

Guidelines for the Selection of Antibacterial Therapy in Children

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Selection of appropriate anti-infective therapy can be challenging to the pediatrician. It is not sufficient to know the likely pathogens causing the infection and which antibiotics have been successful in the past. It also is necessary to know prevalent antibiotic resistance patterns and the effect that treatment might have on promoting the development of resistance in the specific patient being treated and in the general population. The evolution of penicillin-nonsusceptible *Streptococcus pneumoniae*, the increase in community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), and the emergence of multidrug-resistant gram-negative pathogens are examples of how the susceptibility patterns of commonly treated bacteria can change. These changes might alter options for effective therapy dramatically.

Determining the appropriate dose of antibiotics for children also can be difficult. Clinical studies evaluating antimicrobial pharmacokinetics in neonates (from extremely low birth weight to full term), infants, and children are few in number compared with studies performed in adults. Doses often are extrapolated from data derived from adults. Adverse event profiles also are based in large part on studies performed in preclinical animal toxicology models or in clinical trials conducted in older subjects. The clinical relevance of understanding how effectively antibiotics inhibit or kill pathogens at the site of infection, termed *pharmacodynamics*, has been integrated only recently into clinical investigations conducted in adults [1]. Similar studies in children to validate these concepts do not exist. This article reviews factors important in the selection of antimicrobial agents in infants and children. Recommendations for antibiotic therapy for a wide range of infections occurring in children are provided.

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Factors affecting antibiotic selection

When choosing an antibacterial agent, the following factors are the most important to consider.

- *Microbiology*. What are the most common organisms causing the infection? What are the local antibiotic susceptibility patterns? Are resistance mechanisms likely already present in the pathogens; will additional mechanisms become apparent on exposure to the antibiotic?
- *Pharmacodynamics*. Would treatment with the agent result in the type of exposure known to optimize the desired biologic effect on the pathogens?
- *Pharmacokinetics*. Based on the expected absorption, metabolism, elimination, and distribution of the drug to the site of infection, what is the ideal route and dose of drug to prescribe?
- *Monte Carlo simulation* [2]. In the specific population being treated for any given tissue sites of infection and for any given pathogens, what risk of treatment failure is acceptable?
- *Host*. What host factors might affect drug selection and dosing?
- *Antibiotic adverse reactions*. Are there potential side effects that might affect the relative risks and benefits of therapy? What toxicities should be anticipated, either directly or as a result of drug-drug interactions?

Microbiology

Most infections occur as a result of disruption in host defenses (physical or immunologic) in combination with virulence factors of the bacteria. Highly virulent organisms cause disease in healthy and immunocompromised hosts, whereas low-virulence organisms usually are pathogenic only in immunocompromised hosts. In general, most organisms that cause community-acquired infections are part of the child's normal bacterial flora, resulting from exposure to other children in the community. Skin and soft tissue infections are caused most commonly by *S. aureus* or beta-hemolytic streptococci, whereas upper and lower respiratory tract infections are caused commonly by *S. pneumoniae* and nontypable *Haemophilus influenzae*. Resistance to antibiotics can occur with any organism. Local epidemiologic data are key to assessing the prevalent patterns of resistance in a community.

The susceptibility of a specific pathogen to a specific antibiotic can be measured in the microbiology laboratory by defining the lowest concentration of the antibiotic that can inhibit the growth of the pathogen, the *minimum inhibitory concentration* (MIC). Not all isolates of a single pathogen, such as *Escherichia coli*, have exactly the same MIC for a given antibiotic. Although some isolates might remain completely susceptible to an antibiotic, such as ampicillin, a variety of different antibiotic resistance mechanisms involving ampicillin and other antibiotics might exist in other *E. coli* isolates. This variation in susceptibility

gives rise to the concept of a distribution of MICs for specific bacteria infecting a population of children from a defined region over a specified period. This concept of susceptibility distribution has been shown in isolates of pneumococcus with respect to susceptibility to penicillin. The distribution of MICs has been shown to vary by site of isolation of the pneumococcus (middle ear fluid, blood, or cerebrospinal fluid) and by region of the United States [3]. In an ongoing national surveillance project of pneumococcal resistance in children, organisms isolated in Houston, Texas, have tended to be more resistant than organisms isolated in Pittsburgh, Pennsylvania. Organisms isolated in middle ear fluid from children with otitis media on average have been more resistant than organisms isolated from cerebrospinal fluid [4,5].

This observed distribution of susceptibilities in bacterial pathogens is often more apparent in hospitals and long-term care settings, where resistance patterns vary and are notably dependent on the institution. Local clinical laboratory data and hospital antibiograms are helpful in directing empirical therapy. For individual patient care, obtaining bacterial cultures from the site of infection to identify the organism and determine specific antibiotic susceptibility is essential for selecting successful therapy and minimizing the overuse of antibiotics. Hospital-associated infections (eg, wounds, urinary tract infections, ventilator-associated pneumonia) can be particularly difficult to treat because variability in the types of bacteria isolated and in their susceptibility patterns is extensive. For the management of serious infections, a strategy based on susceptibility testing of the isolated pathogen is the standard of care.

