia documented, and infant is <2–3 mos of age, rule out meningitis and treat 14 d IV or IM (AIII)<br>Aminoglycosides at any dose are more nephrotoxic than beta-lactams (AI) |

| | | |
|---|---|---|
| **Recurrent urinary tract infection,** prophylaxis[225,230] | TMP/SMX (2 mg/kg/dose of TMP) PO qd OR nitrofurantoin 1–2 mg/kg PO qd at bedtime; more rapid resistance may develop using beta-lactams (BII) | Prophylaxis for patients with grade IV reflux or frequent infections; resistance eventually develops to every antibiotic; follow resistance patterns for each patient |

## L. MISCELLANEOUS SYSTEMIC INFECTIONS

| | | |
|---|---|---|
| **Actinomycosis**[231–233] | Penicillin G 250,000 U/kg/day IV div q6h, or ampicillin 150 mg/kg/day IV div q8h until improved; then long-term convalescent therapy with penicillin V 100 mg/kg/day (up to 4 g/day) PO x 6–12 mos (AII) | Surgery as indicated<br>Alternatives: amoxicillin, clindamycin, erythromycin; ceftriaxone IM/IV, doxycycline for children >7 years old |
| **Anthrax, sepsis/pneumonia**[14,234] | Ciprofloxacin 20–30 mg/kg/day IV div q12h (regardless of age) (AIII) | On convalescence, can use oral ciprofloxacin or doxycycline; if susceptible, can use penicillin, amoxicillin, or clindamycin<br>For community-associated infection, amoxicillin (75 mg/kg/day div q8h) or doxycycline for children >7 years old should be effective |
| **Appendicitis (see Peritonitis)** | | |
| **Brucellosis**[235–238] | Doxycycline 4 mg/kg/day PO (max 200 mg/day) div bid (for children >7 yrs) AND rifampin (15–20 mg/kg/day div q12h) (BIII); OR TMP/SMX (10 mg/kg/day of TMP) IV, PO div q12h AND rifampin (15–20 mg/kg/day div q12h) BIII); x 4–8 wks | Alternative for children <8 years: TMP/SMX IV, PO div q12h, AND gentamicin 6–7.5 mg/kg/day IV, IM div q8h for the first 2 weeks of therapy (BIII)<br>Consider: ADD gentamicin at least for the first 1–2 wks to decrease the risk of relapse, and for serious disease, particularly with endocarditis, osteomyelitis meningitis; consider prolonged treatment for 4–6 months for these specific infections (AIII) |
| **Cat-scratch disease** *(Bartonella henselae)*[239–241] | Supportive (aspiration of pus); azithromycin 12 mg/kg/day PO qd x 5 d shortens the duration of adenopathy (AIII) | This dosage of azithromycin has been documented to be safe and effective for streptococcal pharyngitis, and may offer greater deep tissue exposure than the dosage studied by Bass et al, used for otitis media<br>No prospective data exist for invasive infections: gentamicin (x 14 d) AND TMP/SMX AND rifampin for hepatosplenic disease and osteomyelitis (AIII). For CNS infection, use cefotaxime AND gentamicin ± TMP/SMX. (AIII)<br>Alternatives ciprofloxacin, doxycycline |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Chickenpox/Shingles** (varicella-zoster virus)[242,243] | Acyclovir 30 mg/kg/day IV div q8h if severe, or 80 mg/kg/day PO div qid, depending on severity; x 5 d AI) | See Chapter 9; therapy for 10 d in immune-compromised children<br>Famciclovir can be made into a suspension with 25 mg and 100 mg sprinkle capsules[244] see Chapter 9 for dosages by body weight. No treatment data in children. (CIII) |
| **Ehrlichiosis** (human monocytic or granulocytic, anaplasmosis)[245–247] | Doxycycline 4 mg/kg/day IV, PO (max 200 mg/day) div bid x 7–10 d (regardless of age) (AIII) | For mild disease, consider rifampin 20 mg/kg/day PO div bid x 7–10 d (BIII) |
| **Febrile neutropenic patient** (empiric therapy of invasive infection: *Pseudomonas*, enteric gram-negative bacilli, staphylococci, streptococci, yeast, fungi)[248,249] | Cefepime 150 mg/kg/day div q8h (AI); or meropenem 60 mg/kg/day div q8h (AII); OR ceftazidime 150 mg/kg/day IV div q8h AND tobramycin 6 mg/kg/day IV q8h (AII)<br>ADD vancomycin 40 mg/kg/day IV div q8h if methicillin-resistant *S aureus* or coag-negative staph suspected (eg, central catheter infection) (AIII)<br>ADD metronidazole to ceftazidime or cefepime if colitis or other deep anaerobic infection suspected (AIII) | Alternatives: other anti-*Pseudomonas* beta-lactams AND anti-staph antibiotics<br>If no response in 3–5 d and no bacterial etiology demonstrated, consider additional empiric therapy with antifungals (BII); dosages and formulations outlined in Chapter 8 |
| **Human immunodeficiency virus infection** | See Chapter 9. | |
| **Infant botulism** | Botulism immune globulin for infants (BabyBIG) 50 mg/kg IV x 1; BabyBIG can be obtained from the California State Health Department: 510/231-7600 or at www.infantbotulism.org ($45,300 for a single dose, August 2009) (AI) | www.infantbotulism.org/ is the Web site organized by the California Dept of Public Health for resources<br>Intensive care unit supportive therapy; aminoglycosides potentiate the neuromuscular effect of botulinum toxin |
| **Kawasaki syndrome**[250–254] | No antibiotics; IVIG 2 g/kg as single dose (AI); may need to repeat dose in up to 10% of children for persisting fever that lasts 24 hours after completion of the IVIG infusion (AII). For subsequent relapse, consult an infectious disease physician. | Aspirin 80–100 mg/kg/day div qid in acute, febrile phase; once afebrile x 24–48 h, initiate low dosage (3–5 mg/kg/day) aspirin therapy for 6–8 wks (assuming echocardiogram is normal)<br>Role of corticosteroids[251,252] and infliximab[253] for IVIG-resistant Kawasaki disease remains to be determined |

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| **Leprosy** (Hansen's disease)[255] | Dapsone 1 mg/kg/day PO qd AND rifampin 10 mg/kg/day PO qd; ADD (for multibacillary disease) clarithromycin 7.5 mg/kg/day PO qd; x 12 months for paucibacillary disease; x 24 months for multibacillary disease (AII) | Clarithromycin has replaced clofazimine for treatment of children: consult the CDC (Hansen's Disease Center) at http://www.hrsa.gov/hansens/clinical/regimens.htm for advice about treatment and free antibiotics: 800/642-2477 |
| **Leptospirosis**[256,257] | Penicillin G 250,000 U/kg/day IV, IM div q6h, or ceftriaxone 50 mg/kg/day q24h; x 7 d (BII)<br>For mild disease, doxycycline (>7 yrs of age) 4 mg/kg/day (max 200 mg/day) PO div bid x 7–10 d (BII) | Alternative: amoxicillin for children ≤7 years of age with mild disease |
| **Lyme disease** *(Borrelia burgdorferi)*[247,258] | Neurologic evaluation, including LP, if there is clinical suspicion of CNS involvement | |
| – Early localized disease | >7 yrs of age: doxycycline 4 mg/kg/day (max 200 mg/day) PO div bid x 14–21 d (AII)<br>≤7 yrs of age: amoxicillin 50 mg/kg/day (max 1.5 g/day) PO div tid x 14–21 d (AII) | Alternative: erythromycin 30 mg/kg/day PO div tid |
| – Early disseminated disease | | |
| Arthritis (no CNS disease) | Oral therapy as outlined above; x 28 d (AIII) | Persistent or recurrent joint swelling after treatment: repeat a 4-wk course of oral antibiotics or give ceftriaxone 75–100 mg/kg IV q24h IV OR penicillin 300,000 U/kg/day IV div q4h; either for 14–28 d |
| Multiple erythema migrans | Oral therapy as outlined above; x 21 d (AIII) | |
| Isolated facial (Bell's) palsy | Oral therapy as outlined above; x 21–28 d (AIII) | LP is not routinely required unless CNS symptoms present |
| Carditis | Ceftriaxone 75–100 mg/kg IV q24h IV OR penicillin 300,000 U/kg/day IV div q4h; either for 14–28 d (AIII) | |
| Neuroborreliosis | Ceftriaxone 75–100 mg/kg IV q24h, or penicillin G 300,000 U/kg/day IV div q4h; x 14–28 d (AIII) | |
| **Melioidosis** *(Burkholderia pseudomallei)*[259-261] | Acute sepsis: meropenem 60 mg/kg/day div q8h; OR ceftazidime 150 mg/kg/day IV div q8h; followed by TMP/SMX (8 mg/kg/day of TMP) PO div bid x 3–6 mos (AII) | Alternative convalescent therapy: amox/clav (90 mg/kg/day amox div tid, not bid) for children ≤7 yrs of age, or doxycycline for children >7 yrs; x 20 wks |

| Clinical Diagnosis | Therapy (evidence grade) | Comments |
|---|---|---|
| **Mycobacteria, nontuberculous**[9,10,262] | | |
| – Adenitis in normal host (see Adenitis under Skin infections)<br>– Pneumonia or disseminated infection in compromised hosts (HIV or gamma interferon receptor deficiency) | Usually treated with 3 or 4 active drugs (eg, clarithromycin OR azithromycin, AND amikacin, cefoxitin, meropenem: also test for ciprofloxacin, TMP/SMX, ethambutol, rifampin, linezolid, clofazimine, and doxycycline (BII) | See Chapter 11 for dosages; cultures are essential, as the susceptibility patterns of nontuberculous mycobacteria are varied |
| **Nocardiosis** *(Nocardia asteroides* and *Nocardia brasiliensis)*[263,264] | TMP/SMX (8 mg/kg/day of TMP) div bid or sulfisoxazole 120–150 mg/kg/day PO div qid x 6–12 wks or longer. For severe infection, particularly in immune-compromised hosts, use ceftriaxone or meropenem AND amikacin 15–20 mg/kg/day IM, IV div q8h. (AIII) | Wide spectrum of disease from skin lesions to brain abscess<br>Surgery when indicated<br>Alternatives: doxycycline (for children >7 yrs of age), amox/clav, or linezolid |
| **Peritonitis** | | |
| – Appendicitis; bowel-associated; (enteric gram-negative bacilli, *Bacteroides* spp, *Enterococcus* spp, increasingly *Pseudomonas)*[265–269] | Meropenem 60 mg/kg/day IV div q8h or imipenem 60 mg/kg/day IV div q6h; OR pip/tazo 240 mg piperacillin/kg/day div q6h; x 7–10 d or longer if suspicion of persisting intraabdominal abscess (AII) | Many other regimens may be effective, including ampicillin 150 mg/kg/day div q8h AND gentamicin 6–7.5 mg/kg/day IV, IM div q8h AND clindamycin 30 mg/kg/day IV, IM div q8h or metronidazole 40 mg/kg/day IV div q8h<br>Source control is critical to achieve cure |
| – Peritoneal dialysis indwelling catheter infection (staphylococci; enteric gram-negatives; yeast)[270,271] | Antibiotic added to dialysate in concentrations approximating those attained in serum for systemic disease (eg, 4 µg/mL for gentamicin; 30 µg/mL for vancomycin, etc) after a larger loading dose (AII) | Selection of antibiotic based on organism isolated from peritoneal fluid; systemic antibiotics if there is accompanying bacteremia/fungemia |
| – Primary (pneumococcus)[272] | Ceftriaxone 50 mg/kg/day q24h, or cefotaxime 150 mg/kg/day div q8h; if penicillin-S, then penicillin G 150,000 U/kg/day IV div q6h; x 7–10 d (AII) | Other antibiotics according to culture and susceptibility tests |
| **Plague** *(Yersinia pestis)*[273–275] | Gentamicin 7.5 mg/kg/day IV div q8h (AII) | Doxycycline 4 mg/kg/day (max 200 mg/day) PO div bid; or ciprofloxacin 30 mg/kg/day PO div bid |

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| **Q fever**<br>*(Coxiella burnetii)*[276,277] | Acute stage: doxycycline 4 mg/kg/day (max 200 mg/day) PO div bid x 14 d (AII)<br>Endocarditis and chronic disease (>12 mos): doxycycline AND hydroxy chloroquine for 18–36 mos (AIII) | CNS: use fluoroquinolone (no prospective data) |
| **Rocky Mountain spotted fever**<br>(fever, petechial rash with centripetal spread;<br>*Rickettsia rickettsii)*[278,279] | Doxycycline 4 mg/kg/day (max 200 mg/day) PO div bid x 7–10 d (AI) | Doxycycline is preferred for all ages<br>Start empiric therapy early |
| **Tetanus**<br>*(Clostridium tetani)*[280,281] | Metronidazole 30 mg/kg/day IV, PO div q8h or penicillin G 100,000 U/kg/day IV div q6h x 10–14 d AND tetanus immune globulin (TIG) 3,000–6,000 U IM (AII) | Wound debridement essential; IVIG may provide antibody to toxin if TIG not available<br>Immunize immediately with Td or Tdap |
| **Toxic shock syndrome**<br>(toxin-producing strains of *S aureus* or group A streptococcus)[6,7,282] | Empiric: Vancomycin 45 mg/kg/day IV div q8h AND nafcillin or oxacillin 150 mg/kg/day IV div q6h, AND clindamycin 30–40 mg/kg/day div q8h ±gentamicin x 7–10 d (AIII) | Clindamycin added for the initial 48–72 h of therapy to decrease toxin production; IVIG may be added to bind circulating toxin<br>For MSSA: nafcillin or oxacillin AND clindamycin ±gentamicin<br>For CA-MRSA: vancomycin AND clindamycin ±gentamicin<br>For group A streptococcus: penicillin G AND clindamycin |
| **Tularemia**<br>*(Francisella tularensis)*[283,284] | Gentamicin 6–7.5 mg/kg/day IM, IV div q8h; x 10–14 d (AII) | Alternatives: doxycycline (x 14–21 d) or ciprofloxacin (x 10 d) |

## 7. Preferred Therapy for Specific Bacterial and Mycobacterial Pathogens

*NOTES*

- For fungal, viral, and parasitic infections see Chapters 8, 9, and 10, respectively.
- Limitations of space do not permit listing of all possible alternative antimicrobials.
- *Abbreviations:* amox/clav, amoxicillin/clavulanate (Augmentin); amp/sul, ampicillin/sulbactam (Unasyn); CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus;* CNS, central nervous system; ESBL, extended spectrum beta-lactamase; IV, intravenous; MRSA, methicillin-resistant *S aureus*; MSSA, methicillin-susceptible *S aureus*; pip/tazo, piperacillin/tazobactam (Zosyn); PO, orally; ticar/clav, ticarcillin/clavulanate (Timentin); TMP/SMX, trimethoprim/sulfamethoxazole; UTI, urinary tract infection.

| Organism | Clinical Illness | Drug of Choice (evidence grade) | Alternatives |
|---|---|---|---|
| *Acinetobacter baumanii*[1,2] | Sepsis, meningitis, nosocomial pneumonia | Meropenem (BIII) | Use culture results to guide therapy: ceftazidime, amp/sul; pip/tazo; TMP/SMX; ciprofloxacin; tigecycline; colistin |
| *Actinobacillus* (now *Aggregatibacter) actinomycetemcomitans*[3] | Abscesses, endocarditis | Ampicillin (amoxicillin) ± gentamicin (CIII) | Doxycycline; TMP/SMX; ciprofloxacin; ceftriaxone |
| *Actinomyces israelii*[4] | Actinomycosis (cervicofacial, thoracic, abdominal) | Penicillin G; ampicillin (CIII) | Amoxicillin; doxycycline; clindamycin; ceftriaxone; imipenem |
| *Aeromonas hydrophila*[5] | Diarrhea<br>Sepsis, cellulitis, necrotizing fasciitis | TMP/SMX (CIII)<br>Ceftazidime (BIII) | <br>Cefepime; ceftriaxone, meropenem; ciprofloxacin |
| *Arcanobacterium haemolyticum*[6] | Pharyngitis | Erythromycin; penicillin (BIII) | Azithromycin, amoxicillin, clindamycin; doxycycline; vancomycin |
| *Bacillus anthracis*[7] | Anthrax | Ciprofloxacin (regardless of age) (AIII) | Doxycycline; amoxicillin, clindamycin; penicillin G; vancomycin, meropenem |
| *Bacillus cereus* or *subtilis*[8,9] | Sepsis, endophthalmitis; toxin-mediated gastroenteritis | Vancomycin (BIII) | Clindamycin; meropenem, ciprofloxacin |
| *Bacteroides fragilis*[10] | Peritonitis, sepsis, abscesses | Metronidazole (AI) | Meropenem or imipenem (AI); ticar/clav; pip/tazo (AI); clindamycin (AI); amox/clav (BII) |

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|---|---|---|---|
| *Bacteroides*, other spp[10] | Pneumonia, sepsis, abscesses | Metronidazole (BII); clindamycin (BII) | Meropenem or imipenem; penicillin G or ampicillin if beta-lactamase negative |
| *Bartonella henselae*[11,12] | Cat-scratch disease | Azithromycin for lymph node disease (BII); gentamicin in combination with TMP/SMX AND rifampin for invasive disease (BIII) | Cefotaxime; ciprofloxacin; doxycycline |
| *Bartonella quintana*[13] | Bacillary angiomatosis, peliosis hepatis | Gentamicin plus doxycycline (BIII); erythromycin; ciprofloxacin (BIII) | Azithromycin; doxycycline |
| *Bordetella pertussis, parapertussis*[14,15] | Pertussis | Azithromycin (AIII); erythromycin (BII); | Clarithromycin; TMP/SMX; ampicillin |
| *Borrelia burgdorferi,* Lyme disease[16,17] | Treatment based on stage of infection (see Lyme disease in Chapter 4) | Doxycycline if >8 years (AII); amoxicillin or erythromycin in children ≤7 years (AIII); Ceftriaxone IV for meningitis (AII) | |
| *Borrelia recurrentis,* Louse-borne relapsing fever[18,19] | Relapsing fever | Single dose doxycycline if >8 years (AIII); penicillin or erythromycin in children ≤7 years (BIII) | |
| *Borrelia hermsii, turicatae, parkeri,* tickborne relapsing fever[18,19] | Relapsing fever | Doxycycline if >8 years (AIII); penicillin or erythromycin in children ≤7 years (BIII) | |
| *Brucella* spp[20–22] | Brucellosis | Doxycycline AND rifampin (BIII); TMP/SMX AND rifampin (BIII) | For serious infection: doxycycline AND gentamicin; or TMP/SMX AND gentamicin (AIII) |
| *Burkholderia cepacia* complex[23,24] | Pneumonia, sepsis in immune-compromised children; pneumonia in children with cystic fibrosis | Meropenem (BIII); for severe disease, ADD tobramycin AND TMP/SMX (AIII) | TMP/SMX; doxycycline; ceftazidime; ciprofloxacin |
| *Burkholderia pseudomallei*[25–27] | Melioidosis | Meropenem (AIII) or ceftazidime (BIII); followed by prolonged TMP/SMX (AIII) | TMP/SMX, doxycycline, or amox/clav for chronic disease |
| *Campylobacter fetus*[28] | Sepsis, meningitis in the neonate | Meropenem (BIII) | Cefotaxime; gentamicin; erythromycin |

| Organism | Clinical Illness | Drug of Choice (evidence grade) | Alternatives |
|---|---|---|---|
| *Campylobacter jejuni*[29] | Diarrhea | Azithromycin (BII); erythromycin (BII) | Doxycycline; ciprofloxacin |
| *Capnocytophaga canimorsus*[30] | Sepsis after dog bite | Amox/clav (BIII); penicillin G (BIII) | Ceftriaxone; meropenem; ciprofloxacin; clindamycin; pip/tazo |
| *Capnocytophaga ochracea*[31] | Sepsis, abscesses | Clindamycin (BIII); amox/clav (BIII) | meropenem; ciprofloxacin; pip/tazo |
| *Chlamydophila* (formerly *Chlamydia) pneumoniae*[32] | Pneumonia | Azithromycin (AII); erythromycin (AII) | Doxycycline; ciprofloxacin |
| *Chlamydophila* (formerly *Chlamydia) psittaci*[33] | Psittacosis | Azithromycin (AIII); erythromycin (AIII) | Doxycycline |
| *Chlamydia trachomatis*[34,35] | Lymphogranuloma venereum | Doxycycline (AII) | Azithromycin; erythromycin |
| | Urethritis, vaginitis | Doxycycline (AII) | Azithromycin; erythromycin; ofloxacin |
| | Inclusion conjunctivitis of newborn | Azithromycin (AIII) | Erythromycin |
| | Pneumonia of infancy | Azithromycin (AIII) | Erythromycin; ampicillin |
| | Trachoma | Azithromycin (AI) | Doxycycline; erythromycin |
| *Chromobacterium violaceum*[36] | Sepsis, pneumonia, abscesses | TMP/SMX AND ciprofloxacin (AIII) | Chloramphenicol ± gentamicin, meropenem |
| *Chryseobacterium (Flavobacterium) meningosepticum*[37,38] | Sepsis, meningitis | Vancomycin (increasing resistance) AND rifampin (BIII); or ciprofloxacin (BIII) | TMP/SMX; clindamycin |
| *Citrobacter* spp[39] | Meningitis, sepsis | Meropenem (AIII) | Cefepime; ceftriaxone AND gentamicin; TMP/SMX; ciprofloxacin |
| *Clostridium botulinum*[40,41] | Botulism: foodborne; wound | Equine antitoxin (AIII)<br>No antibiotic treatment | Equine antitoxin available now only through state health departments (http://www.cdc.gov/ncidod/srp/drugs/formulary.html) |

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| | Infant botulism | Human botulism immune globulin (BabyBIG) (AII)<br>No antibiotic treatment | BabyBIG available nationally from the California State Health Dept at 510/231-7600 (www.dhs.ca.gov/ps/dcdc/InfantBot/ibtindex.htm) |
| *Clostridium difficile*[42,43] | Antibiotic-associated colitis | Metronidazole PO (AI) | Vancomycin PO for metronidazole failures; stop the predisposing antimicrobial therapy, if possible |
| *Clostridium perfringens*[44,45] | Gas gangrene, sepsis;<br>Food poisoning | Penicillin G or clindamycin for invasive infection (BII); no antimicrobials indicated for foodborne illness | Meropenem, metronidazole |
| *Clostridium tetani*[46,47] | Tetanus | Metronidazole (AIII); penicillin G (BIII) | ADD Tetanus immune globulin<br>Alternative antibiotics: meropenem; doxycycline, clindamycin<br>Immunize after recovery |
| *Corynebacterium diphtheriae*[48] | Diphtheria | Equine antitoxin AND erythromycin or penicillin G (AIII) | Antitoxin from the CDC at the Emergency Operations Center 770/488-7100 (http://www.cdc.gov/ncidod/srp/drugs/formulary.html) |
| *Corynebacterium jeikeium*[49] | Sepsis | Vancomycin (AIII) | Penicillin G AND gentamicin |
| *Corynebacterium minutissimum*[50,51] | Erythrasma; bacteremia in compromised hosts | Erythromycin PO for erythrasma (BIII); vancomycin IV for bacteremia (BIII) | Topical clindamycin for cutaneous infection |
| *Coxiella burnetii*[52,53] | Q fever | Doxycycline (all ages) (AII) | Ciprofloxacin |
| *Ehrlichia chafeensis*[54] | Human monocytic ehrlichiosis | Doxycycline (all ages) (AII) | Rifampin |
| *Ehrlichia* (now *Anaplasma phagocytophilum)*[54] | Human granulocytic anaplasmosis | Doxycycline (all ages) (AII) | Rifampin |
| *Eikenella corrodens*[55] | Human bite wounds; abscesses, meningitis | Ampicillin; penicillin G (BIII) | Amox/clav; ticar/clav; pip/tazo; amp/sul; ceftriaxone; ciprofloxacin<br>Resistant to clindamycin |

| Organism | Clinical Illness | Drug of Choice (evidence grade) | Alternatives |
|---|---|---|---|
| *Enterobacter* spp[56,57] | Sepsis, pneumonia, wound infection, UTI | Cefepime; meropenem (BII) | Ertapenem; imipenem; cefotaxime or ceftriaxone AND gentamicin; TMP/SMX; ciprofloxacin |
| *Enterococcus* spp[57–59] | Endocarditis, UTI | Ampicillin AND gentamicin (AI) | Vancomycin AND gentamicin<br>For vancomycin-resistant strains that are also amp-R: linezolid, daptomycin |
| *Erysipelothrix rhusiopathiae*[60] | Sepsis, cellulitis, abscesses, endocarditis | Ampicillin (BIII); penicillin G (BIII) | Ceftriaxone; meropenem; ciprofloxacin |
| *Escherichia coli*[56] | UTI, not hospital-acquired | A 2nd or 3rd generation cephalosporin PO, IM (BI) | Amoxicillin; TMP/SMX if susceptible |
| | Traveler's diarrhea | Azithromycin (AII) | Rifaximin (for nonfebrile, nonbloody diarrhea for children >11 yrs); cefixime |
| | Sepsis, pneumonia, hospital-acquired UTI | A 2nd or 3rd generation cephalosporin IV (BI) | For ESBL-producing strains: meropenem (AIII)<br>Ciprofloxacin if resistant to other antibiotics |
| | Meningitis | Ceftriaxone; cefotaxime (AIII) | For ESBL-producing strains: meropenem (AIII) |
| *Francisella tularensis*[61] | Tularemia | Gentamicin (AII) | Doxycycline; ciprofloxacin |
| *Fusobacterium* spp[62,63] | Sepsis, soft tissue infection, Lemierre's syndrome | Metronidazole (AIII); clindamycin (BIII) | Penicillin G; meropenem |
| *Gardnerella vaginalis*[64] | Bacterial vaginosis | Metronidazole (BII) | Clindamycin |
| *Haemophilus aphrophilus*[65] | Sepsis, endocarditis, abscesses | Ceftriaxone (AII); OR ampicillin AND gentamicin (BII) | Ciprofloxacin, amox/clav |
| *Haemophilus ducreyi*[66] | Chancroid | Azithromycin (AIII); ceftriaxone (BIII) | Erythromycin; ciprofloxacin |