Patterns of resistance change over time. Over 5 years there has been an increase in CA-MRSA [6–8]. In contrast to hospital-acquired MRSA (HA-MRSA), which has been a challenge for adult and pediatric providers for many years, these community-acquired strains frequently are found in otherwise healthy children. The usual predisposing factors for MRSA, including antibiotic exposure and prior hospitalization, often are not present in children infected by CA-MRSA. In contrast to HA-MRSA, the community-acquired strains often retain susceptibility to non- β -lactam antibiotics, such as clindamycin, trimethoprim-sulfamethoxazole, and the macrolides. Resistance to methicillin and the other β -lactam antibiotics is based on an alteration in a specific transpeptidase, penicillin-binding protein 2a, which is conferred by the *mecA* gene. The alteration in protein structure of this transpeptidase is the same one as that seen in HA-MRSA. The differences in susceptibility between HA-MRSA and CA-MRSA can be explained, however, by the antibiotic resistance cassette in which the *mecA* gene is found.

Many strains of CA-MRSA contain a much smaller cassette (SCCmec IV) composed of resistance genes only for the β -lactam antibiotics [9–11]. There is evidence that some of these community-acquired strains have evolved from community-acquired methicillin-susceptible strains of *S. aureus* and not from HA-MRSA [12]. Evolving patterns of resistance underscore the need to obtain cultures and antibiotic susceptibilities, especially when the patient does not respond clinically to antibiotic therapy previously believed to be effective. Mecha-

Table 1

Examples of pediatric bacterial pathogens with emergence of antibiotic resistance, mechanism of resistance, and relevance to patient care

Organism	Mechanism of resistance	Clinical implication
<i>Streptococcus pneumoniae</i>	Alteration in the binding site of the antibiotic to one or more transpeptidases (penicillin binding proteins)	Relative resistance to β -lactam agents (penicillins and cephalosporins)
	Alteration in the ribosomal binding site of antibiotics	Resistance to macrolide agents
	Efflux pump to expel an antibiotic from the cytoplasm	Relative resistance to macrolide agents
<i>Staphylococcus aureus</i>	Alteration in the binding site of a specific transpeptidase (mec A)	Resistance to all β -lactams
	Alteration at ribosomal binding site	Resistance to macrolides and clindamycin
	Efflux pump to expel antibiotics from the cytoplasm	Relative resistance to macrolides
<i>Escherichia coli</i> , <i>Klebsiella</i>	β -lactamases with activity extended beyond ampicillin (extended-spectrum β -lactamases)	Resistance to cefotaxime, ceftriaxone, and ceftazidime
	Chromosomal β -lactamases that are deregulated and hyperproduced	Resistance to cefotaxime, ceftriaxone, and ceftazidime
<i>Enterobacter</i> , <i>Serratia</i> , and some other Enterobacteriaceae	Multiple β -lactamases each with activity against different β -lactam antibiotics	Resistance to multiple β -lactam agents, including ceftazidime
	Cell wall porin protein-deficient bacteria	Carbapenem resistance
	Multiple efflux pumps to expel antibiotics from the cytoplasm	Resistance to β -lactams, fluoroquinolones, others

Data from references [23–25].

nisms of antibiotic resistance in pediatric bacterial pathogens and their resulting clinical implications are outlined in Table 1.

Pharmacodynamics

Pharmacodynamics is recognized as an important concept in predicting the microbiologic and clinical success of antibiotic treatment. Depending on the class of antibiotic and the particular pathogen in question, the ability of the antibiotic to inhibit or kill an organism over minutes to hours might be quite different. In general, antibiotic effect is related directly to either the concentration attained at the site of infection or the time during which an effective concentration of the antibiotic is present at the site of infection. For some antibiotics, such as aminoglycosides and fluoroquinolones [1,13,14], higher concentrations and greater drug exposure result in more rapid killing. Drug exposure is related to the total area under the curve, depicted by plotting serum drug concentrations from the

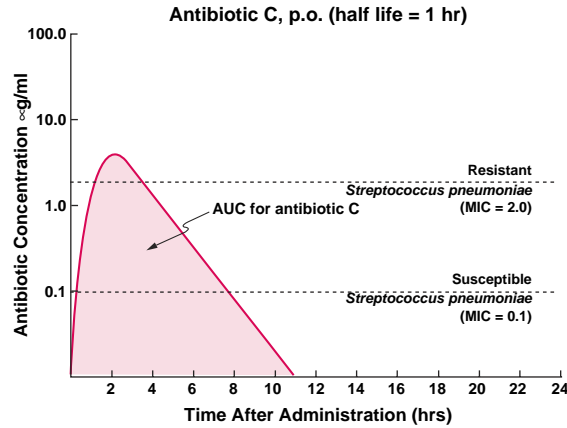
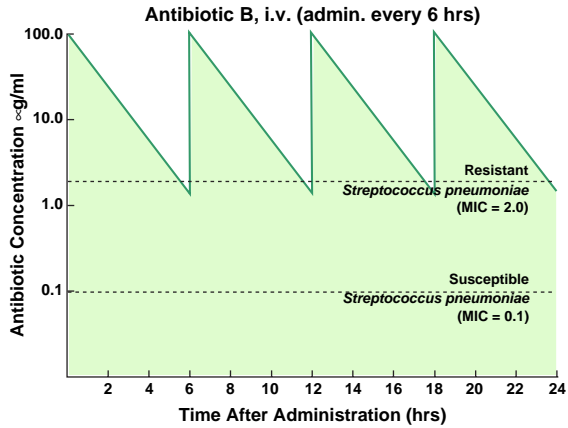
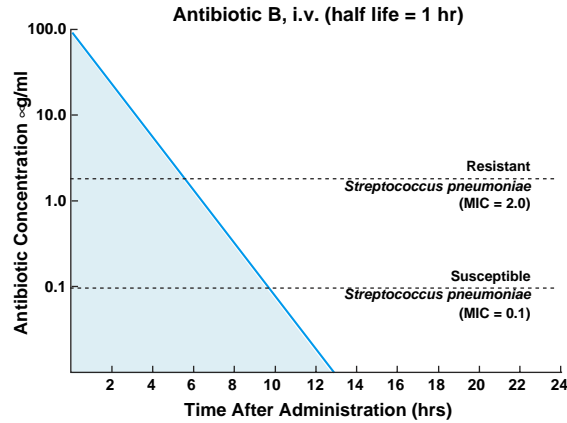
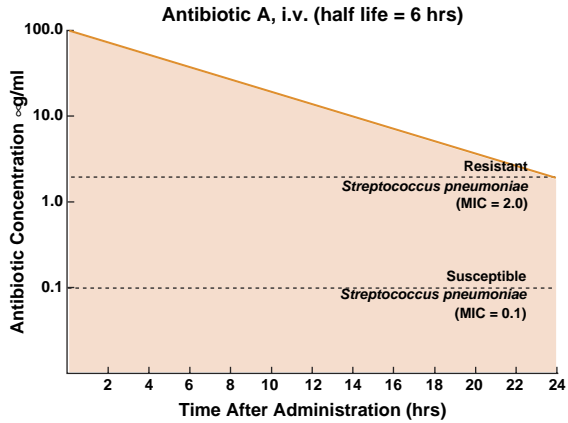
time of administration to the time of elimination (Fig. 1). For β -lactams, optimal activity is related to time during which the antibiotic concentration remains above the MIC at the site of infection over a dosing interval, or the “percent-time-above-MIC.” Inhibitory activity can be optimized by achieving antibiotic concentrations at the site of infection for a duration that is greater than 40% of the dosing interval (eg, for 4.8 hours out of every 12 hours for antibiotics that are administered every 12 hours) for some antibiotic-pathogen combinations. For these interactions, having greater antibiotic concentrations at the site of infection would not achieve a greater inhibitory effect. In addition to the time-above-MIC effect, the macrolides, clindamycin, vancomycin, and linezolid all exhibit a postantibiotic effect, with organisms requiring substantial time to begin regrowth after exposure to the antibiotic [14].

Pharmacokinetics

Dosing guidelines usually are based on information obtained from clinical trials conducted on a few relatively normal, healthy children. For many antibiotics, dosing guidelines have been extrapolated from studies conducted in adults. The absorption, concentration profile, distribution, metabolism, and excretion of an antibiotic in a sick child who might have compromised organ function might not be predicted accurately from existing literature. Patient-to-patient variability in pharmacokinetics must be anticipated. Selecting the most appropriate antibiotic dose when switching from intravenous to oral therapy depends most on the absorption characteristics of the oral agent. In general, most antibiotics when given parenterally result in higher, more reproducible serum concentrations than when given orally (see Fig. 1). Most β -lactam antibiotics administered orally have fair bioavailability; serum concentrations usually are approximately 5% to 10% of those obtained when β -lactam antibiotics are given parenterally [15]. Quinolones and the oxazolidinone antibiotic, linezolid, have excellent bioavailability, however, with serum concentrations and antibiotic exposure after an oral dose being close to that found after an intravenous dose [16–18].

Compliance is not an issue with parenteral treatment, although an indwelling catheter is needed, and complications with the catheters and administration devices might occur. Oral therapy is associated with fewer serious complications. Absorption, compliance, and the palatability of the drug present a different set of problems with oral therapy, however.