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| *Haemophilus influenzae*[67] | | | |
| – non-encapsulated strains | Upper respiratory tract infections | Beta-lactamase neg: ampicillin IV (AI); amoxicillin PO (AI) | Levofloxacin; azithromycin; TMP/SMX |
| – type b strains | Meningitis, arthritis, cellulitis, epiglottitis, pneumonia | Beta-lactamase pos: ceftriaxone IV, IM (AI), or cefotaxime IV (AI); amox/clav (AI) OR 2nd or 3rd generation cephalosporins PO (AI) | Full IV course (10 d) for meningitis |
| *Helicobacter pylori*[68] | Gastritis, peptic ulcer | Amoxicillin AND clarithromycin AND omeprazole (AII) | Other regimens include metronidazole, other proton pump inhibitors |
| *Klebsiella* spp *(K pneumoniae, K oxytoca)*[57,69,70] | UTI | A 2nd or 3rd generation cephalosporin (AII) | Use most narrow spectrum agent active against pathogen: TMP/SMX; gentamicin<br>ESBL producers should be treated with a carbapenem |
| (meropenem, ertapenem, imipenem) | Sepsis, pneumonia, meningitis | Ceftriaxone; cefotaxime, cefepime (AIII) | Carbapenem or ciprofloxacin if resistant to other antibiotics<br>Meningitis caused by ESBL producer: meropenem<br>Carbapenemase producers: ciprofloxacin, colistin |
| *Klebsiella granulomatis*[66] | Granuloma inguinale | Doxycycline (AII) | Azithromycin; TMP/SMX; ciprofloxacin |
| *Kingella kingae*[71] | Osteomyelitis, arthritis | Ampicillin; penicillin G (AII) | Ceftriaxone; TMP/SMX; oxacillin; cephalexin; ciprofloxacin |
| *Legionella* spp[72] | Legionnaires' disease | Azithromycin (AI) | Erythromycin; levofloxacin; doxycycline |
| *Leptospira* spp[73] | Leptospirosis | Penicillin G(AII); ceftriaxone(AII) | Amoxicillin; doxycycline |
| *Leuconostoc*[74] | Bacteremia | Penicillin G (AIII); ampicillin (BIII) | Clindamycin; erythromycin; doxycycline (resistant to |

vancomycin)

| Organism | Clinical Illness | Drug of Choice (evidence grade) | Alternatives |
|---|---|---|---|
| *Listeria monocytogenes*[75] | Sepsis, meningitis in compromised host; neonatal sepsis | Ampicillin (ADD gentamicin for severe infection) (AII) | TMP/SMX; vancomycin |
| *Moraxella catarrhalis*[76] | Otitis, sinusitis, bronchitis | Amox/clav (AI) | TMP/SMX; A 2nd or 3rd generation cephalosporin |
| *Morganella morganii*[77,78] | UTI, sepsis, wound infection | Cefepime (AIII); meropenem(AIII) | Pip/tazo; ceftriaxone |
| *Mycobacterium abscessus*[79,80] | Skin and soft tissue infections; pneumonia in cystic fibrosis | Clarithromycin or azithromycin (AIII); ADD amikacin ± cefoxitin for invasive disease (AIII) | Also test for susceptibility to: tigecycline, linezolid |
| *Mycobacterium avium complex*[80,81] | Cervical adenitis | Clarithromycin (AII); azithromycin (AII) | Surgical excision may be curative<br>May increase cure rate with addition of rifampin ± ethambutol |
| | Disseminated disease in competent host, or disease in immune-compromised host | Clarithromycin or azithromycin AND ethambutol AND rifampin (AIII) | Depending on susceptibilities, and the severity of illness: ADD amikacin ± ciprofloxacin |
| *Mycobacterium bovis*[82] | Tuberculosis (adenitis; abdominal tuberculosis; meningitis) | Isoniazid AND rifampin (AII); add ethambutol for suspected resistance (AIII) | Add streptomycin for severe infection.<br>*M bovis* is resistant to pyrazinamide |
| *Mycobacterium chelonae*[80,83] | Abscesses; catheter infection | Clarithromycin or azithromycin (AIII); ADD amikacin ± cefoxitin for invasive disease (AIII) | Also test for susceptibility to: cefoxitin; TMP/SMX; doxycycline; gentamicin, imipenem; moxifloxacin, linezolid |
| *Mycobacterium abscessus*[79,80] | Skin and soft tissue infections; pneumonia in cystic fibrosis | Clarithromycin or azithromycin (AIII); ADD amikacin ± cefoxitin for invasive disease (AIII) | Also test for susceptibility to: tigecycline, linezolid |
| *Mycobacterium fortuitum complex*[80,84] | Skin and soft tissue infections; catheter infection | Amikacin AND imipenem (AIII) ± ciprofloxacin (AIII) | Also test for susceptibility to: cefoxitin; doxycycline; linezolid |
| *Mycobacterium leprae*[85] | Leprosy | Dapsone AND rifampin (for paucibacillary) (AII) ADD clarithromycin for lepromatous, | For alternatives: http://www.hrsa.gov/hansens/clinical/regimens.htm |

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| | | multibacillary disease (AII) | |
| *Mycobacterium marinum/balnei*[80,86] | Papules, pustules, abscesses (swimmer's granuloma) | Clarithromycin ± rifampin (AIII) | TMP/SMX AND rifampin; doxycycline; ethambutol |
| *Mycobacterium tuberculosis*[82] | Tuberculosis (pneumonia; meningitis; cervical adenitis; mesenteric adenitis; osteomyelitis) | Isoniazid AND rifampin AND pyrazinamide (AI) | Add ethambutol for suspect resistance; add streptomycin for severe infection<br>Corticosteroids should be added to regimens for meningitis, mesenteric adenitis and endobronchial infection (AIII) |
| *Mycoplasma hominis*[66,87,88] | Non-gonococcal urethritis; neonatal infection | Clindamycin (AIII) | Fluoroquinolones; doxycycline<br>Usually erythromycin-resistant |
| *Mycoplasma pneumoniae*[87,89] | Pneumonia | Azithromycin (AI); erythromycin (BI) | Doxycycline; fluoroquinolones |
| *Neisseria gonorrhoeae*[66] | Gonorrhea | Ceftriaxone (AI); cefixime (AI) | Spectinomycin IM |
| *Neisseria meningitidis*[90] | Sepsis, meningitis | Ceftriaxone (AI); cefotaxime (AI) | Penicillin G or ampicillin<br>For prophylaxis following exposure: rifampin or ciprofloxacin (cipro-resistant strains have now been reported) |
| *Nocardia asteroides* or *brasiliensis*[91] | Nocardiosis | TMP/SMX (AII); sulfisoxazole (BII); (AND amikacin for severe infection) (AII) | Meropenem; ceftriaxone; doxycycline; linezolid |
| *Oerskovia* (now known as *Cellulosimicrobium cellulans*)[92] | Wound infection; catheter infection | Vancomycin ± rifampin (AIII) | Resistant to beta-lactams, macrolides, aminoglycosides |
| *Pasteurella multocida*[93] | Sepsis, abscesses, animal bite wound | Penicillin G (AIII); ampicillin (AIII); amoxicillin (AIII) | Amox/clav; ticar/clav; pip/tazo; doxycycline; ceftriaxone |
| *Peptostreptococcus*[94] | Sepsis | Penicillin G (AII); ampicillin (AII) | Clindamycin; vancomycin; meropenem/imipenem, metronidazole |

| Organism | Clinical Illness | Drug of Choice (evidence grade) | Alternatives |
|---|---|---|---|
| *Plesiomonas shigelloides*[95,96] | Diarrhea, meningitis | Antibiotics may not be necessary to treat diarrhea: 2nd and 3rd generation cephalosporins (AIII); azithromycin (BIII); ciprofloxacin (CIII) | For meningitis/sepsis: meropenem; pip/tazo; ceftriaxone |
| *Prevotella (Bacteroides) melaninogenicus*[97] | Deep head/neck space abscess; dental abscess | Metronidazole (AII); meropenem/ imipenem (AII) | Pip/tazo; clindamycin |
| *Propionibacterium acnes*[98,99] | In addition to acne: sepsis, postop wound infection | Penicillin (AIII); vancomycin (AIII) | Cefotaxime; doxycycline; clindamycin; ciprofloxacin; linezolid |
| *Proteus mirabilis*[100–102] | UTI, sepsis, meningitis | Ampicillin (AII) | Increasing resistance, particularly in nosocomial isolates. Use most narrow spectrum agent active against pathogen; TMP/SMX; a cephalosporin; an aminoglycoside. |
| *Proteus vulgaris*, other spp (indole-positive strains)[100] | UTI, sepsis, meningitis | Ceftriaxone (AII); cefotaxime (AII) | Cefepime; meropenem; gentamicin; ciprofloxacin; TMP/SMX |
| *Providencia* spp | Sepsis | Ceftriaxone (AII); cefotaxime (AII) | Cefepime; meropenem; gentamicin; ciprofloxacin; TMP/SMX |
| *Pseudomonas aeruginosa*[57,103–105] | UTI | Ceftazidime (AI); other anti-pseudomonal beta-lactams | Tobramycin; amikacin; ciprofloxacin |
| | Nosocomial sepsis, pneumonia | Cefepime (AI) or meropenem (AI); OR ceftazidime AND tobramycin (BI) | Pip/tazo AND tobramycin (BI); ciprofloxacin AND tobramycin |
| | Pneumonia in cystic fibrosis[106] | Cefepime (AII) or meropenem (AI); OR ceftazidime AND tobramycin (BII); ADD aerosol tobramycin (AI) | Many organisms are multi-drug resistant; consider ciprofloxacin or colistin parenterally; in vitro synergy testing may suggest effective combinations[107]<br>For multi-drug resistant organisms, colistin aerosol (AIII) |

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| *Pseudomonas cepacia, mallei* or *pseudomallei* (see *Burkholderia*) | | | |
| *Rhodococcus equi*[108] | Necrotizing pneumonia | Imipenem AND vancomycin (AIII) | Amikacin; erythromycin; rifampin; ciprofloxacin |
| *Rickettsia*[53,109] | Rocky Mountain spotted fever, Q fever, typhus, rickettsial pox | Doxycycline (all ages) (AII) | Chloramphenicol; a fluoroquinolone |
| *Salmonella, non-typhi*[110] | Gastroenteritis; focal infections; bacteremia | Ceftriaxone (AII); cefixime (AII); azithromycin (AII) | For susceptible strains: ciprofloxacin; TMP/SMX; ampicillin |
| *Salmonella typhi*[110–112] | Typhoid fever | Ceftriaxone (AII); azithromycin (AII); ciprofloxacin (AII) | For susceptible strains: TMP/SMX; ampicillin |
| *Serratia marcescens*[57,113] | Nosocomial sepsis, pneumonia | Cefepime (AII); a carbapenem (AII) | Ceftriaxone or cefotaxime AND gentamicin; or ciprofloxacin |
| *Shigella* spp[113,114] | Enteritis, UTI, prepubertal vaginitis | Ceftriaxone (AII); azithromycin (AII); cefixime (AII); ciprofloxacin (AII) | Use most narrow spectrum agent active against pathogen: ampicillin (not amoxicillin); TMP/SMX |
| *Spirillum minus*[115,116] | Rat-bite fever (Sodoku fever) | Penicillin G IV (AII); for endocarditis, ADD gentamicin or streptomycin (AIII) | Ampicillin; doxycycline; cefotaxime, vancomycin, streptomycin |
| *Staphylococcus aureus*[117,118] See Chapter 4: CA-MRSA. | Skin infections, mild–moderate | MSSA: a 1st generation cephalosporin (cefazolin IV, cephalexin PO) (AI); oxacillin/ nafcillin IV (AI), dicloxacillin PO (AI)<br>MRSA: clindamycin IV or PO (AIII) | For MSSA: amox/clav<br>For CA-MRSA: vancomycin IV; linezolid IV, PO; TMP/SMX (if susceptible); clindamycin IV, PO; daptomycin IV |
| For serious infections, treat empirically for CA-MRSA (resistant to all beta-lactam antibiotics) | Pneumonia, sepsis, myositis, osteomyelitis, etc | MSSA: oxacillin/nafcillin IV (AI); a 1st generation cephalosporin (cefazolin IV) (AI) ± gentamicin (AIII)<br>MRSA: vancomycin (AII) or clindamycin (AII); ± gentamicin ± rifampin (AIII) | For CA-MRSA: linezolid (AII); OR daptomycin for non-pulmonary infection (AII) |
| *Staphylococcus*, coagulase negative[119] | Nosocomial sepsis, infected CNS shunts, UTI | Vancomycin (AII) | If susceptible: nafcillin (or other anti-staph beta-lactam); rifampin (in combination); linezolid |

| Organism | Clinical Illness | Drug of Choice (evidence grade) | Alternatives |
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| *Stenotrophomonas maltophilia*[120] | Sepsis | TMP/SMX (AII) | Ceftazidime; ticar/clav; doxycycline |
| *Streptobacillus moniliformis*[115,116] | Rat-bite fever (Haverhill fever) | Penicillin G (AIII); ampicillin (AIII); for endocarditis, ADD gentamicin or streptomycin (AIII) | Doxycycline; ceftriaxone; carbapenems; clindamycin; vancomycin |
| *Streptococcus*, group A[121] | Pharyngitis, impetigo, adenitis | Penicillin (AI); amoxicillin (AI) | A 1st generation cephalosporin (cefazolin, or cephalexin) (AI); clindamycin (AI); a macrolide (AI), vancomycin (AIII)<br>For relapsing pharyngitis, clindamycin or amox/clav (AIII) |
| *Streptococcus*, group B[122] | Neonatal sepsis, pneumonia, meningitis | Penicillin (AII) or ampicillin (AII) ± gentamicin (AIII) | Vancomycin (AIII)<br>For outpatient management during convalescence: ceftriaxone (AIII) |
| *Streptococcus*, group C G[59] | Pneumonia, sepsis, skin and soft tissue infection, arthritis, brain abscess, meningitis | Penicillin G (AIII); ampicillin (AIII) ADD gentamicin for serious infection (AIII) | Clindamycin; a 1st generation cephalosporin; vancomycin |
| *Streptococcus pneumoniae*[123,124] | Otitis, sinusitis | Amoxicillin, high-dose (90 mg/kg/day) (AII) | Amox/clav; cefdinir; cefpodoxime; cefuroxime; azithromycin; clarithromycin; OR ceftriaxone IM |
| | Meningitis | Ceftriaxone (AI) or cefotaxime (AI); AND vancomycin for possible ceftriaxone-resistant strains (AIII) | Penicillin G alone for pen-S strains; ceftriaxone alone for ceftriaxone-susceptible strains |
| | Pneumonia, osteomyelitis/arthritis, sepsis | Ceftriaxone (AI); cefotaxime (AI) | Penicillin G for pen-S strains (AI) |
| *Streptococcus*, viridans group (alpha streptococci)[125,126] | Endocarditis | Penicillin G ± gentamicin (AII) OR ceftriaxone ± gentamicin (AII) | Vancomycin |
| *Treponema pallidum*[127] | Syphilis | Penicillin G (AII) | Doxycycline; ceftriaxone |

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| *Ureaplasma urealyticum*[66,128] | Genitourinary infections | Azithromycin (AII) | Erythromycin; doxycycline, ofloxacin (for adolescent genital infections) |
| | Neonatal pneumonia (therapy may not be effective) | Azithromycin (AIII) | |
| *Vibrio cholerae*[129,130] | Cholera | Doxycycline (AI) or azithromycin (AII) | Ciprofloxacin; TMP/SMX |
| *Vibrio vulnificus*[131,132] | Sepsis, necrotizing fasciitis | Doxycycline AND ceftazidime (AIII) | Ciprofloxacin AND cefotaxime |
| *Yersinia enterocolitica*[133,134] | Diarrhea, mesenteric enteritis, reactive arthritis, sepsis | TMP/SMX (AIII); ciprofloxacin (AIII) | Ceftriaxone; gentamicin |
| *Yersinia pestis*[135,136] | Plague | Gentamicin (AIII) | Doxycycline; ciprofloxacin |
| *Yersinia pseudotuberculosis*[137,138] | Mesenteric adenitis; Far East scarlet fever; reactive arthritis | TMP/SMX (AIII); ciprofloxacin (AIII) | Ceftriaxone; gentamicin |

## 8. Preferred Therapy for Specific Fungal Pathogens

*NOTES*

- See Chapter 2 for discussion of amphotericins, azoles, and echinocandins.
- *Abbreviations:* AmB-D, amphotericin B deoxycholate, the oldest, standard AmB (original trade name Fungizone); AmB-LC, amphotericin B lipid complex (Abelcet); AmB-LP, liposomal amphotericin B (AmBisome); AmB-CD, amphotericin B colloidal suspension (Amphotec); bid, twice daily; CNS, central nervous system; CSF, cerebrospinal fluid; qd, once daily; qid, 4 times daily; tid, 3 times daily.

| Infection | Therapy (evidence grade) | Comments |
|---|---|---|
| **SYSTEMIC INFECTIONS** | | |
| **Prophylaxis** | | |
| **Prophylaxis of invasive fungal infection in patients with hematologic malignancies[1–4]** | Fluconazole 5 mg/kg/day for prevention of *Candida* infection (AII) | Fluconazole is not effective against *Aspergillus* and some strains of *Candida*. Posaconazole PO and voriconazole PO are effective in adults in preventing *Aspergillus* and *Candida*, but are not well-studied in children, and should only be used for highest risk patients[5] |
| **Prophylaxis of invasive fungal infection in patients with solid organ transplants[6–8]** | Fluconazole 5 mg/kg/day for prevention of *Candida* infection (AII) | AmB, caspofungin, voriconazole, or posaconazole may be effective in preventing aspergillus infection |
| **Treatment** | | |
| **Aspergillosis[9,10]** | Voriconazole 14 mg/kg/day IV div q12h (no loading dosage in children) (AII). May switch from voriconazole IV to voriconazole 400 mg/day div bid PO for children ages 2–12 yrs when stable (AIII). Total course x 6 wks+<br>Alternatives: Caspofungin 70 mg/m2 IV loading dose on day one (max dose 70 mg), followed by 50 mg/m2 IV (max dose 70 mg) on subsequent days x 6 wks+ (BIII)<br>AmB-LC or AmB-LP 5–10 mg/kg IV daily as 3–4 h infusions (in adults, higher dosages have not produced improved outcome)[13] x 6 wks+ (BII)<br>For less severe, non-CNS disease or convalescent therapy: itraconazole 5 mg/kg/day PO solution (AIII) | Treat for tissue invasion, not colonization; voriconazole provides a better response rate than amphotericin<br>Combination therapy not well-studied prospectively in humans. In vitro data suggest synergy with 2 (but not 3) drug combinations: caspofungin AND voriconazole; OR caspofungin AND AmB[11]<br>Both voriconazole and amphotericin are fungicidal, while caspofungin is fungistatic; both voriconazole and caspofungin act on fungal cell wall, AmB acts on cell membrane<br>Against most *Aspergillus* sp, micafungin[12] demonstrates equivalent activity to caspofungin<br>Posaconazole (PO) also active against *Aspergillus*, clinical efficacy documented in salvage therapy; approved for prophylaxis of *Aspergillus* |

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| **Blastomycosis** (North American)[14–16] | For severe disease: AmB-LC or AmB-LP 5 mg/kg IV daily as 3–4 h infusion, followed by itraconazole 10 mg/kg/day (max 400 mg) PO q24h x 6–12 months (AIII)<br>For mild-moderate disease: itraconazole (limited data in children): 10 mg/kg/day (max 400 mg) PO q24h x 6–12 mos (AIII) | Itraconazole PO solution provides greater and more reliable absorption than capsules<br>Alternative: high-dose fluconazole (BIII) |
| **Candidiasis**[17] (see Chapter 2) | | |
| – Disseminated infection | Caspofungin 70 mg/m2 IV loading dose on day 1 (max dose 70 mg), followed by 50 mg/m2 IV (max dose 70 mg) on subsequent days (AII); OR micafungin 2mg/kg/day q24h for children ≤40 kg, and 100 mg/day q24h for children >40 kg (BIII)[18]; preterm neonates may require up to 15 mg/kg/day to achieve adequate drug exposure (BIII)[19] OR AmB-LC or AmB-LP 3-5 mg/kg/day IV q24h (BII) x 2–4 wks<br>For CNS infections: AmB-D 1 mg/kg/day AND flucytosine 100 mg/kg/day PO div q6h (AII); echinocandins do NOT achieve therapeutic concentrations in CSF | Fluconazole 12 mg/kg/day for susceptible *Candida*<br>For immune-compromised children, start with AmB or echinocandins as some strains of *Candida* are resistant to fluconazole, particularly *Candida krusei*. If responsive to empiric therapy and susceptible, can switch to fluconazole IV or PO.<br>For failures with AmB, add caspofungin or micafungin to regimen<br>Voriconazole and posaconazole are active against many fluconazole-resistant *Candida* sp<br>Little data on CNS efficacy with AmB-LC and AmB-LP |
| – Oropharyngeal, esophageal[17,20] | Fluconazole 3–6 mg/kg once daily PO x 5–7 d (AII) | AmB IV OR an echinocandin IV OR fluconazole IV for severe disease or febrile neutropenic patients<br>Clotrimazole 10 mg troche PO 5 times daily x 7 d<br>Voriconazole and posaconazole also effective |
| – Peritonitis (secondary to peritoneal dialysis)[21] | Fluconazole 200 mg intraperitoneal q24h (AII) | Remove peritoneal dialysis catheter; replace after 4–6 weeks of treatment, if possible.<br>High-dosage oral fluconazole may also be used.<br>AmB should not be instilled into the peritoneal cavity. |
| – Urinary tract infection | Cystitis: fluconazole 3–6 mg/kg once daily IV or PO x 5–7 days (AII)<br>Pyelonephritis: fluconazole 3–6 mg/kg once daily IV or PO x 14 days (AII) | Removing Foley catheter, if present, may lead to a spontaneous cure in the normal host; check for additional upper urinary tract disease<br>Alternative: AmB IV |

| Infection | Therapy (evidence grade) | Comments |
|---|---|---|
| – Vulvovaginal[22] | Topical agents (butoconazole, clotrimazole, miconazole, sertaconazole, tioconazole, terconazole ) OR fluconazole 10 mg/kg as a single dose (AII) | |
| **Chromoblastomycosis[23,24]** | Itraconazole oral soln 5 mg/kg/day PO q24h x 12–18 mos, in combination with surgical excision or repeated cryotherapy (AIII) | Alternative: terbinafine or an AmB |
| **Coccidioidomycosis[25–28]** | For pulmonary disease: fluconazole 6–12 mg/kg IV, PO q24h (AII); OR AmB-D 1 mg/kg/day IV q24h; OR AmB-LC or AmB-LP 5 mg/kg/day IV q24h (BII)<br>For meningitis: fluconazole 12 mg/kg/day IV q24h (AII); for failures, intrathecal AmB-D OR voriconazole IV (AIII)<br>For osteomyelitis: itraconazole solution 10 mg/kg/day q24h seems more effective than fluconazole (AIII) | Mild pulmonary disease does not require therapy in the normal host<br>Posaconazole also active, but little experience in children<br>Treat until serum cocci complement fixation titers drop to 1:8 or 1:4, about 6 wks<br>Disease in immune-compromised hosts may need to be treated longer, potentially life-long<br>Watch for relapse up to 1–2 yrs after therapy |
| **Cryptococcosis[29–31]** | For pulmonary disease: fluconazole 10–12 mg/kg/day IV, PO q24h x 12–24 wks (AII); OR AmB-D 1 mg/kg/day q24h; OR AmB-LC, or AmB-LP 3–5 mg/kg/day q24h x 3–6 wks (AII)<br>For meningitis: AmB-D 0.5–0.7 mg/kg/day IV q24h; OR AmB-LC or AmB-LP 3–5 mg/kg/day q24h; AND flucytosine 100 mg/kg/day PO div q6h x 2 wks, FOLLOWED BY fluconazole x 10 wks (AI) | Monitor flucytosine serum concentrations to keep peaks less than 80–100 mcg/mL to prevent neutropenia<br>For HIV-positive, AmB x 2 wks, then fluconazole 6–12 mg/kg once daily x 10 wks, then 4 mg/kg daily indefinitely |
| **Histoplasmosis[32,33]** | For mild-moderate pulmonary disease, itraconazole 10 mg/kg/day PO solution q24h x 6–12 wks (AII) OR for severe disease: AmB-D 1 mg/kg/day q24h; OR AmB-LC or AmB-LP 3-5 mg/kg/day q24h X 1-2 wks, THEN itraconazole 10 mg/kg/day div bid to complete 12 wks (AIII) | Mild disease may not require therapy<br>For disease with respiratory distress, ADD corticosteroids |
| **Paracoccidioidomycosis[34–36]** | Itraconazole 5–10 mg/kg/day PO solution q24h x 6 mos (AIII); OR ketoconazole 5 mg/kg/day PO q24h x 6 mos (BIII) | Alternatives: voriconazole; sulfadiazine or TMP/SMX for 3–5 years<br>AmB is another alternative, and may be combined with sulfa or azole antifungals |

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| **Phaeohyphomycosis** (dematiaceous, pigmented fungi)[37,38] | Combination therapy with an echinocandin and an azole, an echinocandin and AmB(AIII); OR terbinafine and an azole x 3–12 months<br>For mild disease: itraconazole 10 mg/kg/day PO solution q24h (AIII) | Surgery is essential; susceptibilities are variable.<br>Alternatives for mild disease: voriconazole or posaconazole |
| ***Pneumocystis jiroveci (carinii)* pneumonia**[39] | Serious disease: TMP/SMX 15–20 mg, TMP/kg/day IV div q8h(AI); OR pentamidine isethionate 4 mg base/kg/day IV daily(BII); x 3 wks<br>Mild-moderate disease: TMP/SMX, 20 mg TMP/kg/day PO div qid x 2 wks (AII) | Alternatives: TMP AND dapsone; OR primaquine AND clindamycin; OR atovaquone<br>Prophylaxis: TMP/SMX (5 mg TMP component/kg/day) PO daily or 3x/wk; OR dapsone 1 mg/kg PO once daily<br>Use steroid therapy for more severe disease. |
| ***Pseudallescheria boydii*** (and its asexual form, ***Scedosporium apiospermum)***[38,40] | Voriconazole 14 mg/kg/day IV div q12h (no loading/maintenance dosage in children) (AII) | Resistant to AmB in vitro<br>Alternatives: itraconazole in combination with AmB; echinocandins have been successful at salvage therapy anecdotally; combinations of terbinafine and azoles active in vitro |
| **Sporotrichosis**[41] | Itraconazole 10 mg/kg/day PO solution q24h x 3–6 mos(AII);<br>For serious pulmonary infection, or disseminated sporotrichosis: AmB-LC or AmB-LP, 5–10 mg/kg/day q24h until stable, then step-down therapy with itraconazole PO x 12 mos (AIII) | Alternatives: terbinafine<br>Surgery may be necessary in osteoarticular or pulmonary disease. |
| **Zygomycosis** (mucormycosis)[42–45] | Requires aggressive surgery and combination antifungal therapy: AmB-LC or AmB-LP, 5–10 mg/kg/day q24h AND caspofungin x 6–12 wks or longer (AIII)<br>For AmB failures, posaconazole may be effective against most strains. (AIII) | Following clinical response with AmB, long-term oral step-down therapy with posaconazole can be attempted x 2–6 mos. |

| Infection | Therapy (evidence grade) | Comments |
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| **LOCALIZED MUCOCUTANEOUS INFECTIONS** | | |
| **Dermatophytoses** | | |
| – Scalp (tinea capitis, including kerion); *Trichophyton, Microsporum, Epidermophyton* spp[46–48] | Griseofulvin ultramicrosized 10–15 mg/kg/day or microsized 20–25 mg/kg/day once daily PO x 1–2 mos or longer (AII) (taken with milk or fatty foods to augment absorption)<br>For kerion, treat concurrently with prednisone (1–2 mg/kg/day x 1–2 wks) (AIII) | No need to routinely follow liver function tests in normal healthy children taking griseofulvin<br>2.5% selenium sulfide shampoo, or 2% ketoconazole shampoo, 2–3 x/wk should be used concurrently to prevent recurrences<br>Alternatives: itraconazole solution 5 mg/kg PO qd, or terbinafine PO; or fluconazole PO |
| – Tinea corporis (infection of trunk/limbs/face)<br>– Tinea cruris (infection of the groin)<br>– Tinea pedis (infection of the toes/feet) | Alphabetic order of topical agents: butenafine, ciclopirox, clotrimazole, econazole, haloprogin, ketoconazole, miconazole, naftifine, oxiconazole, sertaconazole, sulconazole, terbinafine, and tolnaftate (AII); apply daily x 4 wks | For unresponsive tinea lesions, use griseofulvin PO in dosages provided above; fluconazole PO, itraconazole PO; OR terbinafine PO<br>For tinea pedis: terbinafine PO or itraconazole PO are preferred over other oral agents<br>Keep skin as clean and dry as possible, particularly for tinea cruris and tinea pedis |
| – Tinea unguium (onychomycosis)[48,49] | Topical 8% ciclopirox nail lacquer solution applied daily X 6–12 mos (AII); OR itraconazole 5 mg/kg PO soln q24h (AII) | Recurrence or partial response common<br>Alternative: terbinafine PO 500 mg daily (adult dosage) for 1 wk per mo x 3 mos (hands) or 6–12 mos (toes) until new nail growth |
| – Tinea versicolor (also pityriasis versicolor) *(Malassezia furfur)*[48,50] | Apply topically: selenium sulfide 2.5% lotion or 1% shampoo daily, leave on 30 min, then rinse; x 7 d, then monthly x 6 mos (AIII); OR ciclopirox 1% cream x 4 wks (BII); OR terbinafine 1% solution (BII); OR ketoconazole 2% shampoo daily x 5 d (BII)<br>For small lesions, topical clotrimazole, econazole, haloprogin, ketoconazole, miconazole, or naftifine | For lesions that fail to clear with topical therapy, or for extensive lesions: fluconazole PO or itraconazole PO are equally effective<br>Recurrence common |