Data are limited regarding the specific concentrations of antibiotics in many tissues and organs. It is predictable, however, that antibiotic concentrations would be different in various body compartments, and that the elimination half-lives of antibiotics at each of these sites would vary. There are limitations to predicting the effectiveness of therapy based on general pharmacokinetic principles. When data are available, pharmacokinetic/pharmacodynamic modeling is informative. Antibiotic therapy of otitis media provides an example of how differences in



antibiotic exposure between the bloodstream and the site of infection affect dosing recommendations. Middle ear fluid concentrations of ceftriaxone are known to approximate the concentrations in serum, with documented peak concentrations in middle ear fluid of 80 $\mu\text{g}/\text{mL}$ [19]. Although ceftriaxone has an elimination half-life of 4 to 6 hours in the serum, its measured elimination half-life in middle ear fluid is closer to 24 hours [19]. Concentrations of ceftriaxone in middle ear fluid remain well above the MIC for most strains of *S. pneumoniae* and nontypable *H. influenzae* for at least 72 hours after a single dose. With validation of clinical and microbiologic efficacy of a single dose of ceftriaxone for otitis media in prospective clinical trials, the US Food and Drug Administration approved this dosing regimen for otitis media.

In the population of children to be treated for a particular infection, one can estimate the antibiotic exposure in infected tissues achieved at a specific antibiotic dose. By combining information on antibiotic exposure with information on the range of antibiotic susceptibilities of the pathogens causing the infection, one can estimate the percent of children who would be cured of their infections at a specific antibiotic dosage.

Monte Carlo simulation

When an antibiotic is prescribed, the clinician should be able to predict the likelihood that a certain dose would cure the infection. The acceptable level of certainty with the prediction varies according to the clinical circumstances. An anticipated cure rate of 80% to 90% might be acceptable in the management of a nonserious infection, such as cystitis caused by *E. coli* in a healthy child. In contrast, this would not be an acceptable cure rate for a child with leukemia hospitalized with neutropenia and pneumonia caused by *Pseudomonas aeruginosa*. The therapy in these two situations would be dramatically different; the dose of the appropriate antibiotic necessary to achieve the desired "target attainment" in both children can be predicted by Monte Carlo simulation [2]. This simulation is performed using a computer program that considers the distributions of MICs of a selected antibiotic against the probable pathogens (*E. coli* or *Pseudomonas* in the examples here), the expected range of antibiotic concentrations at the site of infection for various antibiotic dosages, and knowledge of the pharmacodynamic characteristics of the antibiotic that determine the type of antibiotic exposure required. The computer simulates the distributions of MICs and pharmacokinetics in a population of children with characteristics approxi-

Fig. 1. The area under the curve (*shaded area*) for different antibiotics. The area under the curve provides a measure of antibiotic exposure to bacterial pathogens. The greatest exposure comes with antibiotics that have a long serum half-life and are administered parenterally (*upper left panel, antibiotic A*). The lowest exposure occurs with oral administration (*lower right panel, antibiotic C*). Dosing of antibiotic B once a day (*upper right panel*) provides far less exposure than dosing the same antibiotic every 6 hours (*lower left panel*). (© John S. Bradley, MD.)

Table 2
Antimicrobial therapy for common infections seen in children*

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Skin and soft tissue infections			
<i>Note:</i> Community-acquired methicillin-resistant <i>Staphylococcus aureus</i> (CA-MRSA) is now prevalent (representing >20% of all isolates) in many areas. Penicillins and cephalosporins are not active against these strains. Vancomycin is active against virtually all strains and should be used for all life-threatening and severe infections. Clindamycin, TMP-SMZ and linezolid are potentially active and can be used for mild-to-moderate infections			
Oxacillin, methicillin, and nafcillin are all highly active against methicillin-susceptible <i>Staphylococcus aureus</i> (MSSA) and are considered roughly equivalent in efficacy. Cefazolin, although less active in vitro than the antistaphylococcal penicillins, is therapeutically equivalent in mild-to-moderate infections, can be given less frequently, and is better tolerated than the penicillins			
Bites, animal and human	<i>Pasteurella multocida</i> (animal), <i>Eikenella corrodens</i> (human), <i>Staphylococcus</i> spp. and <i>Streptococcus</i> spp	Augmentin 45 mg/kg/d (amoxicillin component) PO div q8h (amoxicillin:clavulanate ratio of 7:1) × 5–7 d; for hospitalized patients, use ticarcillin/clavulanate, 200 mg ticarcillin/kg/d div q6h <i>or</i> ampicillin and clindamycin	Consider rabies prophylaxis for animal bites; consider tetanus prophylaxis; human bites often have mixed aerobes and anaerobes with a very high rate of infection (do not close open wounds)
Impetigo	<i>S. aureus</i> (methicillin-susceptible or methicillin-resistant), group A strep (<i>S. pyogenes</i>)	Mupirocin topically to lesions tid; <i>or</i> (for extensive lesions) cephalexin 50–75 mg/kg/d PO div tid	Cleanse infected area with soap and water; bathe daily. For CA-MRSA: clindamycin, TMP/SMZ, <i>or</i> linezolid
Lymphadenitis	<i>S. aureus</i> (MSSA <i>or</i> MRSA), group A strep	Empiric IV therapy: oxacillin 150 mg/kg/d IV div q6h <i>or</i> cefazolin 100 mg/kg/d IV div q8h initially; for possible CA-MRSA: clindamycin 30 mg/kg/d IV div q8h <i>or</i> vancomycin 40 mg/kg/d IV q8h	Oral therapy for MSSA: cephalexin <i>or</i> dicloxacillin. For CA-MRSA: clindamycin, TMP/SMZ, <i>or</i> linezolid
Myositis, suppurative (synonyms: tropical myositis, pyomyositis)	<i>S. aureus</i>	Oxacillin 150 mg/kg/d IV div q6h <i>or</i> cefazolin 100 mg/kg/d IV div q8h 14–21 d; alternatives: vancomycin <i>or</i> clindamycin	Surgical drainage or excision when needed; for severe infections, add gentamicin for synergy. For CA-MRSA: clindamycin, TMP/SMZ, <i>or</i> linezolid

Necrotizing fasciitis	<i>S. aureus</i> , group A strep, mixed aerobic/ anaerobic, or staphylococcal, depending on the location of infection, age of the child	Penicillin G 200,000–250,000 U/kg/d div q6h <i>and</i> clindamycin 40 mg/kg/d div q8h; <i>add</i> cefotaxime to the above regimen <i>or</i> use meropenem or imipenem as single drug therapy if gram-negative aerobic bacilli suspected	Aggressive, emergent debridement; consider IVIG to bind bacterial toxins for life-threatening disease; if <i>S. aureus</i> is isolated, use oxacillin or ceftazolin rather than clindamycin, unless MRSA
Pyoderma, abscesses, cervical lymphadenitis	<i>S. aureus</i> , group A strep	Cephalexin 50–75 mg/kg/d PO div tid; <i>or</i> dicloxacillin (as above); × 5–10 d	Incision and drainage when indicated; oxacillin or ceftazolin IV or vancomycin for serious infections. For oral therapy for CA-MRSA: clindamycin, TMP-SMZ, or linezolid
Cellulitis, periorbital (Preseptal infection) Associated with entry site lesion on skin	<i>S. aureus</i> , group A strep	Oxacillin 150 mg/kg/d IV div q6h <i>or</i> ceftazolin 100 mg/kg/d IV div q8h; for regions with high prevalence of CA-MRSA: clindamycin 40 mg/kg/d IV div q8h <i>or</i> vancomycin 40 mg/kg/d div q8h; × 10–14 d	Oral antistaphylococcal antibiotic for less severe infection, or for convalescent therapy after the infection has clearly responded to IV therapy
Bacteremia	<i>S. pneumoniae</i> (pneumococcus) <i>or</i> <i>H. influenzae</i> type b in unimmunized children	Cefuroxime or cefotaxime 100–150 mg/kg/d IV, IM div q8h; <i>or</i> ceftriaxone 50 mg/kg/d once daily × 10–14 d	R/O meningitis
Associated with sinusitis (more commonly presenting as nontender edema, not cellulitis); rarely sinus pathogens may erode anteriorly into soft tissue		As for sinusitis: initially cefuroxime or cefotaxime 100–150 mg/kg/d IV, IM div q8h; <i>or</i> ceftriaxone 50 mg/kg/d once daily 5–7 d, followed by oral antibiotics to complete 21 d	For oral antibiotic therapy, see Otitis media and Sinusitis

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Skin and soft tissue infections			
Cellulitis, orbital (Postseptal infection)		Cefotaxime 150 mg/kg/d div q8h or ceftriaxone 50 mg/kg/d once daily; <i>and</i> antistaphylococcal therapy (oxacillin 150 mg/kg/d IV div q6h or cefazolin 100 mg/kg/d IV div q8h; <i>or</i> for CA-MRSA, consider vancomycin 40 mg/kg/d div q8h or clindamycin 40 mg/kg/d IV div q8h) × 10–14 d	Usually secondary to sinus infection: staphylococcal or respiratory tract flora; surgical drainage of pus, if present by CT scan in orbit or subperiosteal tissue
Bone and joint infections			
Osteomyelitis			
Infants and children, acute infection	<i>S. aureus</i> , group A strep, rarely <i>Kingella</i>	As above: for communities with over 5–10% MRSA, start empirical therapy with clindamycin 40 mg/kg/d IV div q8h <i>or</i> vancomycin 40 mg/kg/d IV div q8h; otherwise start oxacillin 150 mg/kg/d IV div q6h <i>or</i> cefazolin 100 mg/kg/d IV div q8h Transition to oral therapy may be considered with cephalexin 100 mg/kg/d div q6–8h or dicloxacillin 100 mg/kg/d div q6h for MSSA once clinical improvement is documented and compliance ensured. Total therapy (IV plus PO) for 4–6 wk	In children with open fractures secondary to trauma, consider adding ceftazidime for extended aerobic gram-negative activity (pending culture results). Oral therapy alternatives for CA-MRSA include clindamycin, TMP/SMZ, and linezolid