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| **Candidiasis** | | |
| – Benign oropharyngeal (thrush)[20] | Fluconazole 3–5 mg/kg/day PO once daily x 3-5 d (AII); OR topical nystatin suspension 1 mL (infants) or 2 mL (older children) each side of mouth, qid until lesions resolved plus 48 h (BII); OR clotrimazole oral troches (10 mg) 5x daily x 14 d (BII); 5–7 d | Itraconazole solution PO 5 mg/kg/day q24h swished in mouth and swallowed x 5–7 d |
| – Chronic mucocutaneous[17] | Fluconazole 3–5 mg/kg daily PO until lesions clear (AII) | Alternative: itraconazole 5 mg/kg PO solution q24h<br>Relapse common |
| – Cutaneous | Topical therapy (alphabetic): ciclopirox, clotrimazole, econazole, haloprogin, ketoconazole, miconazole, oxiconazole, sertaconazole, sulconazole | Fluconazole 3–5 mg/kg/day PO once daily x 5–7 d |
| – Esophageal[17] | (See Systemic Infections.) | |
| – Vulvovaginal[51,52] | Fluconazole 5 mg/kg (max 150 mg) PO single dose (AII) | Topical vaginal cream/tabs/suppositories (alphabetic order): butoconazole, clotrimazole, econazole, fenticonazole, miconazole, sertaconazole, terconazole, or tioconazole; x 3–7 d<br>Alternate systemic antifungals: itraconazole; ketoconazole<br>Avoid azoles during pregnancy. |

## 9. Preferred Therapy for Specific Viral Pathogens

*NOTE*

- *Abbreviations:* ACV, acyclovir; adamantanes, amantadine and rimantadine; bid, twice daily; CDC, Centers for Disease Control and Prevention; CMV, cytomegalovirus; EBV, Epstein-Barr virus; FDA, US Food and Drug Administration; G-CSF, granulocyte-colony stimulating factor; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; HSV, herpes simplex virus; IG, immune globulin; INF, interferon; NAI, neuraminadase inhibitors (oseltamivir, zanamivir, peramivir); NRTI, nucleoside analog reverse transcriptase inhibitor; qd, once daily; qid, 4 times daily; tid, 3 times daily; VZV, varicella-zoster virus.

| Infection | Therapy (evidence grade) | Comments |
|---|---|---|
| **Adenovirus** (pneumonia or disseminated infection in immune-compromised hosts)[1] | Cidofovir and ribavirin are active in vitro, but no prospective clinical data exist and cidofovir has significant toxicity; contact an infectious diseases specialist for current strategy | |
| **Cytomegalovirus** | | |
| – Neonatal[2] | See Chapter 5. | |
| – Immune-compromised (HIV, chemotherapy, transplant-related)[3–5] | For induction: ganciclovir 10 mg/kg/day IV div q12h x 14-21 d<br>For maintenance: 5 mg/kg IV q24h or 1 g PO tid (adults). Duration dependent on degree of immunosuppression (AII)<br>CMV hyperimmune globulin may decrease morbidity in some solid organ transplants (CIII) | Use foscarnet or cidofovir for ganciclovir-resistant strains; for HIV-positive children on HAART, CMV may resolve without therapy.<br>Also used for prevention of CMV disease post-transplant x 100–120 days<br>Limited data on oral valganciclovir in neonates[6] (30 mg/kg/day PO div bid) and children dosing by body surface area (BSA) (dose [mg] = 7 × BSA × creatinine clearance)[5] |
| – Prophylaxis of infection in immune-compromised hosts[4,7] | Ganciclovir 5 mg/kg IV daily (or 3 x/wk) (started at engraftment for stem cell transplant patients) (BII) | Neutropenia is a complication with GCV prophylaxis and may be addressed with G-CSF.<br>Both prophylaxis and preemptive strategies are effective; neither has been shown clearly superior to the other.[7] |
| **Epstein-Barr virus** | | |
| – Mononucleosis, encephalitis[8–10] | Limited data suggest clinical benefit of valacyclovir in adolescents for mononucleosis (3 g/day div tid x 14 d) (CIII)<br>For EBV encephalitis: ganciclovir IV OR acyclovir IV (AIII) | No prospective data on benefits of acyclovir IV or ganciclovir IV in EBV clinical infections of normal hosts |

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| – Post-transplant lymphoproliferative disorder (PTLD)[11,12] | Ganciclovir (AIII) | Decrease immune suppression if possible; rituximab, methotrexate<br>Preemptive treatment with GCV may decrease PTLD in solid organ transplants. |
| **Hepatitis B virus** (chronic)[13,14] | IFN-alpha x 24–48 wks; OR lamivudine 3 mg/kg/day (max 100 mg) PO q24h x 52 wks (AII); OR adefovir for children >12 yrs (adults 10 mg PO q24h) (BII) | For benign childhood chronic infection, consider no treatment. Follow to confirm benign disease.<br>IFN has many side effects: fever, flu-like syndrome, depression, neutropenia<br>Lamivudine approved for children 2 yrs and older, but antiviral resistance develops on therapy in 30% |
| **Hepatitis C virus** (chronic)[15] | IFN-alpha 3 million IU/m2/dose, 3 times per wk x 48 wks (peg-IFN products approved for adults), AND ribavirin 15 mg/kg/day PO q24h x 48 wk (AII) | Consider postponing treatment during childhood if liver biopsy is benign. See comments above regarding IFN. |
| **Herpes simplex virus**[16,17] | | |
| – Third trimester prophylaxis[18] | Acyclovir prophylaxis for pregnant women reduces HSV recurrences and viral shedding at the time of delivery; insufficient data exist to document prevention of neonatal HSV (BIII) | |
| – Neonatal[19] | See Chapter 5. | |
| – Mucocutaneous (normal host) | Acyclovir 60–80 mg/kg/day PO div tid–qid x 5–7 d; or 15 mg/kg/day IV as 1- to 2-h infusion div q8h (AII)<br>Prophylaxis for frequent recurrence (no pediatric data): 20 mg/kg/dose given bid or tid (up to 400 mg) x 6–12 mos; then reevaluate need (AIII) | Foscarnet for acyclovir-resistant strains<br>Valacyclovir and famciclovir suspensions under investigation for children<br>Immune-compromised hosts may require 10–14 days of therapy |
| – Genital | Adult doses: acyclovir 400 mg PO tid, x 7–10 d; OR valacyclovir 1 g PO bid x 10 d; OR famciclovir 250 mg PO tid x 7–10 d (AI) | All 3 drugs have been used as prophylaxis to prevent recurrence |
| – Encephalitis | Acyclovir 60 mg/kg/day IV as 1- to 2-h infusion div q8h; x 21 d (AIII) | Safety of high-dose acyclovir not well defined |
| – Keratoconjunctivitis | Trifluridine (ophthalmic); or idoxuridine (ophthalmic); vidarabine ophthalmic ointment discontinued in the US (AII) | Treat in consultation with an ophthalmologist<br>Topical steroids may be helpful when used together with antiviral agents. |

| Infection | Therapy (evidence grade) | Comments |
|---|---|---|
| **Human Herpesvirus 6 (HHV-6)** | | |
| – Immune-compromised children[20] | No prospective comparative data; ganciclovir 10–20 mg/kg/day IV div q12h case report (AIII) | May require high dose to control infection; safety and efficacy not defined at high doses |
| **Human immunodeficiency virus (HIV)** | | |
| Current information on HIV treatment for children[21] is posted at http://aidsinfo.nih.gov/guidelines/; other information on HIV programs is available at http://www.cdc.gov/hiv/pubs/guidelines.htm. Consult with HIV expert, if possible, for current recommendations. | | |
| – **Therapy of HIV infection** State-of-the-art therapy is rapidly evolving with introduction of new agents and combinations; currently there are 25 individual antiretroviral agents approved for use by the FDA, 14 of which have pediatric indications, as well as multiple combinations; guidelines for children and adolescents are continually updated on the AIDSINFO and CDC Web site given above. | Aggressive therapy (HAART) consists of ≥3 agents including 2 nucleoside reverse transcriptase inhibitors, plus a protease inhibitor or non-nucleoside reverse transcriptase inhibitor; many different combination regimens give similar treatment outcomes; choice of agents depends on the age of the child, viral load, and extent of immune depletion, in addition to judging the child's ability to adhere to the regimen. | Assess drug toxicity (based on the agents used) and virologic/immunologic response to therapy (quantitative plasma HIV and CD4 count) initially monthly and then every 3–6 mos during the plateau phase. |
| – First year of life[22] | HAART with ≥3 drugs are now recommended for all infants <12 months of life, regardless of clinical status or lab values (eg, zidovudine plus lamivudine plus lopinavir/ritonavir or nevirapine) (AI) | Adherence counseling and appropriate antiretroviral formulations are critical for successful implementation. |
| – 1 to <5 years of age<br>– Asymptomatic or mild symptoms and CD4 count ≥25% of total T cells and plasma HIV RNA <100,000 copies/mL | Defer therapy (BIII) | Many experts would defer therapy and monitor clinical course, CD4 count, and plasma HIV RNA on a 3- to 4-month basis. Therapy considered if HIV RNA >100,000 copies/mL. |

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| – CD4 count <25% or significant symptoms or AIDS | Begin ≥3 drug regimen (HAART) as above (BIII) | Any of these conditions support aggressive HAART therapy. |
| – ≥5 years | | |
| – Asymptomatic or mild symptoms and CD4 count ≥350 cells/mm$^3$ of total T cells and plasma HIV RNA <100,000 copies/mL | Defer therapy (BIII) | Many experts would defer therapy and monitor clinical course, CD4 count, and plasma HIV RNA on a 3- to 4-month basis. Therapy considered if HIV RNA >100,000 copies/mL. |
| – CD4 count <350 cells/mm$^3$ or significant symptoms or AIDS | Begin ≥3 drug regimen (HAART) (BIII) as above | Any of these conditions support aggressive HAART therapy. |
| – Antiretroviral-experienced child | Consult with HIV specialist | Consider past treatment history and drug resistance testing and assess adherence. |
| – **HIV exposures, non-occupational** | Therapy recommendations for exposures available on the CDC Web site given on page 88, based on assessment of risk of HIV exposure | Prophylaxis remains unproven; consider individually regarding risk, time from exposure, and likelihood of adherence; prophylactic regimens administered for 4 wks |
| Negligible exposure risk (urine, nasal secretions, saliva, sweat, or tears—no visible blood in secretions)<br>OR<br>>72 hours since exposure | Prophylaxis not recommended (BIII) | |
| Significant exposure risk (blood, semen, vaginal, or rectal secretions from a known HIV-infected individual)<br>AND<br><72 hours since exposure | Prophylaxis recommended (BIII): combivir (zidovudine/lamivudine) or truvada (tenofovir/emtricitabine) PLUS efavirenz or kaletra (lopinavir/ritonavir) | Preferred prophylactic regimens<br>– Based on treatment regimens for infected individuals<br>– 28-day regimen<br>In the event of poor adherence or toxicity, some experts consider 2 NRTI regimens such as combivir (zidovudine/lamivudine) or truvada (tenofovir/emtricitabine) (BIII) |

| Infection | Therapy (evidence grade) | Comments |
|---|---|---|
| – **HIV exposure, occupational** | See guidelines on CDC Web site given on page 88. | |
| **Influenza virus** | | |
| Frequent changes in recommendations have occurred recently regarding influenza due to antiviral resistance in seasonal influenza strains, and the rapid dissemination of pandemic influenza A H1N1; therefore, the reader should access the AAP Web site (www.aap.org) and the CDC Web site (www.flu.gov) for the most current, accurate information (September 2009). | | |
| **Influenza virus, Empiric therapy for 2009–2010** (strains expected to circulate: A:H1N1 seasonal (NOT the swine flu); A:H3N2; A:H1N1 swine flu; B) | Oseltamivir AND an adamantane; OR zanamivir for children >7 yrs (AIII)<br>Oseltamivir dosing: for children ≥1 yr: 4 mg/kg/day PO div bid x 5 d (AI); for infants 9 mos to 1 yr: 7 mg/kg/day div bid; for infants <9 mos: 6 mg/kg/day div bid (AIII); AND amantadine OR rimantidine 5 mg/kg/day PO div bid x 5d (AI)<br>Zanamivir dosing, by inhalation (for children >7 yrs): 10 mg bid x 5 d (AI) | If oseltamivir-R strains of H1N1 do not circulate in 2009–2010, then adamantanes will not be needed.<br>The sooner antiviral therapy can be started, the greater the impact on clinical course<br>Reactive airway disease a relative contraindication for inhaled zanamivir<br>Prophylaxis with oseltamivir/zanamivir: once daily dosing, for 10 days |
| **Influenza A H1N1 seasonal (not swine flu)** (This virus was oseltamivir-R, zanamivir-S, adamantane-S during the 2008–2009 season) | Amantadine OR rimantidine 5 mg/kg/day PO div bid x 5d (AI): OR zanamivir inhalation (for children >7 yrs) 10 mg bid x 5 d (AI) | Prophylaxis with zanamivir; prophylaxis with adamantanes rapidly leads to resistance |
| **Influenza A pandemic H1N1 (swine flu, or novel H1N1)** (oseltamivir-S, zanamivir-S, adamantane-R) | Oseltamivir (dosing: for children ≥1 yr: 4 mg/kg/day PO div bid x 5 d (AI); for infants 9 mos to 1 yr: 7 mg/kg/day div bid; for infants <9 mos : 6 mg/kg/day div bid (AIII); OR zanamivir inhalation (for children >7 yrs) 10 mg bid x 5 d (AI) | Prophylaxis: dosing once daily for 10 days rather than twice daily as for treatment<br>For obese children, not responding to oseltamivir treatment, consider a 2-fold increase in the oseltamivir dosage |
| **Influenza A H3N2 seasonal** (oseltamivir-S, zanamivir-S, adamantane-R) | Oseltamivir (dosing: for children ≥1 yr: 4 mg/kg/day PO div bid x 5 d (AI); for infants 9 mos to 1 yr: 7 mg/kg/day div bid; for infants <9 mos: 6 mg/kg/day div bid (AIII)); OR zanamivir inhalation (for children >7 yrs) 10 mg bid x 5 d (AI) | Prophylaxis: dosing once daily for 10 days rather than twice daily as for treatment |

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| **Influenza A avian H5N1 (bird flu)** (oseltamivir-S, zanamivir-S, adamantane-R) | Oseltamivir (AIII) (dosing: for children ≥1 yr: 4 mg/kg/day PO div bid x 5 d; for infants 9 mos to 1 yr: 7 mg/kg/day div bid; for infants <9 mos: 6 mg/kg/day div bid); OR zanamivir inhalation (for children >7 yrs) 10 mg bid x 5 d | Preliminary data in vitro and in animal models suggest susceptibility to oseltamivir of most strains, as of September 2009. However, the recommended dosage may be greater and duration of therapy may be longer compared with treatment of seasonal influenza strains. |
| **Influenza B seasonal** (oseltamivir-S, zanamivir-S, adamantane-R) | Oseltamivir (dosing: for children ≥1 yr: 4 mg/kg/day PO div bid x 5 d (AI); for infants 9 mos to 1 yr: 7 mg/kg/day div bid; for infants <9 mos: 6 mg/kg/day div bid (AIII); OR zanamivir inhalation (for children >7 yrs) 10 mg bid x 5 d (AI) | Prophylaxis: dosing once daily for 10 days rather than twice daily as for treatment |
| **Measles**[23] | No prospective data on antiviral therapy. Ribavirin is active against measles virus in vitro.<br>Vitamin A is beneficial to children who may be deficient (once daily dosing for 2 days): for children ≥1yr: 200,000 IU; for infants 6–12 mos: 100,000 IU; for infants <6 mos: 50,000 IU. (BII) | IG prophylaxis for exposed, susceptible children: 0.25 mL/kg IM; and for immune-compromised children: 0.5 mL/kg (max 15 mL) IM |

| Infection | Therapy (evidence grade) | Comments |
|---|---|---|
| **Respiratory syncytial virus (RSV)[24]** | | |
| – Therapy (severe disease in compromised host) | Ribavirin (6-g vial to make 20 mg/mL solution in sterile water), aerosolized over 18–20 h daily x 3–5 d (BII) | Aerosol ribavirin provides a small benefit and should only be used for life-threatening infection with RSV. Airway reactivity with inhalation precludes routine use. |
| – Palivizumab (Synagis®) prophylaxis for high-risk infants (AII) (For definition of high risk see comment) | Palivizumab (Synagis®, a monoclonal antibody) 15 mg/kg IM monthly. For all high-risk groups except premature infants with GA between 32 and 35 wks, a maximum of 5 doses should be provided during the RSV season, with the first dose given on November 1, and the last dose on March 1 (currently defined as the RSV season for most of the US). For infants with GA between 32 wks to <35 wks, a maximum of 3 doses should be provided during the RSV season. No infants should routinely receive a dose of palivizumab after the March 1 dose | Palivizumab will not treat an active infection.<br>In Florida, the RSV season lasts 5 months, but starts earlier that the rest of the US.[24]<br>1. Infants <24 mos with chronic lung disease who are receiving or have received medical therapy (oxygen, bronchodilator, diuretic, or corticosteroid therapy) within 6 months before start of the RSV season (since May 1st)<br>2. Infants <24 mos with hemodynamically significant congenital heart disease (congestive heart failure requiring therapy, moderate to severe pulmonary hypertension, cyanotic heart disease)<br>3. Infants with congenital abnormalities of the airway or a neuromuscular disorder, who will be <12 mos on November 1<br>4. Extremely premature infants: gestational age (GA) <28 wks, and chronologic age (CA) <12 mos on November 1<br>5. Very premature infants: GA 29 to <32 wks (31 wks 6 d), and CA <6 mos on November 1<br>6. Premature infants: GA between 32 wks (32 wks 0 d) to <35 wks (34 wks 6 d), and CA <3 mos on November 1, AND 1 of 2 additional risk factors should be present to receive palivizumab: daycare attendance; or a sibling <5 years of age |

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| **Varicella-zoster virus**[16] | | |
| – Infection in a normal host | Acyclovir 80 mg/kg/day (max 3.2 g/day) PO div qid x 5 d (AI) | The sooner antiviral therapy can be started, the greater the impact. |
| – Severe primary chickenpox, disseminated infection (cutaneous, pneumonia, encephalitis, hepatitis); immune-compromised host with primary chickenpox or disseminated zoster | Acyclovir 30 mg/kg/day IV as 1- to 2-h infusion div q8h; x 10 d (acyclovir doses as high as 60 mg/kg/day IV should be used for disseminated or central nervous system infection). Dosing can also be provided as: 1,500 mg/m2/day IV div q8h. Duration in immune compromised children: 7 to 14 d, based on clinical response. (AI) | Valacyclovir, famciclovir, foscarnet also active |
| **West Nile virus**[25,26] | No treatment regimen prospectively evaluated. Investigational therapy exists (West Nile virus IG, antivirals, INF). | |

## 10. Preferred Therapy for Specific Parasitic Pathogens

*NOTES*

- For some parasitic diseases, therapy may be available only from the CDC, as noted. Consultation is available from the CDC for diagnostic parasitic testing and experimental therapy at 404/639-3670 and for malaria at 770/488-7788 (or 7100). Antiparasitic drugs available from the CDC can be viewed and requested at http://www.cdc.gov/ncidod/srp/drugs/formulary.html.
- *Abbreviations:* bid, twice daily; CNS, central nervous system; CDC, Centers for Disease Control and Prevention; DEC, diethylcarbamazine; div, divided; FDA, US Food and Drug Administration; GI, gastrointestinal; G6PD, glucose-6-phosphate dehydrogenase; HAART, highly active antiretroviral therapy; IV, intravenous; PO, orally; qd, once daily; qid, 4 times daily; tid, 3 times daily; TMP/SMX, trimethoprim/sulfamethoxazole.

| Disease/Organism | Treatment | Comments |
|---|---|---|
| **AMEBIASIS**[1–4] | | |
| **ENTERITIS/LIVER ABSCESS** | | |
| *Entamoeba histolytica* | | |
| – Asymptomatic carrier | Paromomycin 30 mg/kg/day PO div tid x 7 d; OR iodoquinol 30–40 mg/kg/day (max 2 g) PO div tid x 20 d; OR diloxanide furoate (not commercially available in the US) 20 mg/kg/day PO div tid x 10 d (CII) | Follow-up stool examination to ensure eradication of carriage; screen/treat positive close contacts |
| – Mild to moderate colitis | Metronidazole 30–40 mg/kg/day PO div tid x 10 d; OR tinidazole 50 mg/kg/day PO (max 2 g) qd x 3 d FOLLOWED by paromomycin or iodoquinol as above to eliminate cysts (BII) | Avoid antimotility drugs, steroids.<br>Nitazoxanide (see GIARDIASIS) may also be effective. |
| – Severe colitis, liver abscess | Metronidazole 35–40 mg/kg/day IV q8h, switch to PO when tolerated, x 10 d; OR tinidazole 50 mg/kg/day PO (max 2 g) qd x 3–5 d FOLLOWED by paromomycin or iodoquinol as above to eliminate cysts (BII) | Serologic assays >95% positive in extraintestinal amebiasis<br>Percutaneous or surgical drainage may be indicated for large liver abscesses or if response to medical therapy inadequate.<br>Chloroquine plus metronidazole or tinidazole followed by luminal agent considered alternative for liver abscess |

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| **MENINGOENCEPHALITIS**[5–9] | | |
| *Naegleria, Acanthamoeba, Balamuthia, Hartmanella* spp | Amphotericin B 1 mg/kg/day IV qd x 3–4 wks or longer, PLUS azithromycin for *Naegleria*<br>Intrathecal miconazole (10 mg) daily may be helpful (IV no longer available in US)<br>*Acanthamoeba* may be susceptible in vitro to ketoconazole, flucytosine, and pentamidine; *Balamuthia* may be susceptible in vitro to pentamidine, azithromycin/clarithromycin, fluconazole, sulfadiazine, and flucytosine (CIII) | Treatment outcomes usually unsuccessful; early therapy (even before diagnostic confirmation if indicated) may improve survival<br>Voriconazole and miltefosine active against *Acanthamoeba* (alone or in combination with pentamadine)<br>Surgical resection of CNS lesions may be beneficial.<br>Keratitis should be evaluated by an ophthalmologist. |
| *Ancylostoma caninum* | See EOSINOPHILIC COLITIS. | |
| *Ancylostoma duodenale* | See HOOKWORM. | |
| **ANGIOSTRONGYLIASIS**[10,11] | | |
| *Angiostrongylus cantonensis*[3,11] | Mebendazole 100 mg PO bid x 5 d OR albendazole 20 mg/kg/day PO div bid x 9 d (CIII) | Most patients recover without antiparasitic therapy; treatment may provoke severe neurologic symptoms.<br>Corticosteroids, analgesics, and repeat lumbar puncture may be of benefit. |
| *Angiostrongylus costaricensis* | Mebendazole 200–400 mg PO tid x 10 d; OR thiabendazole 50–75 mg/kg/day (max 3 g) PO div tid x 3 d (CII) | |
| **ASCARIASIS**[3,12]<br>*(Ascaris lumbricoides)* | Albendazole 400 mg PO once (BII); OR mebendazole 100 mg PO bid x 3 d (alternative, 500 mg once) (BII); OR ivermectin 150–200 µcg/kg PO once (CII) | Follow-up stool ova and parasite exam after therapy not essential |
| **BABESIOSIS**<br>*(Babesia* spp)[13,14] | Clindamycin 30 mg/kg/day PO div tid, PLUS quinine 25 mg/kg/day PO div tid x 7 d (BII); OR atovaquone 40 mg/kg/day div bid, PLUS azithromycin 12 mg/kg/day x 7 d (CII) | Exchange blood transfusion may be of benefit for severe disease |
| ***Balantidium coli***[15] | Tetracycline (patient >7 yrs) 40 mg/kg/day PO div qid x 10 d (max 2 g/day) (BII); OR metronidazole 35–50 mg/kg/day PO div tid x 5 d; OR iodoquinol 40 mg/kg/day (max 2 g/day) PO div tid x 20 d (CII) | Repeated stool examination may be needed for diagnosis; prompt stool examination may increase detection of rapidly degenerating trophozoites. |

| Disease/Organism | Treatment | Comments |
|---|---|---|
| ***Baylisascaris procyonis***[16,17] (raccoon roundworm) | For CNS infection: albendazole 25–40 mg/kg/day PO div q12h AND high-dose corticosteroid therapy (CIII) | Therapy generally unsuccessful to prevent fatal outcome or severe neurologic sequelae once CNS disease present<br>Retinal worms may be killed by direct photocoagulation.<br>Consider prophylactic albendazole for children who may have ingested soil contaminated with raccoon feces. |
| ***Blastocystis hominis***[18,19] | Metronidazole 30 mg/kg/day PO div tid x 10 d; OR iodoquinol 40 mg/kg/day (max 2 g) PO div tid x 20 d; OR nitazoxanide (as for *Cryptosporidium*) (CII) | Normal hosts may not need therapy; reexamination of stool for other parasites (eg, *Giardia*) may be of value<br>Metronidazole resistance may occur. |
| **CHAGAS DISEASE**[20,21] *(Trypanosoma cruzi)* | See TRYPANOSOMIASIS. | |
| ***Clonorchis sinensis*** | See FLUKES. | |
| **CRYPTOSPORIDIOSIS**[22–25] *(Cryptosporidium parvum)* | Nitazoxanide, age 12–47 months, 5 mL (100 mg) bid x 3 d; age 4–11 years, 10 mL (200 mg) bid x 3 d (BII); OR paromomycin 30 mg/kg/day div bid–qid (CII); OR azithromycin 10 mg/kg/day x 5 d (CII); repeated treatment courses may be needed | Disease may be self-limited in normal hosts.<br>In HIV-infected patients not receiving HAART, medical therapy may have limited efficacy. |
| **CUTANEOUS LARVA MIGRANS or CREEPING ERUPTION**[26–28] (Dog and cat hookworm) *Ancylostoma caninum, Ancylostoma braziliense, Uncinaria stenocephala* | Albendazole 15 mg/kg/day PO qd x 3 d (BII); OR ivermectin 200 µg/kg PO x 1 (BII) | |
| ***Cyclospora spp***[29,30] (Cyanobacterium-like agent) | TMP/SMX (10 mg TMP/kg/day) PO div bid x 5–10 d (BIII) | HIV-infected patients may require higher doses/longer therapy. |