Osteomyelitis of the foot (osteochondritis after a puncture wound)	<i>Pseudomonas aeruginosa</i>	Ceftazidime 150 mg/kg/d IV, IM div q8h <i>or</i> ticarcillin 200–300 mg/kg/d IV div q6h; <i>and</i> tobramycin 67.5 mg/kg/d IM, IV div q8h; <i>or</i> cefepime 150 mg/kg/d IV, div q8h; <i>or</i> meropenem 60 mg/kg/d IV, div q8h; × 10 d	Thorough surgical debridement required (second drainage procedure needed in at least 20% of children). For convalescent therapy after clinical resolution, consider ciprofloxacin 30 mg/kg/d PO, div bid
Arthritis, bacterial Infants	<i>S. aureus</i> , group A strep; consider pneumococcus and <i>H. influenzae</i> type b in unimmunized children	For isolates documented to be MSSA: oxacillin 150 mg/kg/d IV div q6h <i>or</i> cefazolin 100 mg/kg/d IV div q8h × 21 d; empirical therapy in communities with 5–10% MRSA: clindamycin 40 mg/kg/d IV div q8h <i>or</i> vancomycin 40 mg/kg/d div q8h. As for osteomyelitis, transition to oral therapy may be considered once clinically improved	For penicillin-susceptible pneumococci or group A strep: penicillin G 200,000 U/kg/d IV div q6h × 14 d or longer; for penicillin-nonsusceptible pneumococci, ceftriaxone 50–75 mg/kg/d IV, IM, once daily, <i>or</i> cefotaxime 100–150 mg/kg/d IV, IM div q8h
Children	<i>S. aureus</i> , group A strep	For MSSA isolates: oxacillin 150 mg/kg/d IV div q6h <i>or</i> cefazolin 100 mg/kg/d IV div q8h. Total therapy (IV plus PO) for 3 wk; empirical therapy for suspected MRSA as above: clindamycin 40 mg/kg/d IV div q8h <i>or</i> vancomycin 40 mg/kg/d IV div q8h. As for osteomyelitis, transition to oral therapy may be considered once clinically improved	Pneumococcus is unusual past infancy. Oral therapy alternatives for CA-MRSA include clindamycin, TMP/SMZ, and linezolid

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Ear and sinus infections			
External otitis, bacterial	<i>P. aeruginosa</i> , <i>S.aureus</i>	Antibiotic solution delivered to wick inserted into canal: neomycin/polymyxin B or fluoroquinolone (ciprofloxacin or ofloxacin); with hydrocortisone	Optimal therapy not well studied; cleaning canal of detritus important
Otitis media, acute			
<i>Note on acute otitis media:</i> Several antibiotic regimens are effective for acute otitis media. High-dose amoxicillin (80–90 mg/kg/d) is considered the most effective oral agent against <i>S. pneumoniae</i> . Other drugs active against β -lactamase-producing <i>H. influenzae</i> and penicillin-resistant <i>S. pneumoniae</i> should be considered for amoxicillin failures or relapses. The physician should consider advantages and disadvantages regarding antibacterial spectrum, palatability of suspensions, and cost. Some physicians observe the child >2 years for 72 h in milder cases before starting antibiotic therapy, watching for spontaneous resolution (often noted with <i>Moraxella</i> and <i>Haemophilus</i>). Although prophylaxis is only rarely indicated in an attempt to limit antibiotic exposure, amoxicillin or other antibiotics can be used in one half the therapeutic dose once or twice daily to prevent infections.			
Otitis media, acute			
Infants and children	Pneumococcus, nontypable <i>H. influenzae</i> , <i>Moraxella</i> most common	Usual therapy: amoxicillin 90 mg/kg/d PO bid; failures caused by either β -lactamase-producing <i>Haemophilus</i> or penicillin-resistant pneumococcus. The following offer better activity than amoxicillin against β -lactamase-positive <i>Haemophilus</i> and <i>Moraxella</i> : amoxicillin/clavulanate (Augmentin), cefdinir, cefprozil, cefpodoxime, cefuroxime, azithromycin, clarithromycin, erythromycin-sulfisoxazole PO, or ceftriaxone 50 mg/kg/d IM q24h \times 1–3 doses. It is difficult to achieve better activity	High-dose amoxicillin (90 mg/kg/d) should be used for empirical therapy in most regions of the world, given the high prevalence of penicillin-nonsusceptible pneumococci causing otitis. The high serum and middle ear fluid concentrations achieved with 45 mg/kg/dose of amoxicillin, combined with its long middle ear fluid half-life, allow for a therapeutic antibiotic exposure to pathogens in the middle ear with only twice-daily dosing of amoxicillin; Augmentin ES-600 combines high-dose amoxicillin (90 mg/kg/d) with clavulanate. For failure with a second treatment course, tympanocentesis differentiates persisting infection from resolving inflammation