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| **CYSTICERCOSIS**[31,32]<br>*(Cysticercus cellulosae)* | Albendazole 15 mg/kg/day PO div bid (max 800 mg/day) x 8–30 d (CII); OR praziquantel 50–100 mg/kg/day PO div tid x 15–30 d (phenytoin decreases praziquantel conc) (CII)<br>For CNS disease with multiple lesions, give steroids and anticonvulsants before first dose; for CNS disease with few lesions, steroid pretreatment not required<br>Contraindicated for eye or spinal cord lesions (surgery as indicated) | Treatment controversial, especially for single lesion disease[32,33] |
| **DIENTAMEBIASIS**[34,35]<br>*(Dientamoeba fragilis)* | Paromomycin 25 mg/kg/day PO div tid x 7 d; OR tetracycline (patients >7 yrs) 40 mg/kg/day PO div qid x 7–10 d; OR iodoquinol 40 mg/kg/day (max 2 g) PO div tid x 20 d; OR metronidazole 30 mg/kg/day PO div tid x 10 d (BII) | Asymptomatic colonization more common in adults than children |
| ***Diphyllobothrium latum*** | See TAPEWORMS. | |
| **ECHINOCOCCOSIS** | | |
| *Echinococcus granulosus, Echinococcus multilocularis*[36,37] | Albendazole 15 mg/kg/day PO div bid (max 800 mg/day) x 3–6 mos alone (CIII), or combined with praziquantel 50–75 mg/kg/day daily (BII) for 5–14 d ± once weekly dose for additional 3–6 months | Surgical excision may be the only reliable therapy; ultrasound-guided percutaneous aspiration-injection-reaspiration plus albendazole may be effective for hepatic hydatid cysts. |
| ***Entamoeba histolytica*** | See AMEBIASIS. | |
| ***Enterobius vermicularis*** | See PINWORMS. | |
| ***Fasciola hepatica*** | See FLUKES. | |
| **EOSINOPHILIC COLITIS**[38]<br>*(Ancylostoma caninum)* | Mebendazole 100 mg PO bid x 3 d; OR albendazole 15 mg/kg/day PO div bid (max 400 mg/day); OR pyrantel pamoate 11 mg/kg/day (max 1 g/day) x 3 d (BIII) | Endoscopic removal may also be of benefit especially if medical treatment not successful. |
| **EOSINOPHILIC MENINGITIS** | See ANGIOSTRONGYLIASIS. | |

| Disease/Organism | Treatment | Comments |
|---|---|---|
| **FILARIASIS**[39] | | Ivermectin may be effective for killing *Wuchereria, Brugia,* and *loa loa microfilariae;* in heavy infections or when coinfection with *O volvulus* possible, consider ivermectin initially to reduce microfilaremia before giving DEC (decreased risk of encephalopathy or severe allergic or febrile reaction) |
| – River blindness *(Onchocerca volvulus)* | Ivermectin 150 µg/kg PO x 1 (AII); repeat q6–12 mos until asymptomatic and no chronic, ongoing exposure | Antihistamines or corticosteroids are of major benefit for allergic reactions. |
| – *Wuchereria bancrofti, Brugia malayi, Mansonella streptocerca* | *W bancrofti, B malayi, M streptocerca:* DEC (from CDC) 1 mg/kg PO after food on day 1; then 3 mg/kg/day div tid on day 2; then 3–6 mg/kg/day div tid on day 3; then 6 mg/kg/day div tid on days 4–14 (AII) | |
| *Mansonella ozzardi* | Ivermectin 150 µg/kg PO once may be effective | |
| *Mansonella perstans* | Albendazole 400 mg PO bid x 10 d; mebendazole 100 mg PO bid x 30 d | |
| *Loa loa* | DEC (from CDC) as above, then 9 mg/kg/day div tid on days 14–21 (AII) | |
| Tropical pulmonary eosinophilia[40] | DEC (from CDC) 6 mg/kg/day PO div tid x 14 d; antihistamines/corticosteroids for allergic reactions (CII) | |
| **FLUKES** | | |
| Chinese liver fluke *(Clonorchis sinensis)* and others *(Fasciolopsis, Heterophyes, Metagonimus, Metorchis, Nanophyetus, Opisthorchis)*[41,42] | Praziquantel 75 mg/kg PO div tid x 1 d (BII); OR albendazole 10 mg/kg/day PO qd x 7 d (CIII) | |
| Lung fluke *(Paragonimus westermani)*[43] | Praziquantel 75 mg/kg PO div tid x 2 d (BII) | Triclabendazole (5 mg/kg once daily x 3 d or 10 mg/kg bid x 1 d) may also be effective.[41] |

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| Sheep liver fluke<br>*(Fasciola hepatica)*[41] | Bithionol (from CDC) 30–50 mg/kg PO div qid on alternate days x 10–15 doses (BII) OR triclabendazole (from CDC) 10 mg/kg PO once (CII); OR nitazoxanide PO (take with food), age 12–47 mos 100 mg/dose bid x 7 d; age 4–11 yrs, 200 mg/dose bid x 7 d; age ≥12 yrs, 1 tab (500 mg)/dose bid x 7 d (CII) | |
| **GIARDIASIS**[44,45]<br>*(Giardia lamblia)* | Metronidazole 30–40 mg/kg/day PO div tid x 7–10 d (BII); OR nitazoxanide PO (take with food), age 12–47 mos 100 mg/dose bid x 7 d; age 4–11 yrs, 200 mg/dose bid x 7 d; age ≥12 yrs, 1 tab (500 mg)/dose bid x 7 d (BII); OR tinidazole 50 mg/kg/day (max 2 g) x 1 d (BII);<br>Alternatives: quinacrine 2 mg/kg/day in 3 doses x 5 d (max 300 mg/d); OR furazolidone 6 mg/kg/d In 4 doses x 7–10 d; OR paromomycin 30 mg/kg/day div tid x 5–10 d; OR albendazole 10 mg/kg/d PO x 5 d (CII) | If therapy inadequate, another course of the same agent usually curative<br>Prolonged courses may be needed in immunocompromise (eg, hypogammaglobulinema)<br>Treatment of asymptomatic carriers not usually recommended |
| **HOOKWORM**[46]<br>*Necator americanus, Ancylostoma duodenale* | Albendazole 10 mg/kg (max 400 mg) x 1 (repeat dose may be necessary) (BII); OR mebendazole 100 mg PO bid x 3 d (alternative, 500 mg x 1) (BII); OR pyrantel pamoate 11 mg/kg (max 1 g/day) (BII) PO qd x 3 d | Perform repeat stool examination 2 weeks after treatment, re-treat if positive |
| ***Hymenolepis nana*** | See TAPEWORMS. | |
| **ISOSPORIASIS**[47]<br>*(Isospora belli)* | TMP/SMX (10 mg TMP/kg/day) PO div qid x 10 d; then 5 mg TMP/kg/day PO div bid x 3 wks; pyrimethamine may be effective (CII)<br>HIV-infected children may need longer courses of therapy (consider long-term maintenance therapy for multiple relapses) | Infection often self-limited in immunocompetent hosts<br>Repeated stool examinations and special techniques (eg, modified acid-fast bacteria staining or UV microscopy) may be needed to detect low oocyst numbers. |

| Disease/Organism | Treatment | Comments |
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| **LEISHMANIASIS**[48–52] including kala azar | | |
| *Leishmania* spp | Visceral: Liposomal amphotericin B, 3 mg/kg/day on days 1–5, day 14, and day 21 (BII); OR sodium stibogluconate (from CDC) 20 mg/kg/day IM, IV x 20-28 d (or longer) (BIII); OR miltefosine 2.5 mg/kg/day PO (max 150 mg/day) x 28 d (BII); OR amphotericin B 1 mg/kg/day IV daily x 15–20 d or every second day x 4–8 wks (BIII) ; OR paromomycin 15 mg/kg/day IM x 21 d (BII)<br>Cutaneous: Sodium stibogluconate 20 mg/kg/day IM, IV x 20 d (BIII); OR miltefosine (as above) (BII); OR pentamidine isethionate 2–4 mg/kg/day IM daily or every second day x 14 d (BII)<br>Mucosal: Sodium stibogluconate 20 mg/kg/day IM, IV x 28 d; OR amphotericin B 0.5–1 mg/kg/day IV daily x 15–20 d or every second day x 4–8 wks; OR miltefosine (as above) | Consult with tropical medicine specialist if unfamiliar with leishmaniasis.<br>Patients infected in south Asia (especially India, Nepal) should receive an amphotericin regimen because of high rates of antimonial resistance.<br>Azoles (eg, fluconazole, ketoconazole) may be effective for cutaneous disease but should be avoided in treating mucosal or visceral disease. |
| **LICE**[53,54] | | |
| *Pediculus capitis* or *humanus*, *Phthirus pubis* | Follow manufacturer's instructions for topical use: permethrin 1% (BII); OR malathion 0.5% (BIII); OR pyrethrins; OR lindane; for topical therapies repeat in 1 wk; OR ivermectin 200 µg/kg PO x 1<br>Launder bedding and clothing; for eyelash infestation, use petrolatum; for head lice, remove nits with comb designed for that purpose | Administration of 3 doses of ivermectin (1dose/wk separately by weekly intervals) may be needed to eradicate infection. |

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| **MALARIA**[55–59] | | |
| *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae* | CDC Physician's Malaria Hotline 770/488-7788 (or 7100); online information at http://www.cdc.gov/malaria/diagnosis_treatment/index.htm for malaria diagnosis and treatment; consult tropical medicine specialist if unfamiliar with malaria | No antimalarial drug provides absolute protection against malaria; fever after return from an endemic area should prompt an immediate evaluation.<br>Emphasize personal protective measures (insecticides, bed nets, clothing, avoidance of dusk-dawn mosquito exposures). |
| **Prophylaxis** | | |
| For areas with chloroquine-resistant *P falciparum* or *P vivax* | Atovaquone-proguanil (A-P): 11–20 kg, 1 pediatric tab (62.5 mg atovaquone/25 mg proguanil); 21–30 kg, 2 pediatric tabs; 31–40 kg, 3 pediatric tabs; >40 kg, 1 adult tab (250 mg atovaquone/100 mg proguanil) PO daily starting 1–2 d before travel and continuing 7 d after last exposure; for children <10 kg, data on A-P are limited (BII); OR mefloquine (MFQ): for children <5 kg, 5 mg/kg; 5–9 kg, 1/8 tab; 10–19 kg, 1/4 tab; 20–30 kg, 1/2 tab; 31–45 kg, 3/4 tab; >45 kg (adult dose) 1 tab PO once weekly starting 1 wk before arrival in area and continuing for 4 wks after leaving area (BII); OR doxycycline (patients >7 yrs): 2 mg/kg (max 100 mg) PO daily starting 1–2 d before arrival in area and continuing for 4 wks after leaving area (BIII); OR primaquine (check for G6PD deficiency before administering): 0.5 mg/kg base daily starting 1–2 d before travel and continuing for 2 d after last exposure (BII) | Avoid mefloquine for persons with a history of seizures or psychosis, active depression, or cardiac conduction abnormalities<br>*P falciparum* resistance to mefloquine exists along the borders between Thailand and Myanmar and Thailand and Cambodia, Myanmar and China, and Myanmar and Laos; isolated resistance has been reported in southern Vietnam.<br>Take doxycycline with adequate fluids to avoid esophageal irritation and food to avoid GI side effects; use sunscreen and avoid excessive sun exposure. |
| – For areas without chloroquine-resistant *P falciparum* or *P vivax* | Chloroquine phosphate 5 mg base/kg (max 300 mg base) PO once weekly, beginning 1 wk before arrival in area and continuing for 4 wks after leaving area (available in suspension outside the US and Canada) (AII)<br>For heavy or prolonged (months) exposure to mosquitoes: treat with primaquine (check for G6PD deficiency before administering) 0.3–0.6 mg base/kg PO qd with final 2 wks of chloroquine for prevention of relapse with *P ovale* or *P vivax* | |

| Disease/Organism | Treatment | Comments |
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| **MALARIA**[55–59] | | |
| **Treatment of disease** | | Consider exchange blood transfusion for >10% parasitemia, altered mental status, pulmonary edema, or renal failure. |
| – Chloroquine-resistant *P falciparum* or *P vivax* | *Oral therapy:* Atovaquone-proguanil: for children <5 kg,data limited; 5–8 kg, 2 pediatric tabs (62.5 mg atovaquone/25 mg proguanil) PO qd x 3 d; 9–10 kg, 3 pediatric tabs qd x 3 d; 11–20 kg, 1 adult tab (250 mg atovaquone/100 mg proguanil) qd x 3 d; 21–30 kg, 2 adult tabs qd x 3 d; 31–40 kg, 3 adult tabs qd x 3 d; >40 kg, 4 adult tabs qd x 3 d<br>OR quinine 25 mg/kg/day (max 2 g/day) PO div tid x 3–7 d AND doxycycline (patients >7 yrs) 2 mg/kg/day x 7 d, or pyrimethamine-sulfadoxine: <1 yr, 1/4 tab; 1–3 yrs, 1/2 tab; 4–8 yrs, 1 tab; 9–14 yrs, 2 tab; >14 yrs, 3 tabs as a single dose on last day of quinine; or clindamycin 30 mg/kg/day div tid (max 900 mg tid) x 5 d;<br>OR artemether/lumefantrine 6 doses over 3 days at 0, 8, 24, 36, 48, and 60 hours; <15 kg, 1 tab/dose; 15–25 kg, 2 tabs/dose; 25–35 kg, 3 tabs/dose; >35 kg, 4 tabs/dose (not available in US) (BII)<br>*Parenteral therapy* (check with CDC): quinidine 10 mg/kg (max 600 mg) IV (1 h infusion in normal saline) followed by continuous infusion of 0.02 mg/kg/min until oral therapy can be given (after 48-h therapy, decrease dose by 1/3 to 1/2); (BII) alternative: artesunate 2.4 mg/kg/dose IV x 3 d at 0, 12, 24, 48, and 72 h (from CDC) (B1)<br>For prevention of relapse with *P vivax, P ovale:* Primaquine (check for G6PD deficiency before administering) 0.3–0.6 mg base/kg/day PO x 14 d | Mild disease may be treated with oral antimalarial drugs; severe disease (impaired level of consciousness, convulsion, hypotension, or parasitemia >5%) should be treated parenterally.<br>Avoid mefloquine for treatment of malaria if possible given higher dose and increased incidence of adverse events.<br>Continuously monitor electrocardiogram, blood pressure, and glucose in patients receiving quinidine.<br>Use artesunate for when quinidine intolerance, treatment failure, or lack of availability; www.cdc.gov/malaria/features/artesunate_now_available.htm; artemesinins should be used in combination with other drugs to avoid resistance |

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| – Chloroquine-susceptible *P falciparum, chloroquine-susceptible P vivax, P ovale, P malariae* | Oral therapy: Chloroquine 10 mg/kg base (max 600 mg base) PO then 5 mg/kg 6 h, 24 h, and 48 h after initial dose<br>*Parenteral therapy:* Quinidine, as above<br>See above for prevention of relapse due to *P vivax* and *P ovale* | |
| ***Paragonimus westermani*** | See FLUKES. | |
| **PINWORMS**[60] | | |
| *(Enterobius vermicularis)* | Mebendazole 100 mg PO x 1 (BII); OR albendazole 10 mg/kg (max 400 mg) PO x 1 (BII); OR pyrantel pamoate 11 mg/kg (max 1 g) PO x 1 (BII); repeat treatment in 2 wks | Treatment of entire household (and if this fails, consider close child care/school contacts) often recommended to prevent reinfection |
| ***PNEUMOCYSTIS* PNEUMONIA**[61,62] | | |
| *Pneumocystis jiroveci* (previously *Pneumocystis carinii*) | Serious disease: TMP/SMX 15–20 mg TMP/kg/day IV div q8h x 2 wks (AII); OR pentamidine isethionate 4 mg base/kg/day IV daily x 2 wks (BII).<br>Mild-moderate disease: TMP/SMX 20 mg TMP/kg/day PO div qid x 2 wks; OR TMP 5 mg/kg PO tid x 21 d AND dapsone 2 mg/kg/day PO x 21 d (BII); OR primaquine 0.3 mg/kg base PO daily x 21 d AND clindamycin 15-25 mg/kg IV q 6 h x 21 d or 10 mg/kg/dose PO q 6 h x 21 d (CII); OR atovaquone ages 1–3 months, 30 mg/kg/day PO x 21 d; 4–24 months, 45 mg/kg/day PO x 21 d; >24 months, 30 mg/kg/day PO x 21 d (CII) | Use concurrent steroids for severe disease. |
| **SCABIES**[63,64] | | |
| *(Sarcoptes scabei)* | Permethrin 5% cream applied to entire body (including scalp in infants), left on for 8–14 h then bathe (BII); OR lindane lotion applied to body below neck, leave on overnight, bathe in am (BII); OR ivermectin 200 µg/kg PO, 1 dose (BII) | Launder bedding and clothing.<br>Reserve lindane for patients who do not respond to other therapy.<br>Treatment may need to be repeated in 10–14 days. |

| Disease/Organism | Treatment | Comments |
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| **SCHISTOSOMIASIS**[65–67] | | |
| *Schistosoma haematobium, Schistosoma japonicum, Schistosoma mansoni, Schistosoma mekongi, Schistosoma intercalatum* | Praziquantel 40 (for *S haematobium* and *S mansoni)* or 60 (for *S japonicum* and *S mekongi)* mg/kg/day PO div bid–tid x 1 d (AI); OR oxamniquine (not commercially available in the US) 15 mg/kg PO once (West Africa, Brazil), or 40–60 mg/kg/day x 2–3 d (most of Africa) for praziquantel-resistant *S mansoni* infections (BII) | Take praziquantel with food and liquids. |
| **STRONGYLOIDIASIS**[68–70] | | |
| *(Strongyloides stercoralis)* | Ivermectin 200 µg/kg PO qd x 1–2 d (BI); OR thiabendazole 50 mg/kg/day (max 3 g/day) PO div bid x 2 d (5 d or longer for disseminated disease) (BII) | Albendazole is less effective but may be adequate if longer courses used. |
| **TAPEWORMS** | | |
| – *Cysticercus cellulosae* | See CYSTICERCOSIS. | |
| – *Echinococcus granulosus* | See ECHINOCOCCOSIS. | |
| – *Taenia saginata, T solium,*[71] *Hymenolepis nana, Diphyllobothrium latum, Dipylidium caninum*[72] | Praziquantel 5–10 mg/kg PO x 1 (25 mg/kg once for *H nana*) (BII); OR niclosamide tablet 50 mg/kg PO x 1, chewed thoroughly (all but *H nana*) | |
| **TOXOPLASMOSIS** | | |
| *(Toxoplasma gondii)*[73–75] | Pyrimethamine 2 mg/kg/day PO div bid x 3 d (max 100 mg) then 1 mg/kg/day (max 25 mg) PO qd AND sulfadiazine 120 mg/kg/day PO div qid (max 6 g/day); with supplemental folinic acid and leucovorin 10–25 mg with each dose of pyrimethamine (AI)<br>See Chapter 5 for congenital infection<br>For treatment in pregnancy, spiramycin 50–100 mg/kg/day PO div qid (available as investigational therapy through the FDA at 301/827-2335) (CII) | Treatment continued for 2 wks after resolution of illness; concurrent corticosteroids given for ocular or CNS infection. Prolonged therapy if HIV positive.<br>Take pyrimethamine with food to decrease GI adverse effects; sulfadiazine should be taken on an empty stomach with adequate liquids.<br>Atovaquone plus pyrimethamine may be effective for patients intolerant of sulfa-containing drugs. |

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| **TRAVELER'S DIARRHEA**[76–78] | Azithromycin 10 mg/kg once daily x 3–5 d (BII); OR rifaximin 200 mg PO tid x 3 d (ages ≥12 years) (BIII); OR ciprofloxacin (BII); OR cefixime (CII) | Azithromycin preferable to ciprofloxacin for travelers to Southeast Asia given high prevalence of quinolone-resistant *Campylobacter;* rifaximin may not be as efficacious for *Shigella* and other enterics in patients with dysentery |
| **TRICHINELLOSIS**[79] *(Trichinella spiralis)* | Mebendazole 200–400 mg PO tid x 3 d, then 400–500 mg tid x 10 d (BII); OR albendazole 20 mg/kg/day (max 400 mg/dose) PO div bid x 8–14 d (BII) | Neither drug effective for larvae already in muscles<br>Anti-inflammatory drugs, steroids for CNS or cardiac involvement or severe symptoms |
| **TRICHOMONIASIS**[80] *(Trichomonas vaginalis)* | Metronidazole 40 mg/kg (max 2 g) PO x 1 dose, or metronidazole 500 mg PO bid x 7 d (AII); OR tinidazole 50 mg/kg (max 2 g) PO x 1 dose (BII) | Treat sex partners simultaneously.<br>Metronidazole resistance occurs and may be treated with higher-dose metronidazole or tinidazole. |
| ***Trichuris trichiura*** | See WHIPWORM. | |
| **TRYPANOSOMIASIS** | | |
| – **CHAGAS DISEASE**[20,21] *(Trypanosoma cruzi)* | Nifurtimox PO (from CDC): children 1–10 yrs, 15-20 mg/kg/day div qid x 90–120 d; 11–16 yrs, 12.5–15 mg/kg/day div qid x 90–120 d; 17 yrs and older: 8–10 mg/kg/day div tid–qid x 90-120 d (BIII); OR benznidazole PO (not commercially available in the US): children <12 yrs, 10 mg/kg/day div bid x 30–90 d; 12 yrs and older: 5–7 mg/kg/day div bid x 30–90 d (BIII) | Therapy recommended for acute and congenital infection, reactivated infection, and chronic Infection in children aged <18 years.<br>Take benznidazole with meals to avoid GI adverse effects<br>Interferon-γ in addition to nifurtimox may shorten acute disease duration.[81] |

| Disease/Organism | Treatment | Comments |
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| **SLEEPING SICKNESS[82–84]** | | |
| *Trypanosoma brucei gambiense* (West African)<br>*Trypanosoma brucei rhodesiense* (East African)<br>– Acute (hemolymphatic) stage | *T brucei gambiense:* Pentamidine isethionate 4 mg/kg/day (max 300 mg) IM x 7 d (BII); *T brucei rhodesiense:* suramin (from CDC) 20 mg/kg (max 1.5 g) IV on days 1, 3, 7, 14, and 21 (BIII) | Consult with tropical medicine specialist if unfamiliar with trypanosomiasis.<br>Examination of the buffy coat of peripheral blood may be helpful.<br>*T brucei gambiense* may be found in lymph node aspirates |
| – Late (CNS) stage | *T brucei gambiense:* Eflornithine (not available commercially in the US) 400 mg/kg/day IV div q6h x 14 d (BIII); OR melarsoprol (from CDC) 2.2 mg/day (max 180 mg) IV x 10 d (BIII); *T brucei rhodesiense:* melarsoprol, 2–3.6 mg/kg/day IV x 3 d; after 7 d, 3.6 mg/kg/day IV x 3 d; repeat again after 7 days; (max 180 mg); corticosteroids given with melarsoprol to decrease risk of CNS toxicity | CSF examination needed for management (double-centrifuge technique recommended); perform repeat CSF examinations every 6 months for 2 years to detect relapse. |
| **VISCERAL LARVA MIGRANS (TOXOCARIASIS)[3]** | | |
| *Toxocara canis; Toxocara cati* | Albendazole 15 mg/kg/day PO bid x 3–5 d (BII), OR DEC (from CDC) 6 mg/kg/day PO div tid x 7–10 d; OR mebendazole 100–200 mg PO bid x 5 d | Some experts advocate longer therapy (eg, 20 days).<br>Corticosteroids if severe or ocular involvement |
| **WHIPWORM (TRICHURIASIS)[85]** | | |
| *Trichuris trichiura* | Mebendazole 100 mg PO bid x 3 d or 500 mg once (BII); OR albendazole 400 mg PO x 3 d; OR ivermectin 200 µcg/kg/day PO daily x 3 d (BII) | Stool reexamination after treatment usually not necessary. |
| ***Wuchereria bancrofti*** | See FILARIASIS. | |

## 11. Alphabetic Listing of Antimicrobials

### A. Systemic Antimicrobials With Dosage Forms and Usual Dosages

*NOTES*

- Higher dosages in a dose range are generally indicated for more serious illnesses.
- For most antimicrobials, a maximum dosage is provided, based on FDA reviewed and approved clinical data. However, data may be published on higher dosages than originally approved by the FDA, particularly for generic drugs (eg, the oral dosages used to treat bone and joint infections), and whenever possible, these dosages are also provided.
- For obesity, no single accurate adjustment for dosing can be made for all drug classes and tissue sites, and most published data result from single patient reports, or a study of a small group.[1] As a rough guide, to achieve serum concentrations that are achieved in patients of normal body weight

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| Aminoglycosides | Start with standard mg/kg dose based on ideal body weight, then use a 40% correction factor for additional kg of weight above IBW |
| Vancomycin | Mg/kg dose based on total body weight, but may need to dose more frequently, as clearance is increased in obesity |
| Beta-lactams | Mg/kg dose based on total body weight, as drugs generally distribute in all tissues and clearance is increased (variability noted among beta-lactams) |
| Fluoroquinolones | As with aminoglycosides, increase dose based on a 40%–45% correction factor for additional kg of weight above standard mg/kg dosing for IBW |
| Linezolid | Use no more than the adult maximum dose (600 mg), although some studies showed a decrease in drug exposure in obese subjects |

In some situations, the benefits for treatment of a particular infection with a particular drug are greater than the potential for unknown risks at that higher dosage.

- Drugs with FDA-approved pediatric dosage, or dosages based on multiple randomized clinical trials, are given a Level of Evidence "I." Dosages for which data are collected from adults, from noncomparative trials, or from small comparative trials, the Level of Evidence is "II." For dosages that are based on expert or consensus opinion, or case reports, the Level of Evidence given is "III."
- All commercially available dosage forms for children and adults are listed. If no oral liquid form is available, round the child's dose to the nearest value using a combination of commercially available solid dosage form strengths OR consult pharmacist for recommendations on mixing with food (eg, crushing tablets, emptying capsule contents) or the availability of a valid extemporaneously compounded liquid formulation if the child is unable to take solid dosage forms.
- Drugs with an asterisk (*) were available in generic formulations in the United States as of September 2009.

- *Abbreviations:* AOM, acute otitis media; BSA, body surface area; CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*; CMV, cytomegalovirus; FDA, US Food and Drug Administration; HSV, herpes simplex virus; IBW, ideal body weight; IM, intramuscular; IV, intravenous; ivpb, intravenous piggyback; MAC, *Mycobacterium avium* complex; ophth, ophthalmic; PCP, *Pneumocystis carinii* pneumonia; PIP, piperacillin; PK, pharmacokinetic; PO, orallly; SPAG-2, small particle aerosol generator model-2; TB, tuberculosis; TBW, total body weight; SMX, sulfamethoxazole; TMP, trimethoprim; UTI, urinary tract infection; VZV, varicella-zoster virus.

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Abacavir, Ziagen<br>Not approved for use in infants aged <3 months | 100-mg/5 mL soln; 300-mg tab | PO | 16 mg/kg/day (adults 600 mg/day) (I) | q12h |
| Epzicom | Combination tab with 600 mg abacavir + 300 mg lamivudine | PO | Adults 1 tab | q24h |
| Trizivir | Combination tab with 300 mg abacavir, 300 mg zidovudine, 150 mg lamivudine | PO | Adults 1 tab | q12h |
| Acyclovir*, Zovirax | 500-, 1,000-mg vial | IV | 15–60 mg/kg/day (adolescents/adults 15–30 mg/kg/day based on IBW) (I) | q8h |
| | 200-mg/5 mL susp<br>200-mg cap; 400-, 800-mg tab | PO | 60–80 mg/kg/day (adults 1–4 g/day) (I) | q6–8h |
| Albendazole, Albenza | 200-mg tab | PO | 15 mg/kg/day (max 800 mg/day) (I) | q12h |
| Amantadine*, Symmetrel | 100-mg cap, tab; 50-mg/5 mL syrup | PO | 5–9 mg/kg/day (max 150 mg/day if <9 yrs)<br>200 mg/day if ≥9 yrs (I) | q12h |
| Amikacin*, Amikin | 100-, 200-mg pediatric vials 50 mg/mL<br>500-, 1,000-mg adult vials 250 mg/mL<br>500 mg/100 mL ivpb | IV, IM | 15–22.5 mg/kg/day (see Chapter 2 regarding q24h dosing) (I) | q8–24h |
| Amoxicillin*, Amoxil | 250-, 500-mg cap<br>500-, 875-mg tab<br>125-, 200-, 250-, 400-mg/5 mL susp<br>125-, 200-, 250-, 400-mg chew tab<br>50-mg/1 mL suspension drops | PO | 40–100 mg/kg/day if <40kg (II)<br>For otitis media, up to 150 mg/kg/day (III)<br>Adults 750–1750 mg/day (I) | q8–12h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Amoxicillin/clavulanate, Augmentin | **16:1** Formulation (Augmentin XR): 1,000/62.5-mg tab | PO | Adult strength | |
| | **14:1** Formulation* (Augmentin ES-600): **600**/42.9-mg/5 mL susp | PO | **14:1** Formulation: 90-mg amoxicillin component/kg/day if <40 kg (I) | q12h |
| | **7:1** Formulation*: **875**/125-mg tab<br>**200**/28.5-, **400**/57-mg chew tab;<br>**200**/28.5-, **400**/57-mg/5 mL susp | PO | **7:1** Formulation: 25–45-mg amoxicillin component/kg/day (adults 1,750 mg/day) (I) | q12h |
| | **4:1** Formulation*: **500**/125-mg tab<br>**125**/31.25-, **250**/62.5-mg chew tab;<br>**125**/31.25-, **250**/62.5-mg/5 mL susp | PO | **4:1** Formulation: 20–40-mg amoxicillin component/kg/day (adults 1,500 mg/day) (I) | q8h |
| Amphotericin B deoxycholate (AmB-D)*, Fungizone | 50-mg vial | IV | 0.7–1 mg/kg/day (II)<br>Adults 1–1.5 mg/kg/day (I)<br>Some adult dosing regimens are 2X or 3X each week (III) | q24h |
| Amphotericin B cholesteryl sulfate, Amphotec | 50-, 100-mg vial | IV | 3–4 mg/kg/day pediatric and adult dose (I) | q24h |
| Amphotericin B, lipid complex (AmB-LC), Abelcet | 100-mg/20 mL vial | IV | 5 mg/kg/day pediatric and adult dose (I); may push to 10 mg/kg/day to achieve appropriate tissue exposure for life-threatening infection (III) | q24h |
| Amphotericin B, liposomal (AmB-LP), AmBisome | 50-mg vial | IV | 3–5 mg/kg/day pediatric and adult dose (I); may push to 10 mg/kg/day to achieve appropriate tissue exposure for life-threatening infection (III) | q24h |
| Ampicillin/ampicillin trihydrate* | 250-, 500-mg cap<br>125-, 250-mg/5 mL susp | PO | 50–100 mg/kg/day if <20 kg (adults 1–2 g/day) (I) | q6h |
| Ampicillin sodium* | 0.125-, 0.25-, 0.5-, 1-, 2-, 10-g vial | IV, IM | 50–200 mg/kg/day (I)<br>300–400 mg/kg/day endocarditis/meningitis (III)<br>Adults 2–12 g/day (I) | q6h<br>q4–6h |
| Ampicillin and sulbactam*, Unasyn | 1/0.5-, 2/1-, 10/5-g vial | IV/IM | 200 mg/kg/day (ampicillin component) if <40 kg (adults 4–8 g ampicillin/day) (I) | q6h |

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| Anidulafungin, Eraxis | 50-, 100-mg vial | IV | 1.5–3 mg/kg/loading dose followed by 0.75–1.5 mg/kg/day (II)<br>Adult loading dose 100–200 mg followed by 50–100 mg/day (I) | q24h |
| Atazanavir, Reyataz | 100-, 150-, 200-, 300-mg cap | PO | 7.5 mg/kg/day if <20 kg + ritonavir 4 mg/kg/day<br>8 mg/kg/day if 20–39 kg + ritonavir 4 mg/kg/day<br>Adults and children >39 kg: 400 mg if tx naïve or 300 mg + ritonavir 100 mg if not (I) | q24h |
| Atovaquone, Mepron | 750-mg/5 mL susp | PO | 30–40 mg/kg/day if 1 to 3 mos and >24 mos<br>45 mg/kg/day if 4–24 mos (II)<br>Adults 1,500 mg/day | q12–24h |
| Atovaquone and proguanil, Malarone | 62.5/25 mg pediatric tab<br>250/100 mg adult tab | PO | Prophylaxis: 11–20 kg 1 ped tab, 21–30 kg 2 ped tabs, 31–40 kg 3 ped tabs, >40 kg 1 adult tab (I)<br>Treatment: 5–8 kg 2 ped tabs, 9–10 kg 3 ped tabs, 11–20 kg 1 adult tab, 21–30 kg 2 adult tabs, 31–40 kg 3 adult tabs, >40 kg 4 adult tabs (I) | q24h |
| Azithromycin*, Zithromax | 250-, 500-, 600-mg tab<br>100-, 200-mg/5 mL susp<br>27 mg/mL XR susp (Zmax) | PO | Otitis: 10 mg/kg/day x 3 d; or 30 mg/kg x 1 (I)<br>Pharyngitis: 12 mg/kg/day x 5 d (I)<br>Sinusitis: 10 mg/kg/day x 3 d (I)<br>Community-associated pneumonia: 10 mg/kg x 1, then 5 mg/kg/day x 4 d or 60 mg/kg x 1 of XR susp (I)<br>Adult single or total course dose: 1.5–2 g (I)<br>MAC prophylaxis: 5 mg/kg/day (I)<br>See Chapter 6 for other specific disease dosing recommendations. | q24h |
| Azithromycin*, Zithromax | 500 mg vial | IV | 10 mg/kg (II) | q24h |
| Aztreonam, Azactam | 0.5-, 1-, 2-g vial, 1-, 2-g/50 mL ivpb | IV, IM | 90–120 mg/kg/day (adults 3–6 g/day) (I) | q6–8h |
| Capreomycin, Capastat | 1-g vial | IV, IM<br>Adults | 15–30 mg/kg (III)<br>1 g/day, max 20 mg/kg/day (I) | q24h |
| Caspofungin, Cancidas | 50-, 70-mg vial | IV | 70 mg/m$^2$ BSA x1 then 50 mg/m$^2$ BSA/day maximum dose 70 mg (I) | q24h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Cefaclor*, Ceclor | 125-, 187-, 250-, 375-mg/5 mL susp<br>250-, 500-mg cap, 375-, 500-mg ER tab | PO | 20–40 mg/kg/day, max 1 g/day (I) | q12h |
| Cefadroxil*, Duricef | 500-mg cap, 1-g tab<br>125-, 250-, 500-mg/5 mL susp | PO | 30 mg/kg/day (adults 1–2 g/day) (I) | q12–24h |
| Cefazolin*, Ancef | 0.5-, 1-, 10-, 20-g vial,1-, 2-g/ 100 mL ivpb | IV, IM | 25–100 mg/kg/day (adults 3–6 g/day) (I)<br>For serious infections, up to 150 mg/kg/day (III) | q6–8h |
| Cefdinir*, Omnicef | 125-, 250-mg/5 mL susp, 300-mg cap | PO | 14 mg/kg/day, max 600 mg/day (I) | q24h |
| Cefepime*, Maxipime | 0.5-, 1-, 2-g vial | IV, IM | 100 mg/kg/day (adults 2–4 g/day) (I) | q12h |
| | | | 150 mg/kg/day empiric therapy of fever with neutropenia (adults 6 g/day) (I) | q8h |
| Cefditoren, Spectracef | 200-, 400-mg tab | PO | ≥12 yrs and adults, 400–800 mg/day (I) | q12h |
| Cefixime*, Suprax | 100-, 200-mg/5 mL susp<br>400 mg tab | PO | 8 mg/kg/day if <50 kg (adults 400 mg/day) (I)<br>For convalescent oral therapy of serious infections, up to 20 mg/kg/day (III) | q12–24h |
| Cefotaxime*, Claforan | 0.5-, 1-, 2-, 10-, 20-g vial | IV, IM | 50–180 mg/kg/day (adults 3–8 g/day) (I)<br>200–225 mg/kg/day for meningitis (adults 12 g/day) (I) | q6–8h<br>q6–8h |
| Cefotetan*, Cefotan | 1-, 2-, 10-g vial | IV, IM | 60–100 mg/kg/day (II)<br>Adults 2–4 g/day (I) | q12h |
| Cefoxitin*, Mefoxin | 1-, 2-, 10-g vial, 1-, 2-g/50 mL | IV, IM | 80–160 mg/kg/day, max 12 g/day (I) | q6h |
| Cefpodoxime*, Vantin | 50-, 100-mg/5 mL susp<br>100-, 200-mg tab | PO | 10 mg/kg/day, max 400 mg/day (I) | q12h |
| Cefprozil*, Cefzil | 125-, 250-mg/5 mL susp<br>250-, 500-mg tab | PO | 15–30 mg/kg/day (adults 0.5–1 g/day) (I) | q12h |
| Ceftazidime*, Ceptaz, Fortaz | 0.5-, 1-, 2-, 6-g vial | IV, IM | 90–150 mg/kg/day (adults 3–6 g/day) (I) | q8h |
| | 0.5-, 1-, 2-g/50 mL ivpb | | 200–300 mg/kg/day for serious *Pseudomonas* infection (III) | q8h |

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| Ceftibuten, Cedax | 90-mg/5 mL susp, 400-mg cap; | PO | 9 mg/kg/day (adults 400 mg/day) (I) | q24h |
| Ceftizoxime, Cefizox | 1-, 2-g/50 mL ivpb | IV, IM | 150–200 mg/kg/day (adults 2–12 g/day) (I) | q6–8h |
| Ceftriaxone*, Rocephin | 0.25-, 0.5-, 1-, 2-, 10-g vial<br>1-, 2-g/50 mL ivpb | IV, IM | 50–75 mg/kg/day, max 2 g/day (I)<br>100 mg/kg/day for meningitis, max 4 g/day (I)<br>50 mg/kg x1–3 doses IM for AOM, max 1 g (II) | q12–24h |
| Cefuroxime axetil*, Ceftin | 125-, 250-mg/5 mL susp<br>125-, 250-, 500-mg tab | PO | 20 –30 mg/kg/day (adults 0.5–1 g/day) (I)<br>For bone and joint infections, up to 100 mg/kg/day (III) | q12h |
| Cefuroxime sodium*, Zinacef | 0.75-, 1.5-g vial,<br>0.75-, 1.5-g/50 mL ivpb | IV, IM | 100–150 mg/kg/day (adults 1.5–3 g/day) (I) | q8h |
| Cephalexin*, Keflex | 125-, 250-mg/5 mL susp<br>250-, 500-mg caps and tabs | PO | 25–50 mg/kg/day, max 1 g/day (I) | q12h |
| | | | 75–100 mg/kg/day for bone and joint, AOM, or severe infections (adults 2–4 g/day) (II) | q6h |
| Panixine | 125-, 250-mg dispersable tab | | | |
| Chloramphenicol sod succinate*, Chloromycetin | 1-g vial | IV | 50–75 mg/kg/day<br>75–100 mg/kg/day for meningitis (I)<br>Adults max 4 g/day | q6h |
| Chloroquine phosphate*, Aralen | 150-, 300-mg (base) tab | PO | See Chapter 8. | |
| Ciprofloxacin, Cipro | 250-, 500-mg/5 mL susp<br>100-, 250-, 500-, 750-mg tab* | PO | 20–40 mg/kg/day, max 1.5 g/day (I) | q12h |
| | 200-, 400-mg vial, ivpb* | IV | 20–30 mg/kg/day, max 1.2 g/day (I) | q8–12h |
| Cipro XR | 500-, 1,000-mg ER tab* | PO | Adults 500–1,000 mg/day (I) | q24h |
| Clarithromycin*, Biaxin 250-, 500-mg tab | 125-, 250-mg/5 mL susp | PO | 15 mg/kg/day, max 1 g/day (I) | q12h |
| Biaxin XL | 500-mg ER tab | PO | Adults 1,000 mg/day (I) | q24h |
| Clindamycin*, Cleocin | 75 mg/5 mL soln<br>75-, 150-, 300-mg cap | PO | 10–25 mg/kg/day (adults 1.2–1.8 g/day) (I)<br>30–40 mg/kg/day for CA-MRSA, intraabdominal infection, or AOM (III) | q8h |
| | 0.3-, 0.6-, 0.9-g vial, ivpb | IV, IM | 20–40 mg/kg/day (adults 1.8–2.7 g/day) (I) | q8h |
| Clofazimine, Lamprene | 50-mg cap | PO | Adults 100 mg/day (I) | q24h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Clotrimazole*, Mycelex | 10-mg lozenge | PO | ≥3 yrs and adults 10 mg, dissolve in mouth (I) | 5 times daily |
| Colistimethate*, Coly-Mycin M | 150-mg (colistin base) vial | IV, IM | 2.5–5 mg/kg/day based on IBW (I)<br>up to 5–7 mg/kg/day (III) | q8h |
| Cycloserine, Seromycin | 250-mg cap | PO | 10–20 mg/kg/day (III)<br>Adults max 1 g/day (I) | q12h |
| Dapsone | 25-, 100-mg tab | PO | 2 mg/kg/day, max 100 mg/day (II) | q24h |
| Daptomycin, Cubicin | 500-mg vial | IV | Children >6 yrs 4–6 mg/kg/day (II)<br>In children 2–6 yrs 10 mg/kg/day (III)<br>Adults 4–6 mg/kg total body weight/day (I) | q24h |
| Darunavir, Prezista | 75-, 150-, 300-, 400-, 600-mg tab | PO | ≥20–<30 kg 375 mg + ritonavir 50 mg<br>≥30–<40 kg 450 mg + ritonavir 60 mg<br>≥40 kg 600 mg + ritonavir 100 mg (I) | q12h |
| Delavirdine, Rescriptor | 100-, 200-mg tab | PO | ≥16 yrs of age 1,200 mg/day (I) | q8h |
| Demeclocycline*, Declomycin | 150-, 300-mg tab | PO | ≥8 yrs 7–13 mg/kg/day, max 600 mg/day (I) | q6h |
| Dicloxacillin*, Dynapen | 125-, 250-, 500-mg cap | PO | 12–25 mg/kg/day (adults 0.5–1 g/day) (I)<br>For bone and joint infections, up to 100 mg/kg/day (III) | q6h |
| Didanosinex (ddI), Videx | 50-mg/5 mL oral soln | PO | 2 wks–8 months 200 mg/m$^2$ BSA/day<br>>8 months 240 mg/m$^2$ BSA/day<br>Adolescents/adults<br>≥60 kg 400 mg/day<br><60 kg 250 mg/day | q12h |
| Videx-EC* | 125-, 200-, 250-, 400-mg cap | PO | Adolescents <60 kg 250 mg/day<br>Adolescents ≥60 kg 400 mg/day | q24h |
| Diiodohydroxyquin (see Iodoquinol) | | | | |

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| Doxycycline calcium, monohydrate*, and hyclate* | 50-, 75-, 100-mg cap, tab<br>25-, 50-mg/5 mL susp (no generic avail) | PO | ≥8 yrs, ≤45 kg: 2–4 mg/kg/day (adults 100–200 mg/day) (I) | q12h |
| Vibramycin, Monodox | 100-, 200-mg vial | IV | | |
| Efavirenz, Sustiva | 50-, 200-mg cap, 600-mg tab<br>Approved for >3 yrs | PO | 10–<15 kg: 200 mg<br>15–<20 kg: 250 mg<br>20–<25 kg: 300 mg<br>25–<32.5 kg: 350 mg<br>32.5–<40 kg: 400 mg<br>≥40 kg: 600 mg (adults) (I) | q24h |
| Atripla | Combination tab with 200 mg emtricitabine, 300 mg tenofovir, 600 mg efavirenz | PO | Adults 1 tab | q24 |
| Emtricitabine, Emtriva | 50-mg/5 mL soln<br>200-mg cap | PO | ≥3 months 6 mg sol/kg/day, max 240 mg/day<br>>33 kg and adults 200 mg cap/day | q24h |
| Truvada | Combination tab with 200 mg emtricitabine + 300 mg tenofovir | PO | Adults 1 tab | q24h |
| Atripla | Combination tab with 200 mg emtricitabine, 300 mg tenofovir, 600 mg efavirenz | PO | Adults 1 tab | q24h |
| Enfuvirtide, Fuzeon | 108-mg vial (90 mg/mL) | SQ | ≥6 yrs 4 mg/kg/day, max 180 mg/day (I) | q12h |
| Ertapenem, Invanz | 1-g vial | IV, IM | 30 mg/kg/day, max 1 g/day (I) | q12h |
| | | | ≥13 yrs and adults 1 g/day (I) | q24h |
| Erythromycin* base | 250-, 500-mg tab, film coated | PO | 50 mg/kg/day (adults 1–4 g/day) (I) | q6–8h |
| ERYC* | 250-mg cap, enteric coated (EC) | | | |
| PCE | 333-, 500-mg tabs of EC particles | | | |
| Ery-Tab* | 250-, 333-, 500-mg tab, EC | | | |
| Erythromycin ethylsuccinate* EES, EryPed | 200-, 400-mg/5 mL susp | PO | 50 mg/kg/day (adults 1–4 g/day) (I) | q6–8h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
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| Erythromycin ethylsuccinate and sulfisoxazole acetyl*, Pediazole | 200 mg erythromycin and 600 mg sulfisoxazole/5 mL susp | PO | 50 mg/kg/day of erythromycin component, max 2 g/day erythromycin (I) | q6–8h |
| Erythromycin lactobionate*, Erythrocin | 0.5-, 1-g vial | IV | 20 mg/kg/day (adults 1–4 g/day) (I) | q6h |
| Erythromycin stearate* | 250-mg tab, film coated | PO | 50 mg/kg/day (adults 1–4 g/day) (I) | q6–8h |
| Ethambutol*, Myambutol | 100-, 400-mg tab | PO | 15–25 mg/kg/day, max 2.5 g/day (I) | q24h |
| Ethionamide, Trecator | 250-mg tab | PO | 15–20 mg/kg/day, max 1 g/day (III) | q12h |
| Famciclovir*, Famvir | 125-, 250-, 500-mg tab | PO | Adults 0.5–1.5 g/day (I) | q8–12h |
| Fluconazole*, Diflucan | 50-, 100-, 150-, 200-mg tab<br>50-, 200-mg/5 mL susp | PO | 3–12 mg/kg/day, max 600 mg/day (I) | q24h |
| | 200-, 400-mg vial, ivpb | IV | | |
| Flucytosine, Ancobon | 250-, 500-mg cap | PO | 50–150 mg/kg/day (III) | q6h |
| Fosamprenavir, Lexiva | 700-mg tab, 250-mg/5 mL sol | PO | 2–6 yrs 60 mg/kg/day (max 2.8 g/day)<br>≥6 yrs 36 mg/kg/day (max 1,400 mg/day) with ritonavir 6 mg/kg/day (I) | q12h |
| Foscarnet*, Foscavir | 6-, 12-g vial | IV | CMV 180 mg/kg/day x 2–3 weeks | q8h |
| | | | 90–120 mg/kg/day (I) | q24h |
| | | | HSV/VZV: 80–120 mg/kg/day (I) | q8–12h |
| Ganciclovir*, Cytovene | 500-mg vial | IV | 10–15 mg/kg/day x2–3 wk<br>then 5 mg/kg/day (I) | q12h<br>q24h |
| | 250-, 500-mg cap | PO | 90 mg/kg/day (III)<br>Adults 3,000 mg/day (I) | q8h |
| Gemifloxacin, Factive | 320-mg tab | PO | Adults 320 mg/day (I) | q24h |

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| Gentamicin* | 20-mg/2 mL pediatric vial<br>80-mg/2 mL, 800-mg/20 mL adult vial, numerous ivpb | IV, IM | 3–7.5 mg/kg/day (cystic fibrosis 7–10);<br>see Chapter 2 regarding q24h dosing | q8–24h |
| Griseofulvin microsized*, Grifulvin V | 125-mg/5 mL susp<br>250-, 500-mg tab | PO | 10–25 mg/kg/day (adults 0.5–1 g/day) (I) | q24h |
| ultramicrosized, Gris-PEG | 125-, 250-mg tab | PO | 10–15 mg/kg/day (adults 0.375–0.75 g/day) (I) | q24h |
| Imipenem/cilastatin, Primaxin | 250/250-, 500/500-mg vial for IV<br>500/500-mg vial for IM | IV, IM | 60–100 mg/kg/day (I)<br>IM form not approved for <12 yrs | q6h |
| Iodoquinol, Yodoxin | 210-, 650-mg tab | PO | 30–40 mg/kg/day, max 1.95 g/day (I) | q8h |
| Isoniazid*, Nydrazid | 100-, 300-mg tab, 50 mg/5 mL syrup | PO | 10–15 mg/kg/day, max daily dosage 300 mg/day (I) | q12–24h |
| | 1,000-mg vial | IV, IM | With directly observed biweekly therapy, dosage is 20–40 mg/kg, max 900 mg/dose (I) | Twice weekly |
| Itraconazole, Sporanox | 50-mg/5 mL soln<br>100-mg cap* | PO | 5 mg/kg/day (I)<br>For serious infections, up to 10 mg/kg/day (III) | q12h |
| | 250-mg vial | IV | 5 mg/kg/day (II) | q12h |
| Ivermectin, Stromectal | 3-mg tab | PO | 150–200 mcg/kg (I) | 1 dose |
| Kanamycin*, Kantrex | 75-mg pediatric vial 37.5 mg/mL<br>500-, 1,000-mg adult vial | IV, IM | 15–30 mg/kg/day (see page 7 regarding q24h dosing) | q8h |
| Ketoconazole*, Nizoral | 200-mg tab | PO | ≥2 yrs 3.3–6.6 mg/kg/day (II) | q24h |
| Lamivudine, Epivir | 50-mg/5 mL soln<br>150-, 300-mg tab | PO | Neonates (<30 days): 4 mg/kg/day<br>Infants/children 8 mg/kg/day (max 300 mg/day)<br>Adolescents/adults (≥16 yrs; >50 kg): 150 mg/dose q12h or 300 mg once daily (I) | q12h |
| Epivir HBV | 100-mg tab, 25-mg/5 mL soln | PO | 3 mg/kg/day (max 100 mg/day) | q24h |
| Combivir | Combination tab: 300 mg zidovudine + 150 mg lamivudine | | >12 yrs and adults 1 tab/dose | q12h |
| Epzicom | Combination tab with 600 mg abacavir + 300 mg lamivudine | | Adults 1 tab | q24h |
| Trizivir | Combination tab with 300 mg abacavir, 300 mg zidovudine, 150 mg lamivudine | | Adults >40 kg 1 tab/dose | q12h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Lamivir | Combination tab with 150 mg lamivudine + stavudine 30/40 mg | | Pending FDA approval | q12h |
| Triomune | Combination tab with lamivudine 150 mg, stavudine 30/40 mg + nevirapine 200 mg<br>Combination dispersable tab with lamivudine 30/60 mg, stavudine 6/12 mg + nevirapine 50/100 mg | | Pending FDA approval | q12h |
| Levofloxacin, Levaquin | 125-mg/5 mL solution<br>250-, 500-, 750-mg tab,<br>500-, 750-mg vial<br>250-, 500-, 750-mg ivpb | PO, IV | 16 mg/kg/day, max 500 mg/day (I)<br><5 yrs 20 mg/kg/day (II)<br>≥5 yrs 10 mg/kg/day (II) | q12h<br>q12h<br>q24h |
| Linezolid, Zyvox | 100-mg/5 mL susp<br>400-, 600-mg tab | PO, IV | 30 mg/kg/day (I) | q8h |
| | 200-, 400-, 600-mg ivpb | | ≥12 yrs, adults 1,200 mg/day (I) | q12h |
| Lopinavir/ritonavir, Kaletra<br>– adjustments necessary for concomitant use with nevirapine or efavirenz | 400 mg lopinavir/100 mg ritonavir per 5 mL oral soln<br>100 mg lopinavir/25 mg ritonavir tab<br>200 mg lopinavir/50 mg ritonavir tab | PO | <6 months 36 mg/kg/day L (lopinavir)<br>≥6 months<br><15 kg 24 mg/kg/day L<br>15–<40 kg 20 mg/kg/day L<br>≥40 kg 800 mg/day L (adult dose) (I) | q12h |
| Maraviroc (Selzentry) | 150- and 300-mg tab | PO | Not approved for use in children <16 yrs<br>Adolescents ≥16 yrs/adults: 300–1,200 mg/day (depends on co-administered drugs) (I) | q12h |
| Mebendazole*, Vermox | 100-mg chewable tab | PO | See Chapter 10. | |
| Mefloquine*, Lariam | 250-mg tab | PO | See Chapter 10. | |
| Meropenem, Merrem | 0.5-, 1-g vial | IV | 60 mg/kg/day, max 3 g/day (I)<br>120 mg/kg/day for meningitis, max 6 g/day (I) | q8h<br>q8h |