Sinusitis, acute	Nontypable <i>H. influenzae</i> , pneumococcus, other streptococci, <i>Moraxella</i>	against penicillin-resistant pneumococci with oral therapy than with high-dose amoxicillin; options include ceftriaxone 50 mg/kg/d IM q24h × 1–3 doses, <i>or</i> a macrolide-class antibiotic (azithromycin, clarithromycin, <i>or</i> erythromycin-sulfisoxazole); caution: 40% of penicillin-resistant pneumococci are also macrolide-resistant, <i>or</i> clindamycin (not active against <i>H. influenzae</i> <i>or</i> <i>M. catarrhalis</i>)	Little prospective data exist on bid therapy with high-dose amoxicillin (90 mg/kg/d) in sinus infections, but this dosing regimen should be as effective as in otitis. Sinus irrigations for severe disease <i>or</i> failure to respond
Oropharyngeal infections			
Dental abscess	Oral aerobic and anaerobic flora	Clindamycin 30 mg/kg/d PO, IV, IM div q6–8h <i>or</i> penicillin G 100,000–200,000 U/kg/d IV div q6h	Usually oral aerobes and anaerobes; tooth extraction may be necessary
Epiglottitis (aryepiglottitis, supraglottitis)	<i>H. influenzae</i> type b; consider <i>S. aureus</i> in immunized children	Cefuroxime 100–150 mg/kg/d IV, IM div q8h <i>or</i> cefotaxime 150 mg/kg/d IV div q8h <i>or</i> ceftriaxone 50 mg/kg/d IV, IM q24h × 7–10 d	Provide airway. For staphylococci, consider oxacillin 150 mg/kg/d IV div q6h <i>or</i> cefazolin 100 mg/kg/d IV div q8h <i>or</i> vancomycin 40 mg/kg/d IV div q8h
Peritonsillar cellulitis <i>or</i> abscess	Group A strep with mixed oral flora	Clindamycin 30 mg/kg/d PO, IV, IM div q8h <i>and</i> cefotaxime 150 mg/kg/d IV div q8h	Consider incision and drainage for abscess. Alternatives: meropenem <i>or</i> imipenem; piperacillin/tazobactam

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Oropharyngeal infections			
Pharyngitis	Group A strep	Penicillin V 50–75 mg/kg/d PO div bid or tid, or amoxicillin 50–75 mg/kg/d div bid or tid 10 d or benzathine penicillin 25,000 U/kg IM (max 1.2 million U) as a single dose; erythromycin for penicillin-allergic patients	For the uncommon failures, or frequent relapses, amoxicillin/clavulanate, cephalosporins, or clindamycin may be more effective
Retropharyngeal or lateral pharyngeal cellulitis or abscess	Mixed aerobic and anaerobic oral flora	Clindamycin 30 mg/kg/d PO, IV, IM div q8h and cefotaxime 150 mg/kg/d IV div q8h or ceftriaxone 50 mg/kg/d IV q24h	Consider incision and drainage; possible airway compromise, mediastinitis Alternatives: meropenem or imipenem
Tracheitis, bacterial	<i>S. aureus</i> (consider CA-MRSA), group A strep, pneumococcus, <i>H. influenzae</i> , type b	Vancomycin 40 mg/kg/d IV div q8h, or oxacillin 150 mg/kg/d IV div q6h or cefazolin 100 mg/kg/d IV div q8h and cefotaxime 150 mg/kg/d div q8h or ceftriaxone 50 mg/kg/d q24h	May represent bacterial superinfection of viral laryngotracheobronchitis
Lower respiratory tract infections			
Abscess, lung - primary (severe, necrotizing)	Pneumococcus, <i>S. aureus</i> (consider CA-MRSA), group A strep	Empirical therapy with ceftriaxone 50–75 mg/kg/d q24h or cefotaxime 150 mg/kg/d div q8h and vancomycin 40 mg/kg/d IV div q8h × 14–21 d or longer	Bronchoscopy necessary if abscess fails to drain; surgical excision rarely necessary For MSSA: oxacillin 150 mg/kg/d IV div q6h or cefazolin 100 mg/kg/d IV div q8h; or for CA-MRSA: clindamycin 30–40 mg/kg/d IV div q8h
Pertussis		Erythromycin (estolate may be preferable) 40 mg/kg/d PO div qid × 14 d; limited clinical data suggest that azithromycin (10 mg/kg/d × 5 d) or clarithromycin (15 mg/kg/d × 14 d) may be used as alternatives	Hospitalize young infants; avoid mist therapy; avoid cough suppressants; Isolate for the first 5 d of therapy; Provide macrolide prophylaxis to family members