| | | | | |
|---|---|---|---|---|
| Methenamine hippurate*, Hiprex | 1-g tab | PO | >12 yrs 2 g/day (I)<br>6–12 yrs 1–2 g/day (I) | q12h |
| Metronidazole*, Flagyl | 250-, 500-mg tab, 375-mg cap | PO | 30–50 mg/kg/day (adults 750–2250 mg/day) (I) | q8h |
| | 500-mg vial, ivpb | IV | 22.5–40 mg/kg/day (II)<br>Adults 1,500 mg/day (I) | q8h |
| Micafungin, Mycamine | 50-, 100-mg vial | IV | 2–4 mg/kg/day (II)<br>Preterm infants may require up to 15 mg/kg/day (see Chapter 8) (III) | q24h |
| Minocycline*, Minocin 100-mg vial | 50-, 75-, 100-mg cap, tab<br>IV | PO | ≥8 yrs 4 mg/kg/day (adults 200 mg/day) (I) | q12h |
| Solodyn | 45-, 90-, 135-mg ER tab | PO | ≥12 yrs 1 mg/kg/day (acne) (I) | q24h |
| Moxifloxacin, Avelox | 400-mg tab, 400-mg/250 mL ivpb | PO, IV | Adults 400 mg/day (I) | q24h |
| Nafcillin*, Nallpen | 0.5-, 1-, 2-, 10-g vial, 1-, 2-g ivpb | IV, IM | 150–200 mg/kg/day (II)<br>Adults 3–6 g/day q4h (I) | q6h |
| Nelfinavir, Viracept | 250-, 625-mg tab<br>50 mg/g scoop oral powder | PO | >2 yrs 90–110 mg/kg/day max 2.5 g/day (I) | q12h |
| Neomycin sulfate*, Neo-fradin | 500-mg tab, 87.5 mg/5mL solution | PO | 50–100 mg/kg/day (III) | q6–8h |
| Nevirapine, Viramune | 50-mg/5 mL susp, 200-mg tab | PO | 300–400 mg/m$^2$ BSA/day (max 400 mg/day) | q12h |
| | | | Note: initiate therapy with half dose (150 mg/m$^2$/once daily) for 14 days, followed by full q12h dose (300–400 mg/m$^2$/day) (I) | |
| Nitazoxanide, Alinia | 500-mg tab; 100-mg/5 mL susp | PO | 1–3 years of age: 200 mg/day<br>4–11 years of age: 400 mg/day<br>≥12 years of age: 1 g/day (I) | q12h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Nitrofurantoin, Furadantin | 25 mg/5 mL susp | PO | 5–7 mg/kg/day<br>1–2 mg/kg once daily for UTI prophylaxis (I) | q6h |
| Nitrofurantoin, macrocrystalline*, Macrodantin | 25-, 50-, 100-mg cap | | 5–7 mg/kg/day<br>1–2 mg/kg once daily for UTI prophylaxis (I) | q6h |
| Nitrofurantoin monohydrate and macrocrystalline*, Macrobid | 100-mg cap | | >12 yrs 200 mg/day (I) | q12h |
| Norfloxacin*, Noroxin | 400-mg tab | PO | Adults 800 mg/day (I) | q12h |
| Nystatin*, Mycostatin | 500,000-unit/5 mL susp | PO | Infants 2 mL/dose, children 4–6 mL/dose, to coat oral mucosa | q6h |
| Oseltamivir, Tamiflu | 60-mg/5 mL susp<br>30-, 45-, 75-mg cap, | PO | For infants <9 mos 6 mg/kg/day (III)<br>For infants 9 mos to 1 yr 7 mg/kg/day (III)<br>For children ≥1 yr 4 mg/kg/day, max 150 mg/day (I) | q12h |
| | | | 2 mg/kg/day (prophylaxis) (I) | q24h |
| Oxacillin*, Bactocill | 250-, 500-mg, 1-, 2-, 10-g vial<br>150–200 mg/kg/day for meningitis (III) | IV, IM | 100 mg/kg/day (adults 4–12 g/day) (I) | q4–6h |
| Palivizumab, Synagis | 50-, 100-mg vial | IM | 15 mg/kg (I) | Monthly |
| Paromomycin*, Humatin | 250-mg cap | PO | 25–35 mg/kg/day (adult max 4 g/day) (I) | q8h |
| Penicillin G benzathine, Bicillin L-A | 600,000 units/mL in 1-, 2-, 4-mL syringe sizes | IM | 50,000 units/kg for newborns and infants<br>children <60 lbs 300,000–600,000 units<br>children ≥60 lbs 900,000 units (I) | 1 dose |
| Penicillin G benzathine/ procaine, Bicillin C-R | 600,000 units/mL as 300,000 units benzathine + 300,000 units procaine per mL in 2-mL syringe size | IM | <30 lbs 600,000 units<br>30–60 lbs 900,000–1,200,000 units<br>>60 lbs 2,400,000 units (I) | 1 dose |
| Penicillin G procaine | 600,000 units/mL in 1-, 2-mL syringe sizes | IM | 50,000 units/kg/day, max 1,200,000 units per dose (I) | q12–24h |

| | | | | |
|---|---|---|---|---|
| Penicillin G K*, Pfizerpen<br>Penicillin G sodium* | 1-, 5-, 20-million-unit vial<br>5-million-unit vial | V, IM<br>IV, IM | 100,000–250,000 units/kg/day (I)<br>Same as Pen G K | q4–6h |
| Penicillin V K* | 125-, 250-mg/5 mL soln<br>250-, 500-mg tab | PO | 25–50 mg/kg/day | q6–8h |
| Pentamidine, Pentam | 300-mg vial* | IV, IM | 4 mg/kg/day (I) | q24h |
| Nebupent | 300-mg vial | Inhaled | 300 mg q month for prophylaxis (I) | q24h |
| Piperacillin*, Pipracil | 2-, 3-, 4-, 40-g vial | IV | 200–300 mg/kg/day<br>≥12 years and adults 8–18, max 24 g/day (I) | q6–8h |
| Piperacillin/tazobactam, Zosyn | 2/0.25-, 3/0.375-, 4/0.5-g vial, ivpb<br>36/4.5-g vial | IV | ≤40 kg; 240–300 mg PIP/kg/day (adults 12–16 g PIP/day q6h) (I) | q8h |
| Posaconazole, Noxafil | 200-mg/5 mL susp | PO | ≥13 yrs and adults 600–800 mg/day (I) | q8–12h |
| Praziquantel, Biltricide | 600-mg triscored tab | PO | 20–25 mg/kg q4–6h x 3 doses (I) | |
| Primaquine phosphate | 15-mg (base) tab | PO | 0.3 mg (base)/kg/day (with clindamycin) for PCPmax 30 mg/day (III)<br>See also Chapter 10. | q24h |
| Pyrantel pamoate*, Antiminth | 250-mg (base) chew tab<br>250-mg (base)/5 mL susp<br>62.5-mg (base) tabs, caps | | 11 mg (base)/kg, max 1 g (I) | Once |
| Pyrazinamide* | 500-mg tab | PO | 15–30 mg/kg/day, max 2 g/day (I) | q24h |
| | | | Directly observed therapy biweekly therapy, 50–70 mg/kg (I) | Twice weekly |
| Pyrimethamine, Daraprim (see also Sulfadoxine) | 25-mg tab | PO | See Chapter 10. | |
| Quinupristin/dalfopristin Synercid | 150/350-mg vial (500 mg total)<br>180/420-mg vial (600 mg total) | IV | 22.5 mg/kg/day (II)<br>Adults 15–22.5 mg/kg/day (I) | q8h<br>q8–12h |
| Raltegravir, Isentress | 400-mg tab | PO | ≥16 yrs and adults 800 mg/day (I) | q12h |
| Ribavirin, Rebetol | 200-mg cap*, 200-mg/5 mL soln | PO | 15 mg/kg/day (with interferon 3 x/week) | q12h |
| Virazole | 6-g vial | Inhaled | 1 vial by SPAG-2 | q24h |
| Rifabutin, Mycobutin | 150-mg cap | PO | 5 mg/kg/day for MAC<br>10–20 mg/kg/day for TB, max 300 mg/day (II) | q24h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Rifampin*, Rifadin | 150-, 300-mg cap, 600-mg vial | PO, IV | 10–20 mg/kg/day, max 600 mg for TB (I) | q24h |
| | | | With directly observed biweekly therapy, dosage is still 10–20 mg/kg/dose (max 600 mg) | Twice weekly |
| | | | 20 mg/kg/day x 2 days for meningococcus prophylaxis, adult dose 1,200 mg/day (I) | q12h |
| Rifampin/Isoniazid*, Rifamate | 300/150-mg cap | PO | Refer to individual agents | |
| Rifampin/isoniazid/ pyrazinamide, Rifater | 120/50/300-mg tab | PO | Refer to individual agents | |
| Rifapentine, Priftin | 150-mg tab | PO | ≥12 yrs and <45 kg: 450 mg/dose<br>≥45 kg and adults: 600 mg/dose (I) | Twice weekly |
| Rifaximin, Xifaxan | 200-mg tab | PO | ≥12 yrs and adults: 600 mg/day (I) | q8h |
| Rimantadine*, Flumadine | 100-mg tab | PO | <10 years, 5 mg/kg/day, max 150 mg/day<br>≥10 years and adults, 200 mg/day (I)<br>If <40 kg but ≥10 years, 5 mg/kg/day (III) | q24h<br>q12h<br>q24h |
| Ritonavir, Norvir | 100-mg cap, 400-mg/5 mL soln | | As pharmacokinetic enhancer of other HIV protease inhibitors: 3–12 mg/kg/day (I) | q12h |
| Saquinavir, Invirase<br>– recommended only in combination with ritonavir | 200-mg hard gel cap<br>500-mg tab | PO | Adolescent/adults 1,000 mg/dose + 100 mg ritonavir/dose | q12h |
| Stavudine*, Zerit | 5-mg/5 mL soln<br>15-, 20-, 30-, 40-mg cap | PO | Birth–13 days of age 1 mg/kg/day<br>Ped dose (to 30 kg) 2 mg/kg/day<br>30–<60 kg: 60 mg/day<br>≥60 kg 80 mg/day (I) | q12h<br>q12h<br>q12h<br>q12h |
| Streptomycin* | 1-g vial | IM, IV | 20–30 mg/kg/day, max 1 g/day (I) | q12h |

| | | | | |
|---|---|---|---|---|
| Sulfadiazine* | 500-mg tab | PO | 120–150 mg/kg/day, max 4–6 g/day (I)<br>Rheumatic fever secondary prophylaxis<br>500 mg once daily if ≤27 kg<br>1,000 mg once daily if >27 kg (II) | q6h<br>q24h |
| | | | See also Chapter 10. | |
| Sulfadoxine/ pyrimethamine, Fansidar | 500-/25-mg tab | PO | See Chapter 10. | |
| Sulfisoxazole, Gantrisin | 500-mg/5 mL susp | PO | 120–150 mg/kg/day, max 6 g/day (I) | q6h |
| | | | 10–20 mg/kg/day for UTI prophylaxis (II) | q12h |
| | | | Rheumatic fever secondary prophylaxis:<br>500 mg once daily if ≤27 kg<br>1,000 mg once daily if >27 kg (III) | q24h |
| Telbivudine, Tyzeka | 600 mg tab | PO | ≥16 yrs and adults 600 mg/day | q24h |
| Telithromycin, Ketek | 300-, 400-mg tab | PO | Adults 800 mg/day (I) | q24h |
| Tenofovir, Viread | 300-mg tab<br>Investigational: 75 mg tab | PO | Adults 300 mg/dose (I) | q24h |
| Truvada | Combination tab with 200 mg emtricitabine + 300 mg tenofovir | PO | Adults 1 tab | q24h |
| Atripla | Combination tab with 200 mg emtricitabine, 300 mg tenofovir, 600 mg efavirenz | PO | Adults 1 tab | q24h |
| Terbinafine, Lamisil | 125-, 187.5-mg oral granules<br>250-mg tab* | PO | >4 yrs <25 kg 125 mg/day<br>25–35 kg 187.5 mg/day<br>>35 kg 250 mg/day (I) | q24h |
| Tetracycline* | 250-, 500-mg cap, tab | PO | ≥8 yrs 25–50 mg/kg/day (I) | q6h |
| Ticarcillin/clavulanate, Timentin | 3/0.1-g vial, ivpb, 30/1-g vial | IV | 200–300 mg ticarcillin component/kg/day (adults 12–15 g/day) (I) | q4–6h |
| Tinidazole, Tindamax | 250-, 500-mg tab | PO | 50 mg/kg/day, max 2 g/day (I)<br>See also Chapter 10. | q24h |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Tipranavir, Aptivus | 500-mg/5 mL sol, 250-mg cap | PO | 28 mg/kg/day + ritonavir 12 mg/kg/day (adults: 1,000 mg/day + ritonavir 400 mg/day) (I) | q12h |
| Tobramycin*, Nebcin | 20-mg pediatric vial 10 mg/mL<br>80-mg/2 mL, 1.2-g vial | IV, IM | 3–7.5 mg/kg/day (cystic fibrosis 7–10); see Chapter 2 regarding q24h dosing | q8–24h |
| Tobi | 300-mg ampule | Inhaled | ≥6 yrs 600 mg/day | q12h |
| Trimethoprim/ sulfamethoxazole*, Bactrim, Septra | 80-mg TMP/400-mg SMX tab (single strength)<br>160-mg TMP/800-mg SMX tab (double strength)<br>40-mg TMP/200-mg SMX per 5-mL susp<br>16-mg TMP/80-mg SMX per mL inj soln in 5-,10-, 30-mL vials | PO<br><br><br><br>IV | 8–10 mg TMP/kg/day (I)<br>2 mg TMP/kg/day for UTI prophylaxis (I)<br>15–20 mg TMP/kg/day for *Pneumocystis* pneumonia treatment (I)<br>150 mg TMP/m2/day div bid, 3 times each week (Mon, Tue, Wed; OR Mon, Wed, Fri) for *Pneumocystis* pneumonia prophylaxis (I) | q12h<br>q6–8h<br><br>3 times a week |
| Valacyclovir, Valtrex | 500-mg, 1-g tab | PO | HSV (cold sores): ≥12 yrs, 2 g/day x 1 day (I)<br>VZV: ≥3 mos to 12 yrs, 60 mg/kg/day (III)<br>HSV: ≥3 mos to 12 yrs, 40 mg/kg/day (III)<br>Adults 0.5–3 g/day (I) | q12h<br>q8h<br>q12h<br>q8–24h |
| Valganciclovir, Valcyte | 450 mg-tab | PO | 30 mg/kg/day (II)<br>Adults 900–1,800 mg/day (I) | q12h<br>q12–24h |
| Vancomycin*, Vancocin | 125-, 250-mg cap<br>0.5-, 1-, 5-, 10-g vial<br>0.5-, 1-g IVPB | PO<br>IV | 40 mg/kg/day (I), max 500 mg/day (III)<br>30–40 mg/kg/day (adjusted based on therapeutic drug monitoring) (I)<br>For life-threatening invasive CA-MRSA infection, 60 mg/kg/day to achieve trough serum concentrations above 15 µg/mL (III) | q6h<br>q6–8h |
| Voriconazole, Vfend | 200-mg/5 mL susp<br>50-, 200-mg tab<br>200-mg vial | IV, PO | Aspergillosis: 12–16 mg/kg/day (IV) or 16 mg/kg/day (PO) loading dose (max 800 mg/day) x 1 day, then 14 mg/kg/day (max 400 mg/day) (I); see also Section VI<br>Adults 200–400 mg/day (I) | q12h |

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|---|---|---|---|---|
| Zanamivir, Relenza | 5-mg blister cap for inhalation | Inhaled | Prophylaxis: ≥5 yrs 2 x 5 mg inhalations<br>Treatment: ≥7 yrs 2 x5 mg inhalations | q24h<br>q12h |
| Zidovudine, Retrovir | 50-mg/5 mL syrup*<br>100-mg cap*, 300-mg tab*<br>200-mg/20 mL vial | PO | 4–<9 kg 24 mg/kg/day<br>9–<30 kg 18 mg/kg/day<br>≥30 kg and adults 600 mg/day (I)<br>Or 480 mg/m$^2$/day (max 600 mg/day) (I) | q12h |
| | | IV | 480 mg/m$^2$/day (max 600 mg/day) (II) | q6h |
| | | | 20 mg/m$^2$/hour continuous infusion (II) | |
| Combivir | Combination tab: 300 mg zidovudine + 150 mg lamivudine | | >12 yrs and adults 1 tab/dose (I) | q12h |
| Trizivir | Combination tab with 300 mg abacavir, 300 mg zidovudine, lamivudine | | Adults 1 tab/dose (I) | q12h |

* Available in a generic formulation.

## B. Topical Antimicrobials (Skin, Eye, Ear)

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Acyclovir, Zovirax | 5% cream | Topical | ≥12 yrs Apply to oral lesion | 5 times a day |
| | 5% ointment[a] | | Apply to genital lesion | 6 times a day |
| Azithromycin, Azasite | 1% ophth soln | Ophth | 1 gtt | bid x 2 d then daily x 5 d |
| Bacitracin | ophth ointment | Ophth | Topical Apply to affected eye | q3–4h |
| | ointment[b,c] | Topical | Apply to affected area | bid–qid |
| Besifloxacin, Besivance | 0.6% ophth susp | Ophth | ≥1 yr 1 gtt to affected eye | tid |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Butenafine, Mentax | 1% cream | Topical | ≥12 yrs apply to affected area | qd |
| Butoconazolea, Gynazole-1 | 2% cream | Vaginal | Insert intravaginally | qd x 1 d |
| Femstat-3 | | | | qd x 3 d |
| Chloramphenicol, Chloromycetin | 1% ophth ointment | Ophth | Apply to affected eye | q3h |
| Ciclopiroxb, Loprox | 0.77% cream, gel, lotion | Topical | ≥10 yrs apply to affected area | bid |
| | 1% shampoo[a] | | | q3–4 d |
| | 8% nail lacquer[a] | | | qd |
| Ciprofloxacin, Ciloxan | 0.3% ophth soln[b] | Ophth | ≥12 yrs apply to affected eye | q2h x 2 d then q4h x 5 d |
| | 0.3% ophth ointment[a] | | | q8h x 2 d then q12h x 5 d |
| Ciprofloxacin, Cetraxal Cipro HC (plus hydrocortisone) Otic | 0.2% otic soln | Otic | ≥1 yr apply 3 drops to affected ear | bid x 7 d |
| Ciprofloxacin + dexamethasone, Ciprodex | 0.3% otic soln | Otic | ≥6 months apply 4 drops to affected ear | bid x 7 d |
| Clindamycin, Clindesse | 2% cream | Vaginal | Adolescents 1 applicatorful intravaginally | One time |
| Cleocin[b] | 100-mg supp | | 1 supp intravaginally | qhs x 3 d |
| | 2% cream | | 1 applicatorful intravaginally | qhs x 3 d–7 d |
| Cleocin-T[b] | 1% solution, gel, lotion | Topical | Apply to affected area | qd–bid |
| Evoclin | 1% foam | | | qd |

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|---|---|---|---|---|
| Clindamycin + benzoyl peroxide, Benzaclin, Acanya | 1% gel<br>1.2% gel | Topical | ≥12 yrs apply to affected area<br>Apply small amount to face | bid<br>q24h |
| Clindamycin + tretinoin, Ziana | 1.2% gel | Topical | Apply small amount to face | hs |
| Clotrimazole[b,c], Lotrimin | 1% cream, lotion, solution | Topical | Apply to affected area | bid |
| Gyne-Lotrimin-7 | 1% cream,100-mg supp | Vaginal | Adolescents intravaginally | qhs x 7–14 d |
| Gyne-Lotrimin-3 | 2% cream, 200-mg supp | | | qhs x 3d |
| Clotrimazole + betamethasone, Lotrisoneb | 1% cream, lotion | Topical | ≥12 yrs apply to affected area | bid |
| Coly-Mycin S Colistin + neomycin + hydrocortisone | otic suspension | Otic | Apply 3–4 drops to affected ear canal; may use with wick | q6–8h |
| Cortisporin x Bacitracin + neomycin + polymyxin b + hydrocortisone | ointment[a] | Ophth<br>Topical | Apply to affected eye<br>Apply to affected area | q4h<br>bid–qid |
| Neomycin + polymyxin b + hydrocortisone | ophth solution[a]<br>otic soln, suspension<br>cream[a] | Ophth<br>Otic<br>Topical | 1–2 drops to affected eye<br>3 drops to affected ear<br>Apply to affected area | q4h<br>tid–qid |
| Econazole[b], Spectazole | 1% cream | Topical | Apply to affected area | bid |
| Erythromycin | 0.5% ophth ointment[b] | Ophth | Apply to affected eye | q4h |
| Eryderm, Erygel | 2% solutionb, gel[a,b] | Topical | Apply to affected area | bid |
| Ery Pads | 2% pledgets[b] | | | |
| Akne-mycin | 2% ointment | | | |
| Erythromycin + benzoyl peroxide, Benzamycin[b] | 3% gel | Topical | ≥12 yrs apply to affected area | qd–bid |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Gatifloxacin, Zymar | 0.3% ophth soln | Ophth | Apply to affected eye | q2h x 2 d then q6h x 5 d |
| Gentamicin[b], Garamycin | 0.1% cream, ointment | Topical | Apply to affected area | tid–qid |
| | 0.3% ophth soln, ointment | Ophth[a] | Apply to affected eye | q1–4h (sol) q4–8h (oint) |
| Gentamicin + prednisolone, Pred-G[a] | 0.3% ophth soln, ointment | Ophth | Apply to affected eye | q1–4h (sol) qd–tid (oint) |
| Ketoconazole | | | | |
| Nizoral | shampoo[a,b] | Topical | Apply to affected area | qd (x1 for sham-poo) |
| | 2% cream[b] | Topical | ≥12 yrs apply to affected area | q3–4 d |
| Nizoral A-D[c] | 1% shampoo | Topical | ≥12 yrs apply to affected area | bid |
| Extina®, Xolegel | 2% foam, gel | Topical | ≥12 yrs apply to affected area | bid |
| Levofloxacin | | Ophth | Apply to affected eye | |
| Iquix | 1.5% ophth soln | | | q1–4h |
| Quixin | 0.5% ophth soln | | | q1–4h |
| Mafenide, Sulfamylon | 8.5% cream | Topical | Apply to burn | qd–bid |
| | 5-g powder for reconstitution | | To keep burn dressing wet | q4–8h as needed |
| Malathion, Ovide | 0.5% solution | Topical | ≥6 yrs apply to hair and scalp | Once |
| Maxitrola,[b], neomycin + polymyxin b + dexamethasone | suspension, ointment | Ophth | Apply to affected eye q1–4h (susp) | q4h (oint) |

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|---|---|---|---|---|
| Metronidazole[a] | | | | |
| Metrogel-Vaginal[b] | 0.75% vag gel | Vaginal | 1 applicatorful intravaginally | qd–bid |
| Metrocream-gel, – lotion | 0.75% cream[b], gel[b], lotion[b] | Topical | | bid qd |
| Noritate, Metrogel | 1% cream, gel | | | |
| Miconazole | | | | |
| Micatin[b,c] and others | 2% cream, pwd, ointment, spray, lotion, gel | Topical | Apply to affected area | qd–bid |
| Fungoid[c] | 2% tincture | | | bid |
| Vusion | 0.25% ointment | | ≥1 month: to diaper dermatitis | Each diaper change x 7 d |
| Monistat-1 | 1.2-g vag supp | Vaginal | Adolescents: Intravaginally | once |
| Monistat-3[b,c] | 4% cream, 200-mg supp | | | qhs x 3 d |
| Monistat-7[b,c] | 2% cream, 100-mg supp | | | qhs x7 d |
| Moxifloxacin, Vigamox | 0.5% ophth soln | Ophth | Apply to affected eye | tid |
| Mupirocin, Bactroban | 2% ointment[b], cream, nasal ointment | Topical | Apply to infected skin or nasal mucosa | tid |
| Naftifine, Naftin[a] | 1% cream, gel | Topical | Apply to affected area | Cream qd; Gel bid |
| Natamycin, Natacyn[a] | 5% ophth soln | Ophth | Apply to affected eye | q1–4h |
| Neosporin[b] | | | | |
| Bacitracin + neomycin + polymyxin B | ophth ointment[a] | Ophth | Apply to affected eye | q4h |
| | topical ointment[c] | Topical | Apply to affected area | bid–qid |
| Gramicidin + neomycin + polymyxin B | ophth soln[a] | Ophth | Apply to affected eye | q4h |
| Nystatin[b], Mycostatin | 100,000 units/g cream, ointment, powder | Topical | Apply to affected area | bid–qid |
| | 100,000 vag tablet | Vaginal | Adolescents: intravaginally | qd |
| Nystatin + triamcinolone 0.1% Mycolog II[b] | 100,000 units/g cream, ointment | Topical | Apply to affected area | bid |

| Generic and Trade Names | Dosage Form | Route | Dose (evidence grade) | Interval |
|---|---|---|---|---|
| Ofloxacin[b], Floxin Otic | 0.3% otic soln | Otic | 5–10 drops to affected ear | qd–bid |
| Ocuflox | 0.3% ophth soln | Ophth | Apply to affected eye | q1–6h |
| Oxiconazole, Oxistat | 1% cream, lotion | Topical | Apply to affected area | qd–bid |
| Penciclovir, Denavir | 1% topical cream | Topical | Apply to affected area | q2h while awake x4d |
| Permethrin, Nix[b,c] | 1% cream | Topical | Apply to hair/scalp | Once x 10 minutes |
| Elimite[b] | 5% cream | | Apply to all skin surfaces | Once x 8–14h |
| Polysporin[b] | ophth ointment[a] | Ophth | Apply to affected eye | q4–6h |
| polymyxin B + bacitracin | ointmentc, powder[c] | Topical | Apply to affected area | |
| Polytrim[b] trimethoprim + polymyxin B | ophth soln | Ophth | Apply to affected eye | q3–4h |
| Pyrethrins[b], Rid | 0.3% lotion, gel, shampoo | Topical | Apply to affected area | Once x 10 minutes |
| Retapamulin, Altabax | 1% ointment | Topical | Apply thin layer to affected area | bid x 5 d |
| Sertaconazole, Ertaczol | 2% cream | Topical | Apply to tinea pedis | bid x 4 weeks |
| Silver Sulfadiazine[a,b], Silvadene | 1% cream | Topical | Apply to affected area | qd–bid |
| Sulconazole, Exelderm | 1% solution, cream | Topical | Apply to affected area | qd–bid |

| | | | | |
|---|---|---|---|---|
| Sulfacetamide sodium[b]<br>Sodium- Sulamyd | 10, 15, 30% soln<br>10% ophth ointment | Ophth | Apply to affected eye | q1–3h<br>qid |
| Klaron | 10% topical lotion | Topical | ≥12 yrs apply to affected area | bid–qid |
| Sulfacetamide sodium + prednisolone, Blephamide[b] | 10% ophth ointment<br>10% opth soln | Ophth | Apply to affected eye | tid–qid<br>q4h |
| Sulfacetamide sodium + fluorometholone, FML-S | 10% opth soln | Ophth | Apply to affected eye | qid |
| Terbinafine[c], Lamisil-AT | 1% cream[b], spray, gel, soln | Topical | Apply to affected area | qd–bid |
| Terconazole[a,b], Terazol-3<br>Terazol-7 | 0.4% cream, 80 mg supp<br>0.8% cream | Vaginal | | |
| Tobramycin[b], Tobrex | 0.3% ophth soln, ointment | Ophth | Apply to affected eye | q1–4h (sol)<br>q4–8h (oint) |
| Tobramycin + dexamethasone, Tobradex | 0.3% ophth soln[b], ointment | Ophth | Apply to affected eye | q2–6h (sol)<br>q6–8h (oint) |
| Tobramycin + fluorometholone, Tobrasone | 0.3% ophth soln[b], ointment | Ophth | Apply to affected eye | q2–6h (sol)<br>q6–8h (oint) |
| Trifluridine[b], Viroptic | 1% ophth soln | Ophth | 1 drop (max 9 drops/day) | q2h |
| Tolnaftate, Tinactin | 1% cream, soln, powder, spray | Topical | Apply to affected area | bid |

[a] Not approved for children.
[b] Generic available.
[c] Over-the-counter.

## 12. Alphabetic Listing of Trade Names

**Trade Name** (Company)
—generic name, dosage form if topical
(Some named brands may no longer be commercially available.)

### A

**Abelcet** (Enzon)
— amphotericin B, lipid complex
**Acanya** (Arcutis)
— clindamycin 1.2%/benzoyl peroxide 2.5% topical gel
**Albenza** (GlaxoSmithKline)
— albendazole
**Alinia** (Romark)
— nitazoxanide
**AmBisome** (Astellas)
— amphotericin B liposomal
**Amikin** (Apothecon; generic)
— amikacin
**Amoxil** (GlaxoSmithKline; generic)
— amoxicillin
**Amphotec** (Three Rivers)
— amphotericin B cholesteryl sulfate
**Ancef** (GlaxoSmithKline; generic)
— cefazolin
**Ancobon** (ICN)
— flucytosine
**Antiminth**
— pyrantel pamoate
**Aptivus** (Boehringer Ingelheim)
— tipranavir
**Aralen** (Sanofi; generic)
— chloroquine phosphate
**Atripla** (Bristol-Myers Squibb)
— efavirenz/emtricitabine/tenofovir
**Augmentin** (GlaxoSmithKline; generic)
— amoxicillin/clavulanate potassium
**Avelox** (Bayer)
— moxifloxacin
**Azactam** (Bristol-Myers Squibb)
— aztreonam

### B

**Bactrim** (Roche; generic)
— trimethoprim/sulfamethoxazole
**Bactroban** (GlaxoSmithKline; generic)
— mupirocin 2% ointment, cream (topical)
**Benemid** (Merck; generic)
— probenecid
**Besivance** (Bausch & Lomb)
— besifloxacin 0.6% ophthalmic suspension
**Biaxin** (Abbott; generic)
— clarithromycin
**Bicillin C-R** (King; generic)
— benzathine/procaine penicillin G
**Bicillin L-A** (King; generic)
— benzathine penicillin G
**Biltricide** (Bayer)
— praziquantel
**Blephamide** (Allergan)
— prednisolone acetate/sulfacetamide sodium 10% (ophth drops)
**Blephamide** S.O.P. (Allergan)
— prednisolone acetate/sulfacetamide sodium 10% (ophth ointment)
**Bleph-10** (Allergan; generic)
— sulfacetamide sodium 10% (ophth drops)
**Bleph-30** (Allergan; generic)
— sulfacetamide sodium 30% (ophth drops)

### C

**Cancidas** (Merck)
— caspofungin
**Capastat** (Lilly)
— capreomycin
**Ceclor** (Lilly; generic)
— cefaclor
**Cedax** (Shionogi)
— ceftibuten
**Cefizox** (Astellas)
— ceftizoxime
**Cefotan** (AstraZeneca)
— cefotetan
**Ceftin** (GlaxoSmithKline; generic)
— cefuroxime axetil
**Cefzil** (Bristol-Myers Squibb; generic)
— cefprozil
**Cetraxal** (Laboratorios Salvat)
— ciprofloxacin 0.2% otic solution

**Chloromycetin** (Parkedale; generic)
— chloramphenicol
**Ciloxan** (Alcon; generic)
— ciprofloxacin (ophth drops, ointment)
**Cipro** (Bayer; generic)
— ciprofloxacin
**Cipro HC** (Allergan; generic)
— ciprofloxacin (otic drops)
**Claforan** (Sanofi-Aventis; generic)
— cefotaxime
**Cleocin** (Pharmacia & Upjohn; generic)
— clindamycin
**Coly-Mycin M** (Parkedale)
— colistimethate (colistin)
**Coly-Mycin S** (Parkedale)
— colistin/neomycin/hydrocortisone (otic drops)
**Combivir** (GlaxoSmithKline)
— zidovudine/lamivudine
**Copegus** (Roche; generic)
— ribavirin
**Cortisporin** (Monarch; generic)
— bacitracin/hydrocortisone/neomycin/polymyxin B (topical ointment, ophth ointment)
— hydrocortisone/neomycin/polymyxin B (topical cream, ophth drops, otic)
**Crixivan** (Merck)
— indinavir
**Cubicin** (Cubist)
— daptomycin
**Cytovene** (Roche; generic)
— ganciclovir

## D

**Daraprim** (GlaxoSmithKline)
— pyrimethamine
**Declomycin** (Lederle; generic)
— demeclocycline
**Denavir** (Novartis)
— penciclovir 1% cream
**Diflucan** (Pfizer; generic)
— fluconazole
**Doryx** (Faulding)
— doxycycline
**Doxy** (APP)
— doxycycline inj
**Duricef** (Warner Chilcott; generic)
— cefadroxil
**Dynapen** (Bristol-Myers Squibb; generic)
— dicloxacillin

## E

**E. E. S.** (Abbott; generic)
— erythromycin ethylsuccinate
**Elimite Cream** (Allergan; generic)
— permethrin 5% (topical)
**Emtriva** (Gilead)
— emtricitabine
**E-Mycin** (Abbott; generic)
— erythromycin base
**Epivir** (GlaxoSmithKline; generic)
— lamivudine
**Epzicom** (GlaxoSmithKline)
— lamivudine/abacavir
**Eraxis** (Roerig)
— anidulafungin
**ERYC** (Mayne Pharma; generic)
— erythromycin base
**Erygel** (Merz; generic)
— 2% erythromycin gel (topical)
**EryPed** (Abbott; generic)
— erythromycin ethylsuccinate
**Ery-Tab** (Abbott; generic)
— erythromycin base
**Erythrocin** (Abbott; generic)
— erythromycin lactobionate
**Erythrocin Stearate** (Abbott; generic)
— erythromycin stearate
**Exelderm** (Westwood Squibb)
— sulconazole 1% (topical)

## F

**Factive** (Oscient)
— gemifloxacin
**Famvir** (Novartis; generic)
— famciclovir
**Fansidar** (Roche)
— sulfadoxine/pyrimethamine
**Flagyl** (Searle; generic)
— metronidazole
**Floxin** (Ortho-McNeil; generic)
— ofloxacin

**Floxin otic** (Daiichi; generic)
— ofloxacin (otic soln)
**Flumadine** (Forest; generic)
— rimantadine
**FML-S** (Allergan)
— fluorometholone/sulfacetamide sodium (ophth drops)
**Fortaz** (GlaxoSmithKline; generic)
— ceftazidime
**Fortovase** (HLR)
— saquinavir
**Foscavir** (AstraZeneca; generic)
— foscarnet
**Fulvicin-U/F** (Schering; generic)
— griseofulvin microcrystalline
**Fungizone** (Apothecon; generic)
— amphotericin B desoxycholate
**Furadantin** (Sciele)
— nitrofurantoin
**Fuzeon** (Roche)
— enfuvirtide

## G

**Gantrisin** (Roche)
— sulfisoxazole
**Garamycin** (Schering; generic)
— gentamicin 0.3% (ophth drops)
**Grifulvin V** (OrthoNeutrogena; generic)
— griseofulvin microcrystalline
**Gris-PEG** (Pedinol)
— griseofulvin ultramicrocrystalline

## H

**Hepsera** (Gilead)
— adefovir
**Hiprex** (Sanofi-Aventis)
— methenamine hippurate
**Hivid** (Roche)
— zalcitabine
**Humatin** (Parke-Davis; generic)
— paromomycin

## I

**Intelence** (Tibotec)
— etravirine
**Invanz** (Merck)
— ertapenem
**Invirase** (Roche, HLR)
— saquinavir mesylate
**Iquix** (Santen)
— levofloxacin 1.5% (ophth drops)
**Isentress** (Merck)
— raltegravir
**Isopto-Cetamide** (Alcon; generic)
— sulfacetamide sodium 15% (ophth drops)

## K

**Kaletra** (Abbott)
— lopinavir/ritonavir
**Kantrex** (Bristol-Myers Squibb; generic)
— kanamycin
**Keflex** (Advancis; generic)
— cephalexin
**Keftab** (Lilly; generic)
— cephalexin
**Kefurox** (Lilly; generic)
— cefuroxime
**Kefzol** (Lilly; generic)
— cefazolin
**Ketek** (Sanofi)
— telithromycin
**Klaron** (Dermik)
— sulfacetamide sodium 10% (topical)
**Kwell** (Reed & Carnrick; generic)
— lindane

## L

**Lamisil** (Novartis; generic)
— terbinafine
**Lamprene** (Novartis)
— clofazimine
**Lariam** (Roche; generic)
— mefloquine
**Levaquin** (Ortho-McNeil; generic)
— levofloxacin
**Lexiva** (GlaxoSmithKline)
— fosamprenavir
**Lincocin** (Pfizer)
— lincomycin
**Lipsovir** (Medivir)
— acyclovir 5%/hydrocortisone 1% cream (topical)
**Loprox** (Medicis; generic)
— ciclopirox 0.77% (topical)

**Lotrimin** (Schering; generic)
— clotrimazole 1% (topical)

## M

**Macrodantin** (Procter & Gamble; generic)
— nitrofurantoin macrocrystalline
**Malarone** (GlaxoSmithKline)
— atovaquone/proguanil
**Maxipime** (Bristol-Myers Squibb; generic)
— cefepime
**Maxitrol** (Falcon; generic)
— dexamethasone/neomycin/polymyxin B (ophth)
**Mefoxin** (Merck; generic)
— cefoxitin
**Mentax** (Bertek; generic)
— butenafine 1% (topical)
**Mepron** (GlaxoSmithKline)
— atovaquone
**Merrem** (AstraZeneca)
— meropenem
**Minocin** (Wyeth; generic)
— minocycline
**Monistat** (Ortho; generic)
— miconazole
**Monodox** (Watson; generic)
— doxycycline
**Monurol** (Zambon)
— fosfomycin tromethamine
**Moxatag** (MiddleBrook)
— amoxicillin XR
**Myambutol** (Stat-Trade; generic)
— ethambutol
**Mycamine** (Fujisawa)
— micafungin
**Mycifradin** (Pharmacia & Upjohn, generic)
— nystatin
**Mycelex** (Bayer; generic)
— clotrimazole
**Mycobutin** (Pharmacia & Upjohn)
— rifabutin
**Mycostatin** (Bristol-Myers Squibb; generic)
— nystatin

## N

**Naftin** (Merz)
— naftifine 1% (topical)
**Nallpen** (GlaxoSmithKline; generic)
— nafcillin
**Nebcin** (Lilly; generic)
— tobramycin
**Nebupent** (APP)
— pentamidine (for inhalation)
**NegGram** (Sanofi; generic)
— nalidixic acid
**Neosporin** (Pfizer; generic)
— bacitracin/neomycin/polymyxin B (topical)
**Neosporin** (Monarch; generic)
— bacitracin/neomycin/polymyxin B (ophth ointment)
— gramicidin/neomycin/polymyxin B (ophth drops)
**Neosporin G.U. Irrigant** (Monarch)
— neomycin/polymyxin B
**Nix** (Insight; generic)
— permethrin 1% (topical)
**Nizoral** (Janssen, McNeil; generic)
— ketoconazole
**Noroxin** (Merck; generic)
— norfloxacin
**Norvir** (Abbott)
— ritonavir
**Noxafil** (Schering)
— posaconazole
**Nydrazid** (Sandoz; generic)
— isoniazid

## O

**Ocuflox** (Allergan; generic)
— ofloxacin (ophth)
**Omnicef** (Abbott; generic)
— cefdinir
**Omnipen** (Wyeth-Ayerst; generic)
— ampicillin
**Oxistat** (GlaxoSmithKline)
— oxiconazole 1% (topical)

## P

**PCE** (Abbott)
— erythromycin base
**Pediazole** (Ross; generic)
— erythromycin ethylsuccinate/sulfisox-azole acetyl

**Penlac** (Dermik; generic)
— ciclopirox 8% (topical)
**Pentam** (APP; generic)
— pentamidine isethionate
**Pen-Vee K** (Wyeth-Ayerst; generic)
— penicillin V potassium
**Pfizerpen** (Pfizer; generic)
— penicillin G potassium
**Pin-X** (Effcon; generic)
— pyrantel pamoate
**Plaquenil** (Sanofi; generic)
— hydroxychloroquine
**Polysporin** (Pfizer; generic)
— polymyxin B/bacitracin (topical)
**Polysporin** (Monarch; generic)
— polymyxin B/bacitracin (ophth)
**Polytrim** (Allergan; generic)
— trimethoprim/polymyxin B (ophth)
**Pred-G** (Allergan)
— prednisolone/gentamicin (ophth)
**Prezista** (Tibotec)
— darunavir
**Priftin** (Sanofi-Aventis)
— rifapentine
**Primaquine** (Sanofi)
— primaquine phosphate
**Primaxin** (Merck)
— imipenem/cilastatin
**Proloprim** (Monarch)
— trimethoprim

## Q

**Quixin** (Santen)
— levofloxacin 0.5% (ophth drops)

## R

**Rebetol** (Schering; generic)
— ribavirin
**Relenza** (GlaxoSmithKline)
— zanamivir
**Rescriptor** (Agouron)
— delavirdine
**Retrovir** (GlaxoSmithKline; generic)
— zidovudine
**Reyataz** (Bristol-Myers Squibb)
— atazanavir
**Rifadin** (Sanofi-Aventis; generic)
— rifampin
**Rifamate** (Sanofi-Aventis; generic)
— rifampin/isoniazid
**Rifater** (Sanofi-Aventis)
— rifampin/isoniazid/pyrazinamide
**Rocephin** (Roche; generic)
— ceftriaxone

## S

**Selzentry** (Pfizer)
— maraviroc
**Septra** (Burroughs-Wellcome; generic)
— trimethoprim/sulfamethoxazole
**Seromycin** (Lilly)
— cycloserine
**Spectazole** (J and J; generic)
— econazole 1% (topical)
**Spectracef** (Cornerstone)
— cefditoren
**Sporanox** (Janssen; generic)
— itraconazole
**Stromectol** (Merck)
— ivermectin
**Suprax** (Wyeth; generic)
— cefixime
**Sustiva** (Bristol-Myers Squibb)
— efavirenz
**Symmetrel** (Endo; generic)
— amantadine
**Synagis** (MedImmune)
— palivizumab
**Synercid** (Sanofi-Aventis; generic)
— Quinupristin/dalfopristin

## T

**T-Stat** (Westwood Squibb; generic)
— erythromycin 2% (topical soln)
**Tamiflu** (Roche)
— oseltamivir
**Tazicef** (GlaxoSmithKline; generic)
— ceftazidime
**Tazidime** (Lilly; generic)
— ceftazidime
**Thalomid** (Celgene)
— thalidomide
**Timentin** (GlaxoSmithKline)
— ticarcillin/clavulanate
**Tindamax** (Mission)
— tinidazole

**Tobi** (Chiron)
— tobramycin inhalational
**Tobradex** (Alcon; generic)
— dexamethasone/tobramycin (ophth)
**Tobrex** (Falcon; generic)
— tobramycin (ophth)
**Trecator-SC** (Wyeth)
— ethionamide
**Trizivir** (GlaxoSmithKline)
— zidovudine/lamivudine/abacavir
**Truvada** (Gilead)
— emtricitabine/tenofovir
**Tygacil** (Wyeth)
— tigecycline
**Tyzeka** (Novartis)
— telbivudine

## U

**Unasyn** (Pfizer; generic)
— ampicillin/sulbactam
**Unipen** (Wyeth Ayerst; generic)
— nafcillin

## V

**Valtrex** (GlaxoSmithKline; generic)
— valacyclovir
**Vancocin** (Lilly; generic)
— vancomycin
**Vantin** (Pfizer; generic)
— cefpodoxime
**Vasocidin** (Novartis; generic)
— sulfacetamide sodium/prednisolone (ophth)
**Vermox** (McNeil; generic)
— mebendazole
**Vfend** (Pfizer)
— voriconazole
**Vibramycin** (Pfizer; generic)
— doxycycline
**Vibra-Tabs** (Pfizer)
— doxycycline hyclate
**Videx** (Bristol-Myers Squibb; generic)
— didanosine
**Vigamox** (Alcon)
— moxifloxacin (ophth)
**Viracept** (Agouron)
— nelfinavir
**Viramune** (Boehringer Ingelheim; generic)
— nevirapine
**Virazole** (Valeant)
— ribavirin (inhalation)
**Viread** (Gilead)
— tenofovir
**Viroptic** (Monarch; generic)
— trifluridine (ophth)
**Vistide** (Gilead)
— cidofovir

## W

**Wycillin** (Wyeth-Ayerst; generic)
— penicillin G procaine

## X

**Xifaxan** (Salix)
— rifaximin

## Y

**Yodoxin** (Glenwood)
— iodoquinol

## Z

**Zerit** (Bristol-Myers Squibb, generic)
— stavudine
**Ziagen** (GlaxoSmithKline)
— abacavir
**Zinacef** (GlaxoSmithKline; generic)
— cefuroxime sodium
**Zithromax** (Pfizer; generic)
— azithromycin
**Zosyn** (Wyeth)
— piperacillin/tazobactam
**Zovirax** (GlaxoSmithKline; generic)
— acyclovir
**Zymar** (Allergan; generic)
— gatifloxacin (ophth)
**Zyvox** (Pfizer)
— linezolid

## 13. Sequential Parenteral-Oral Antibiotic Therapy for Serious Infections

Bacterial pneumonias, bone and joint infections, and deep tissue abscesses often require prolonged antibiotic therapy. Many other infections, such as cellulitis or pyelonephritis, require initial parenteral therapy to control the growth and spread of pathogens. However, intravenous (IV) therapy is unpleasant for the child and carries a hazard of nosocomial infection during hospitalization. For the beta-lactam class of antibiotics, absorption of orally administered antibiotics in standard dosages provides peak serum concentrations that are only 5% to 10% of those achieved with IV or intramuscular administration. However, many newer antibiotics of the fluoroquinolone and oxazolidinone class have excellent absorption of their oral formulations and provide virtually the same tissue antibiotic exposure at a particular mg/kg dose, compared with the exposure when the antibiotic is given at that dose IV. Following initial parenteral therapy of serious infections, it may be possible to provide oral antibiotic therapy to achieve the tissue antibiotic exposure that is required for cure. One must also assume that the parent and child are compliant with the administration of each antibiotic dose, and that the parents will seek medical care if the clinical course does not continue to improve for their child.

High-dose oral beta-lactam antibiotic therapy of osteoarticular infections, associated with achieving a particular level of bactericidal activity in serum, has been associated with treatment success since 1978. While most hospital laboratories no longer offer bactericidal assays, the need to achieve bactericidal activity with high-dose oral therapy, explained below, remains important.

**Convalescent Oral Beta-Lactam Therapy**

1. Comparable mg/kg dosages of parenteral and oral beta-lactam medications often result in comparable tissue concentrations 4 to 6 hours after a dose.
2. The momentary high serum concentrations that occur during IV administration of beta-lactam antibiotics may provide for better tissue penetration, but killing of bacteria by beta-lactam antibiotics is not dependent on the height of the antibiotic concentration, but on the time that the antibiotic is present at the site of infection at concentrations above the minimum inhibitory concentrations.
3. For abscesses in soft tissues, joints, and bones, most organisms are removed by surgical drainage and killed by the initial parenteral therapy. When the signs and symptoms of infection begin to resolve, usually within 5 to 7 days, continuing IV therapy may not be required as a normal host response begins to assist in clearing the infection.
4. Large dosage oral beta-lactam therapy (based on in vitro susceptibilities) provides the tissue antibiotic exposure required to eradicate remaining pathogens as the tissue perfusion improves. Begin with a dosage 2 to 3 times normal dosage (eg, 75–100 mg/kg/day of dicloxacillin or 100–150 mg/kg/day of cephalexin).
5. Follow the child clinically for a continued response on oral therapy; follow C-reactive protein concentrations and erythrocyte sedimentation rate to make sure that the infection is continuing to respond to the antibiotic and dosage you selected. High-dose prolonged oral beta-lactam therapy may be associated with reversible neutropenia; checking for hematologic toxicity every few weeks during therapy should be considered.

## 14. Antibiotic Therapy in Patients With Renal Failure

For antiinfective drugs recently approved by the US Food and Drug Administration (FDA), information on drug exposure in patients with varying degrees of renal failure is placed in the package label and posted on the FDA Web site (http://dailymed.nlm.nih.gov/dailymed/about.cfm). Information on older agents is often lacking, and information on children in particular may never have been collected prospectively. A complete list of antibiotics and dosing recommendations in renal failure, and for children on dialysis, is beyond the scope of this chapter, but an exhaustive, annually updated reference that includes information on dosing adjustments in renal failure exists: *AHFS Drug Information 2009,* published and available for computer or PDA by the American Society of Hospital Pharmacists, Inc., Bethesda, MD (http://www.ahfsdruginformation.com/).

Many commonly used antimicrobials are excreted primarily by the kidneys; therefore, when significant renal impairment is present, either downward adjustments in dosages must be made or the intervals between doses must be lengthened. Drugs that are excreted by the kidney and have a narrow therapeutic index, with toxicity documented at serum concentrations not too much greater than therapeutic concentrations, must be monitored closely. The aminoglycosides and vancomycin are prime examples of these antibiotics. For those antibiotics excreted by the kidney, but with little toxicity at high serum concentrations, such as the beta-lactam antibiotics, only moderate changes in dosages need to be made. Drugs such as metronidazole that are metabolized by the liver and those excreted significantly by the liver, such as azithromycin, nafcillin, and ceftriaxone, do not require adjustments in dosing.

In some circumstances, dosing drugs in children with decreased renal function is best achieved by therapeutic drug monitoring of serum antibiotic concentrations. Many computer programs are available that integrate information on the serum creatinine (or creatinine clearance) and antibiotic half-life, which allows for estimation of the best mg/kg dosage, administered at a specified interval in order to attain therapeutic but non-toxic peak and trough serum concentrations. Many hospital-based pharmacists can assist with this determination. The following calculation (commonly known as the Schwartz method[1,2]) is used for estimating creatinine clearance (and therefore antibiotic clearance) in infants and children (1–18 years of age) with stable renal function:

CrCl (mL/min/1.73 m2 BSA) = (κ x height in cm) ÷ (serum creatinine), where BSA is body surface area and κ (a proportionality constant that varies with age and sex) is:

| | |
|---|---|
| Preterm infants | 0.33 |
| Full-term infants | 0.45 |
| Children and adolescent girls | 0.55 |
| Adolescent boys | 0.78 |

In the absence of computer programs, one can administer the customary initial loading mg/kg dose, and until antibiotic assay results are available, make an estimate of the appropriate dosage based on past experience of rates of excretion related to the degree of renal failure. Alterations in dosage and/or interval are made to achieve serum concentrations and therefore exposure of antibiotic at the site of infection, similar to those in patients with normal renal function.

## 15. Adverse Reactions to Antimicrobial Agents

A good rule of clinical practice is to be suspicious of an adverse drug reaction when a patient's clinical course deviates from the expected. This section focuses on reactions that may require close observation or laboratory monitoring either because of their frequency or because of their severity. For more detailed listings of reactions, review the US Food and Drug Administration (FDA)-approved package labels or reference texts (such as *AHFS Drug Information 2009,* American Society of Hospital Pharmacists, Inc., Bethesda, MD). In addition, FDA-approved package labels for most drugs can be accessed online at the National Library of Medicine (NLM) site, with information from the FDA at http://dailymed.nlm.nih.gov/dailymed/about.cfm. For many of the more recently approved antibiotics, adverse reaction rates in both antibiotic- and comparator-treated populations are provided to allow you to draw your own conclusions about safety and the risk of adverse reactions. The NLM provides an online drug information service (Medline Plus), accessed at http://www.nlm.nih.gov/medlineplus/ druginformation.html.

### Antibacterial Drugs

#### *Aminoglycosides*

Any of the aminoglycosides can cause serious nephrotoxicity and ototoxicity. Monitor all patients receiving aminoglycoside therapy for more than a few days for renal function with periodic determinations of the blood urea nitrogen and creatinine to assess potential problems of drug accumulation with deteriorating renal function. Common practice is to measure the peak serum concentration 0.5 to 1.0 hour after a dose to make sure one is in a safe and therapeutic range and to measure a trough serum concentration immediately preceding a dose to assess for drug accumulation and pending toxicity. Monitoring is especially important in patients with any degree of renal insufficiency. Elevated trough concentrations (>2 mg/mL for gentamicin and tobramycin, and >10 mg/mL for amikacin) suggest drug accumulation and should be a warning to decrease the dose, even if the peak is not yet elevated. Renal toxicity may be related to the total exposure of the kidney to the aminoglycoside over time. With once daily administration regimens, peak values are 2 to 3 times greater, and trough values are usually very low. Nephrotoxicity seems to be less common in adults with once daily (as opposed to 3 times daily) dosing regimens; but data are lacking in children.[1]

The "loop" diuretics (furosemide and bumetanide) potentiate the ototoxicity of the aminoglycosides. Aminoglycosides potentiate botulinum toxin and are to be avoided in young infants with infant botulism.

The aminoglycosides are well tolerated via intramuscular and intravenous (IV) routes of administration. Minor side effects, such as allergies, rashes, and drug fever, are rare.

#### *Beta-Lactam Antibiotics*

The most feared reaction to penicillins, anaphylactic shock, is extremely rare, and no absolutely reliable means of predicting its occurrence exists. For most infections, alternative therapy to penicillin or beta-lactams exists. However, in certain situations, the benefits of penicillin or a beta-lactam may outweigh the risk of anaphylaxis, requiring that skin testing and desensitization be performed in a medically supervised environment. The commercially available skin testing material, benzylpenicilloyl polylysine (Pre-Pen, AllerQuest) was approved and marketed in September 2009. It contains the major determinants thought to be primarily responsible for urticarial reactions, but does not contain the minor determinants that are more often associated with anaphylaxis. No commercially available minor determinant mixture is available. Some authorities use a dilute solution of freshly prepared benzyl penicillin G as the skin test material in place of a standardized mixture of minor determinants. Testing should be

performed on children with a credible history of a possible reaction to a penicillin before these drugs are used in either oral or parenteral formulations. Anaphylaxis has been reported in adults receiving penicillin skin testing. A recent review provides a more in-depth discussion,[2] with additional information on desensitization available at the Centers for Disease Control and Prevention Web site (www.cdc.gov/STD/treatment/2006/penicillin-allergy.htm#skintesting). Cross-reactions between classes of beta-lactam antibiotics (penicillins, cephalosporins, carbapenems, and monobactams) occur at a rate of between 5% to 20%. No commercially available skin testing reagent has been developed for beta-lactam antibiotics other than penicillin.

Amoxicillin and other aminopenicillins are associated with minor adverse effects. Diarrhea, oral or diaper area candidiasis, morbilliform, and blotchy rashes are not uncommon. The kinds of non-urticarial rashes that may occur while a child is receiving amoxicillin are not known to predispose to anaphylaxis and may not actually be caused by amoxicillin itself; they do not represent a routine contraindication to subsequent use of amoxicillin or any other penicillins. Rarely, beta-lactams cause serious, life-threatening pseudomembranous enterocolitis due to suppression of normal bowel flora and overgrowth of toxin-producing strains of *Clostridium difficile*. Drug-related fever may occur; serum sickness is uncommon. Reversible neutropenia and thrombocytopenia may occur with any of the beta-lactams and seem to be related to dose and duration of therapy.

The cephalosporins have been a remarkably safe series of antibiotics. The third-generation cephalosporins cause profound alteration of normal flora on mucosal surfaces, and all have caused pseudomembranous colitis on rare occasions. Ceftriaxone commonly causes loose stools, but it is rarely severe enough to require stopping therapy. Ceftriaxone in high dosages may cause fine "sand" (a calcium complex of ceftriaxone) to develop in the gallbladder. In adults, and rarely in children, these deposits may cause biliary tract symptoms; these are not gallstones, and the deposits are reversible after stopping the drug. In neonates receiving calcium-containing hyperalimentation concurrent with IV ceftriaxone, precipitation of ceftriaxone-calcium in the bloodstream resulting in death has been reported, leading to an FDA warning against the concurrent use of ceftriaxone and parenteral calcium in infants younger than 28 days (http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm109103.htm). As ceftriaxone may also displace bilirubin from albumin-binding sites and increase free bilirubin in serum, the antibiotic is not routinely used in neonatal infections until the normal physiologic jaundice is resolving after the first few weeks of life. Cefotaxime is the preferred IV third-generation cephalosporin for neonates.

Imipenem-cilastatin, meropenem, and ertapenem have rates of adverse effects on hematopoietic, hepatic, and renal systems that are similar to other beta-lactams. However, children treated with imipenem for bacterial meningitis were noted to have an increase in probable drug-related seizures not seen with meropenem therapy in controlled studies.[3] For children requiring carbapenem therapy, meropenem is preferred for those with any underlying central nervous system inflammatory condition.

***Fluoroquinolones (FQs)***

All quinolone antibiotics (nalidixic acid, ciprofloxacin, levofloxacin, gatifloxacin, and moxifloxacin) cause cartilage damage to weight-bearing joints in toxicity studies in various immature animals; however, no conclusive data indicate similar toxicity in young children. Studies to evaluate cartilage toxicity and failure to achieve predicted growth have not consistently found statistically significant differences between those children treated with FQs and controls, although in an FDA-requested, blinded, prospective study of complicated urinary tract infections, the number of muscular/joint/tendon events was greater in the ciprofloxacin-treated

group than in the comparator (http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM162536.pdf). This continues to be an area of active investigation by the pediatric infectious diseases community as well as the FDA. Fluoroquinolone toxicities in adults, which vary in incidence considerably between individual agents, include cardiac dysrhythmias, hepatotoxicity, and photodermatitis; other reported side effects include gastrointestinal symptoms, dizziness, headaches, tremors, confusion, seizures, and alterations of glucose metabolism producing both hyper- and hypoglycemia.

***Lincosamides***

Clindamycin can cause nausea, vomiting, and diarrhea. Pseudomembranous colitis due to suppression of normal flora and overgrowth of *C difficile* is uncommon, especially in children, but potentially serious. Urticaria, glossitis, pruritus, and skin rashes occur occasionally. Serum sickness, anaphylaxis, and photosensitivity are rare, as are hematologic and hepatic abnormalities. Extensive use of clindamycin since 2000 for treatment of community-associated methicillin-resistant *Staphylococcus aureus* infections has not been accompanied by reports of increasing rates of *C difficile*–mediated colitis in children.

***Macrolides***

Erythromycin is one of the safest antimicrobial agents. However, it commonly produces nausea and epigastric distress. Azithromycin and clarithromycin cause fewer gastrointestinal side effects than erythromycin. Alteration of normal flora is generally not a problem, but oral or perianal candidiasis occasionally develops. Transient cholestatic hepatitis is a rare complication that occurs with approximately equal frequency among the various formulations of erythromycin. Intravenous erythromycin lactobionate causes phlebitis and should be administered slowly (1–2 hours); the gastrointestinal side effects seen with oral administration also accompany IV use. However, IV azithromycin is better tolerated than IV erythromycin, and has been evaluated for pharmacokinetics in limited numbers of children.[4]

Erythromycin therapy has been associated with pyloric stenosis in newborns and young infants; due to this toxicity and with limited data on safety of azithromycin in the first months of life, azithromycin is now the preferred macrolide for treatment of pertussis in neonates and young infants.[5]

***Oxazolidinones***

Linezolid represents the first oxazolidinone antibiotic approved for all children, including neonates, by the FDA. Toxicity is primarily hematologic, with thrombocytopenia and neutropenia that is dependent on dosage and duration of therapy, occurring most often with treatment courses of 2 weeks or longer. Routine monitoring for toxicity every 1 to 2 weeks is recommended for children on long-term therapy.

***Sulfonamides and Trimethoprim***

The most common adverse reaction to sulfonamides is a hypersensitivity rash, which occurs much more commonly in children with HIV infection on therapy. The frequency and types of reactions to the trimpethoprim/sulfamethoxazole (TMP/SMX) combination are said to be the same as with sulfamethoxazole alone, but it is not clear whether the most significant reaction, Stevens-Johnson syndrome, is caused more often by the combination than by sulfamethoxazole alone. Neutropenia and anemia occur occasionally. Mild depression of platelet counts occurs in approximately one-half the patients treated with sulfas or TMP/SMX, and seems to be dosage-related, but this rarely produces clinical bleeding problems. Sulfa drugs can precipitate hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency. Drug fever

and serum sickness are infrequent hypersensitivity reactions. Hepatitis with focal or diffuse necrosis is rare. A rare idiosyncratic reaction to sulfa drugs is acute aseptic meningitis.

***Tetracyclines***

Tetracyclines are used infrequently in pediatric patients because the major indications are uncommon diseases (rickettsial infections, brucellosis, Lyme disease), with the exception of acne. Side effects include minor gastrointestinal disturbances, photosensitization, angioedema, browning of the tongue, glossitis, pruritus ani, and exfoliative dermatitis. Potential adverse drug reactions from tetracyclines involve virtually every organ system. Hepatic and pancreatic injuries have occurred with accidental overdosage and in patients with renal failure. (Pregnant women are particularly at risk for hepatic injury.) Tetracyclines are deposited in growing bones and teeth, with depression of linear bone growth, dental staining, and defects in enamelization in deciduous and permanent teeth. This effect is dose-related, and the risk extends up to 8 years of age. A single treatment course of tetracyclines has not been found to cause dental staining, leading to the recommendation for tetracyclines as the drugs of choice in children for a number of uncommon pathogens. A new parenteral tetracycline approved for adults in 2005, tigecycline, produces the same "staining" of bones in experimental animals as seen with previous tetracyclines.

***Vancomycin***

Vancomycin can cause phlebitis if the drug is injected rapidly or in concentrated form. Vancomycin has the potential for ototoxicity and nephrotoxicity, and serum concentrations should be monitored for children on more than a few days of therapy. Hepatic toxicity is rare. Neutropenia has been reported. If the drug is infused too rapidly, a transient rash of the upper body with itching may occur from histamine release (red man syndrome). It is not a contraindication to continued use and the rash is less likely to occur if the infusion rate is increased to 60 to 120 minutes and the children are pretreated with oral or IV antihistamines.

**Antituberculous Drugs**

Isoniazid (INH) is generally well tolerated and hypersensitivity reactions are rare. Peripheral neuritis (preventable or reversed by pyridoxine administration) and mental aberrations from euphoria to psychosis occur more often in adults than in children. Mild elevations of alanine transaminase in the first weeks of therapy, which disappear or remain stable with continued administration, are common. Rarely, hepatitis develops, but is reversible if INH is stopped; if INH is not stopped, liver failure may develop in these children. Monitoring of liver functions is not routinely required in children receiving INH single drug therapy for latent tuberculosis as long as the children can be followed closely and liver functions can be drawn if the child develops symptoms of hepatitis.

Rifampin can also cause hepatitis; it is more common in patients with preexisting liver disease or in those taking large dosages. The risk of hepatic damage increases when rifampin and INH are taken together in dosages of more than 15 mg/kg/day of each. Gastrointestinal, hematologic, and neurologic side effects of various types have been observed on occasion. Hypersensitivity reactions are rare.

Pyrazinamide also can cause hepatic damage, which again seems to be dosage-related. Ethambutol has the potential for optic neuritis, but this toxicity seems to be rare in children at currently prescribed dosages, and routine screening for color vision is no longer recommended.

**Antifungal Drugs**

Amphotericin B (deoxycholate) causes chills, fever, flushing, and headaches, the most common of the many adverse reactions. Some degree of decreased renal function occurs in virtually all patients given amphotericin B. Anemia is common and, rarely, hepatic toxicity and neutropenia occur. Patients should be monitored for hyponatremia and hypokalemia. However, much better tolerated (but more costly) lipid formulations of amphotericin B are now commonly used (see Chapter 2). For reasons of safety and tolerability, the lipid formulations should be used whenever possible.

Ketoconazole produces hepatic damage on rare occasions. The most common side effect is gastric distress; this can often be alleviated by dividing the daily dose. Gynecomastia is not rare in adult males. Itraconazole has a smaller incidence of adverse effects than ketoconazole.

Fluconazole is usually very well tolerated from both clinical and laboratory standpoints. Gastrointestinal symptoms, rash, and headache occur occasionally. Transient, asymptomatic elevations of hepatic enzymes have been reported but are rare.

Voriconazole, a new antifungal suspension, may interfere with metabolism of other drugs the child may be receiving due to hepatic P450 metabolism. However, a poorly understood visual field abnormality has been described, usually at the beginning of a course of therapy, and uniformly self-resolving, in which objects appear to glow. There is no pain and no known anatomic or biochemical correlate of this side effect; no lasting effects on vision have yet been reported. Hepatic toxicity has also been reported, but is not so common as to preclude the use of voriconazole for serious fungal infections.

Caspofungin is very well tolerated, is now FDA-approved for use in children down to 3 months of age, and has minimal side effects. Fever, rash, headache, and phlebitis at the site of infection have been reported in adults. Uncommon hepatic side effects have also been reported. Micafungin and anidulofungin seem to have the same benign side effect profile in adults as caspofungin. Neither of these 2 echinocandins is well studied in children.

Flucytosine (5-FC) is seldom used due to the availability of safer, equally effective therapy. The major toxicity is bone marrow depression, which is dosage related, especially in patients treated concomitantly with amphotericin B. Renal function should be monitored.

**Antiviral Drugs**

After extensive clinical use, acyclovir has proved to be a safe drug with rare serious adverse effects. Renal dysfunction with IV acyclovir has occurred mainly with too rapid infusion of the drug. Rash, headache, and gastrointestinal side effects are uncommon. There has been little controlled experience in children with famciclovir and valacyclovir.

Ganciclovir causes hematologic toxicity that is dependent on the dosage and duration of therapy. Gastrointestinal disturbances and neurologic damage are rarely encountered.

Amantadine produces dizziness, drowsiness, and insomnia in many patients, but these effects are usually not severe. Rimantadine has fewer side effects. Visual disturbances, confusion, and psychosis are rare.

Oseltamivir is well tolerated except for nausea with or without vomiting, which may be more likely to occur with the first few doses, but usually resolves within a few days while still on therapy. Neuropsychiatric events have been reported, primarily from Japan, in patients with influenza treated with oseltamivir (a rate of approximately 1:50,000). These adverse events have not been reported in patients taking oseltamivir prophylaxis. Based on an FDA assessment (which is ongoing), it seems that these spontaneously reported side effects may be a function of influenza itself, oseltamivir itself, possibly a genetic predisposition to this clinical event, or a combination of all 3.

Foscarnet can cause renal dysfunction, anemia, and cardiac rhythm disturbances. Seizures and neuropathy are other serious but rare toxicities.

The many antiviral drugs for treatment for HIV infection have many adverse effects; consult the current FDA-approved package labels.

## 16. Drug Interactions

*NOTES*

- Antimicrobial drug-drug interactions that are known to be or have the potential to be clinically significant in children are listed in this chapter. Interactions involving probenecid, synergy-antagonism, and physical incompatibilities are not listed. Interactions involving antiretrovirals can be found at http://aidsinfo.nih.gov/contentfiles/PediatricGuidelines.pdf. Citations at the end of this section provide more extensive details of all reported and theoretical interactions, including antimicrobial drug-disease interactions.
- *Abbreviations:* ACE, angiotensin-converting enzyme; Conc, concentration; Decr, decrease; EIAED, enzyme-inducing antiepileptic drugs; FQs, fluoroquinolones; Incr, increase; MAO, monoamine oxidase; Poss, possible; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitors; SRI, serotonin reuptake inhibitors; TMP/SMX, trimethoprim/sulfamethoxazole.

| Antiinfective Agent | Interacting Drug(s) | Adverse Effect |
|---|---|---|
| Acyclovir/valacyclovir | Nephrotoxins[a] | Additive nephrotoxicity |
| | Phenytoin, valproic acid | Decr seizure control |
| Albendazole | EIAED[b] | Decr conc of albendazole |
| Amantadine | Anticholinergics[c] | Additive anticholinergic toxicity |
| | Bupropion | Additive neurotoxicity |
| | Trimethoprim | Incr amantadine conc |
| Amikacin | (See Aminoglycosides[d]) | |
| Aminoglycosides[d] (parenteral) | Nephrotoxins[a] | Additive nephrotoxicity |
| | Neuromuscular blocking agents | Incr neuromuscular blockade |
| | Indomethacin, ibuprofen | Incr aminoglycoside conc<br>Additive nephrotoxicity |
| | Carbo-/cisplatin, ethacrynic acid | Additive ototoxicity |
| Amphotericin B | Nephrotoxins[a] | Additive nephrotoxicity |
| | Cisplatin, corticosteroids, diuretics | Additive hypokalemia |
| Atovaquone | Metoclopramide, rifamycins, tetracyline | Decr atovaquone conc |
| Carbapenems | Valproic acid | Decr conc of valproic acid |
| Caspofungin | Cyclosporine | Transient elevated hepatic enzymes |
| | Tacrolimus, sirolimus | Decr tacrolimus/sirolimus conc |
| | Rifampin, EIAED[b] | Decr caspofungin conc |
| Cefaclor, cefdinir, cefpodoxime, cefuroxime (oral) | Antacids, H2 antagonists[e], PPI[f] | Decr antibiotic conc |
| Ceftriaxone | Calcium intravenous | Precipitation, cardiopulmonary embolism |
| Chloramphenicol[g] | Phenytoin, PPI[f], sulfonylureas | Incr conc of interacting drug |
| | EIAED[b], rifamycins | Decr chloramphenicol conc |
| Cidofovir | Nephrotoxins[a] | Additive nephrotoxicty |

| Antiinfective Agent | Interacting Drug(s) | Adverse Effect |
|---|---|---|
| Ciprofloxacin[h] | Caffeine, clozapine, diazepam, duloxetine, glyburide, methadone, olanzapine, sildenafil, theophylline, warfarin | Incr conc of interacting drug |
| | Phenytoin | Incr or decr conc of phenytoin |
| | Foscarnet | Additive seizure toxicity |
| | Antacids, bismuth, calcium, iron, sucralfate, zinc | Decreased oral absorption |
| Clarithromycin[g] | (See Erythromycin.) | |
| Clindamycin | Neuromuscular blocking agents | Incr neuromuscular blockade |
| Dapsone | Rifampin | Decr dapsone conc |
| Daptomycin | Statins | Additive myopathy |
| Doxycycline | Antacids, bismuth, calcium, iron, magnesium, sucralfate, zinc | Decreased oral absorption |
| | EIAED[b], rifamycins | Decreased doxycycline conc |
| Erythromycin[g] | Theophylline | Incr conc of interacting drug |
| | Class IA and III antiarrhythmics, doxapram, droperidol, haloperidol, methadone, pimozide, FQs[h], ziprasidone | Additive arrhythmic cardiotoxicity |
| | Azole antifungals, diltiazem, verapamil | Incr macrolide conc |
| | Rifamycins | Decr macrolide conc |
| Fluconazole[g] | Celecoxib, ibuprofen, irbesartan, naproxen, fluvastatin, phenytoin, sulfonylureas, warfarin | Incr conc of interacting drug-CYP 2C9 inhibition |
| | Losartan | Decr losartan activity |
| | Rifampin | Decr fluconazole conc |
| Foscarnet | Pentamidine | Hypocalcemia |
| | Ciprofloxacin | Additive seizure toxicity |
| | Nephrotoxins[a] | Additive nephrotoxicty |
| Ganciclovir/valganciclovir | Imipenem | Additive seizure toxicity |
| | Hemotoxins[i] | Additive hemotoxicity |
| | Nephrotoxins[a] | Additive nephrotoxicity |
| Gentamicin | (See Aminoglycosides[d].) | |
| Griseofulvin | EIAED[b] | Decr griseofulvin conc |
| Imipenem | Cyclosporine, ganciclovir | Additive neurotoxicity |

| Antiinfective Agent | Interacting Drug(s) | Adverse Effect |
|---|---|---|
| Isoniazid[j] | Acetaminophen, carbamazepine | Hepatotoxicity |
| | Cycloserine | Dizziness, drowsiness |
| | Carbamazepine, valproate | Inc conc of interacting drug |
| | Atomoxetine, linezolid | Poss MAO inhibition toxicity |
| | Amphetamines, buspirone, mirtazipine, SRI[k] tramadol | Poss serotonin syndrome |
| Itraconazole, ketoconazole | Aripiprazole, benzodiazepines[l] buspirone, busulfan, calcium-channel blockers[m], carbamazepine, chlorpheniramine, corticosteroids, cyclophosphamide, cyclosporine, digoxin, ergotamine, fentanyl, fexofenadine, fluoxetine, haloperidol, loperamide, methadone, pimozide, quetiapine quinidine, rifabutin, sertraline, sildenafil, sirolimus, statins[n], tacrolimus, trazadone, vinca-alkaloids, warfarin, zolpidem | Incr conc of interacting drug-CYP 3A4-7 inhibition |
| | Antacids, H2 antagonists[e] PPI[f] sucralfate | Decr azole conc, itraconazole oral solution less effected |
| | EIAED[b] rifamycins | Decr azole conc |
| | Erythromycin, quinolones, ziprasodone | Incr conc of interacting drugs with poss incr cardiotoxicity |
| | Loratadine, haloperidol, phenytoin | Incr conc of interacting drug |
| Levofloxacin[h] | See ciprofloxacin for drugs that decr oral absorption of FQ | |
| Linezolid | Atomoxetine, isoniazid | Poss MAO inhibition toxicity |
| | Sympathomimetics | Poss hypertension |
| | Amphetamines, buspirone, mirtazipine, SRI[k] tramadol | Poss serotonin syndrome |
| Metronidazole | Amiodarone, busulfan, carbamazepine, cyclosporine, 5-fluorouacil, lithium, phenytoin, tacrolimus, warfarin | Incr conc of interacting drug |
| | EIAED[b] | Decr metronidazole conc |
| Micafungin | Cyclosporine, sirolimus | Incr conc of interacting drug |
| Minocycline | Antacids, bismuth, calcium, iron, magnesium, sucralfate, zinc | Decreased oral absorption |
| Nafcillin | Cyclosporine | ± cyclosporine conc |
| | Calcium channel blockers[m] | Decr conc of interacting drug |
| | Warfarin | Warfarin resistance |
| Norfloxacin | Cyclosporine | Incr cyclosporine conc |
| | See ciprofloxacin for drugs that decr oral absorption of FQ | |

| Antiinfective Agent | Interacting Drug(s) | Adverse Effect |
|---|---|---|
| Penicillins | Methotrexate | Incr methotrexate conc |
| Posaconazole[g] | Phenytoin | Decr conc of posaconazole |
| Praziquantel | EIAED[b] | Decr conc of praziquantel |
| Quinupristin/dalfopristin[g] | (See Itraconazole for list of interacting drugs.) | |
| Rifampin, Rifabutin | Numerous including: amiodarone, anticonvulsants, antidepressants, antipsychotics, barbiturates, benzodiazepines[l], beta-adrenergic blockers, buspirone, coxibs, calcium channel blockers[m], oral contraceptives, corticosteroids, digoxin, immunosuppressants, NSAIDs, opioids, statins, sulfonylureas, warfarin, zolpidem | Decr conc of interacting drug<br>See also *Clinical Pharmacokinetics* 2003;42(9):819–850 |
| Streptomycin | (See Aminoglycosides[d]) | |
| Telithromycing | (See Erythromycin.) | |
| Terbinafine | Most SRI[k], tricyclic antidepressants | Incr conc of interacting drug |
| | Rifampin | Decr terbinafine conc |
| Tetracycline | Antacids, bismuth, calcium, iron, magnesium, sucralfate, zinc | Decreased oral absorption |
| | Atovaquone | Decr atovaquone conc |
| | Isotretinoin | Additive intracranial hypertension |
| TMP/SMX | Cyclosporine, losartan | Decr conc of interacting drug |
| | Azathioprine, methotrexate | Additive hematological toxicity |
| | Rifamycins | Decr TMP/SMX conc |
| | Celecoxib, dapsone, digoxin, dofetilide, fluoxetine, fluvastatin, methotrexate, NSAIDs, phenytoin, procainamide, sulfonylureas, voriconazole, warfarin | Incr conc of interacting drug |
| | ACE Inhibitors, spironolactone | Hyperkalemia |
| Tobramycin | (See Aminoglycosides[d].) | |
| Vancomycin | Indomethacin, ibuprofen | Incr vancomycin conc |
| Voriconazole[g,j] | Methadone, omeprazole | Incr conc of interacting drug |
| | EIAED[b], rifamycins | Decr voriconazole conc |

[a] Potentially nephrotoxic drugs include: aminoglycosides, acyclovir, cidofovir, ganciclovir, foscarnet, ACE inhibitors, cyclosporine, diuretics, NSAIDs, contrast agents, pentamidine, tacrolimus, tenofovir.
[b] EIAED: carbamazepine, phenobarbital, phenytoin, and primidone.
[c] Examples of anticholinergics: atropine, belladonna, benztropine, clidinium, dicyclomine, diphenhydramine, glycopyrrolate, homatropine, hyoscyamine, promethazine, propantheline, scopolamine.
[d] Gentamicin, tobramycin, amikacin, streptomycin.
[e] Famotidine, ranitidine.
[f] Pantoprazole, rabeprazole, omeprazole, lansoprazole, esomeprazole.

[g] Antibiotic is known to have or may potentially have the same interactions as itraconazole due to similar inhibition of CYP3A4-7 drug metabolism.
[h] FQs as a class have dose- and drug-dependant cardiac QTc interval prolongation effects. When used with other drugs that share this cardiac effect, there may be an additive cardiotoxic interaction. Ciprofloxacin and levofloxacin are FQs sometimes used in children; their risk of prolonging the QTc interval is low compared to other FQs.
[i] Notable hemotoxic drugs include: antineoplastics, clozapine, dapsone, flucytosine, mycophenolate, pentamidine, primaquine, pyrimethaine, TMP/SMX, zidovudine.
[j] Antibiotic is known to have or may potentially have the same interactions as fluconazole due to similar inhibition of CYP2C9 drug metabolism.
[k] SRI: buproprion, citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, nefazodone, paroxetine, sertraline, venlafaxine.
[l] CYP3A4 oxidized benzodiazepines: alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, midazolam, and triazolam.
[m] Amlodipine, bepridil, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nimodipine, verapamil.
[n] Atorvastatin, lovastatin, simvastatin.

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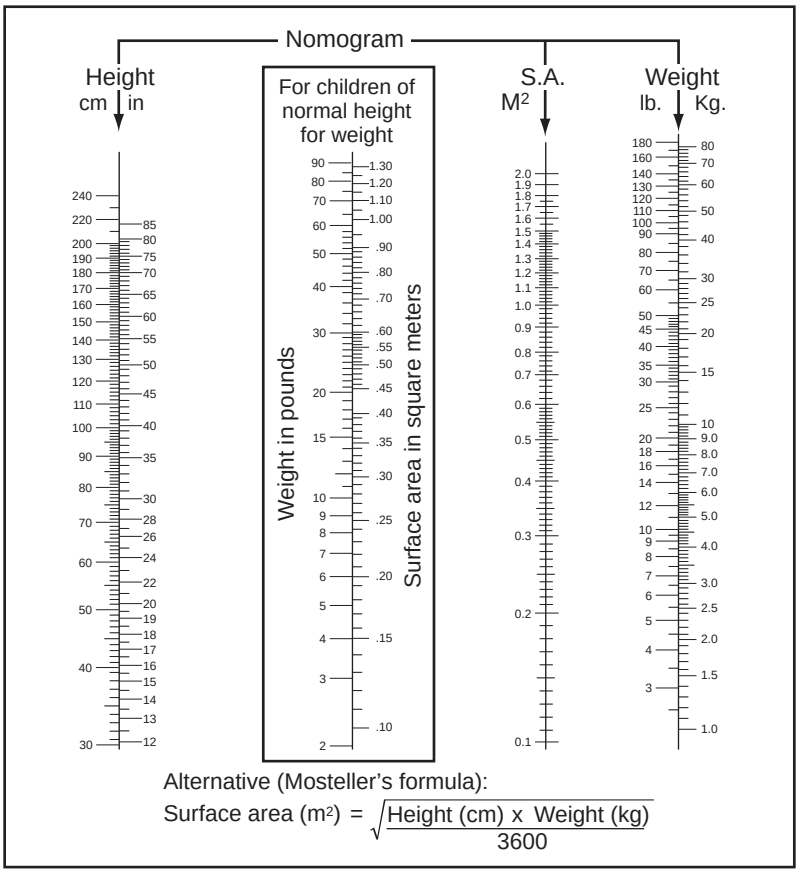
## Appendix
## Nomogram for Determining Body Surface Area

Based on the nomogram shown in Figure C-4, a straight line joining the patient's height and weight will intersect the center column at the calculated body surface area (BSA). For children of normal height and weight, the child's weight in pounds is used, then the examiner reads across to the corresponding BSA in meters$^2$. Alternatively, Mosteller's formula can be used.




Nomogram and equation to determine body surface area. (From: Robertson J, Shilkofski N, eds. *The Harriet Lane Handbook.* 17th ed. St Louis, MO: Mosby; 2005. |Data from Briars GL, Bailey BJ. Surface area estimation: pocket calculator v nomogram. *Arch Dis Child.* 1994;70[3]:246. Reprinted with permission from Elsevier.)

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