Pneumonia, aspiration	Polymicrobial infection with oral aerobes and anaerobes	Clindamycin 30–40 mg/kg/d PO, IM, IV div q8h <i>or</i> meropenem 60 mg/kg/d IV div q8h if additional gram-negative aerobic coverage is needed; $\times \geq 10$ d	Alternatives: imipenem IV or piperacillin/tazobactam IV or ticarcillin/clavulanate IV
Pneumonia: lobar or segmental consolidation			Consider <i>H. influenzae</i> type b in immunized child
Community-acquired	Pneumococcus (even if immunized), group A strep, and <i>S. aureus</i> more likely in younger infants; <i>Mycoplasma pneumoniae</i> and other atypical agents may cause lobar pneumonia in school-age children and adolescents	Empirical therapy for hospitalized children: cefuroxime 150 mg/kg/d IV, IM div q8h, <i>or</i> ceftriaxone 50 mg/kg/d IV, IM q24h, <i>or</i> cefotaxime 150 mg/kg/d div q8h; $\times 10$ –14 days; for suspect mycoplasma and other atypical pneumonia pathogens, <i>add</i> a macrolide (erythromycin IV or PO, azithromycin IV or PO, clarithromycin PO) Empirical oral outpatient therapy for less severe illness: amoxicillin 80–90 mg/kg/d PO div q8h; for atypical pneumonia, <i>add</i> agents as above	Change to PO after improvement (decreased fever, no oxygen needed); Alternative IV agents include clindamycin for susceptible strains of staphylococcus and pneumococcus. Oral therapy for bacterial pathogens may also be successful with: amoxicillin/clavulanate, cefdinir, cefprozil, cefpodoxime or cefuroxime.
	Pneumococcal, penicillin-susceptible Pneumococcal, penicillin-resistant	Penicillin G 150,000 U/kg/d IV div q4–6h $\times 10$ d Ceftriaxone 50 mg/kg/d q24h, <i>or</i> cefotaxime 150 mg/kg/d div q8h for 10–14 d	Change to PO penicillin V 50–75 mg/kg/d div qid to tid after improvement Addition of vancomycin has <i>not</i> been required for eradication of penicillin-resistant strains causing lobar or bronchopneumonia
With empyema	Same pathogens as for community-acquired pneumonia; consider CA-MRSA	Empirical therapy: ceftriaxone 50–75 mg/kg/d q24h <i>or</i> cefotaxime 150 mg/kg/d div q8h <i>and</i> vancomycin 40 mg/kg/d IV div q8h $\times 10$ –14 d	Initial therapy based on Gram stain of empyema fluid; typically clinical improvement is slow, with persisting but decreasing “spiking” fever for 2–3 wk; for susceptible strains of staph, use β -lactam therapy; for susceptible CA-MRSA: clindamycin

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Lower respiratory tract infections			
Pneumonia: lobar or segmental consolidation			
With empyema	Group A strep	Penicillin G 150,000 U/kg/d IV div q4–6h × 10 d	Closed chest tube drainage of purulent fluid; change to PO penicillin V 50–75 mg/kg/day, div qid to tid, or amoxicillin 75 mg/kg/d div tid after clinical improvement
	Pneumococcal	(See above, Pneumonia: Lobar or segmental consolidation)	Definitive therapy is based on susceptibility of strain
	<i>S. aureus</i> (consider CA-MRSA)	Vancomycin 40 mg/kg/d div q8h. For susceptible strains of MSSA: oxacillin or cefazolin. For susceptible strains of MRSA: clindamycin × ≥21 d	Closed chest tube drainage of empyema; consider adding gentamicin for synergy; may benefit from video-assisted thoroscopic drainage
Pneumonia, nosocomial	<i>P. aeruginosa</i> , gram-negative enteric bacilli (<i>Enterobacter</i> , <i>Klebsiella</i> , <i>Serratia</i> , <i>E. coli</i>), <i>Acinetobacter</i> , <i>Stenotrophomonas</i> and gram-positive organisms including MRSA and <i>enterococcus</i> , including vancomycin-resistant strains (VRE)	Should be institution-specific, based on hospital's nosocomial pathogens and their susceptibilities. Commonly used regimens include meropenem 60 mg/kg/d div q8h or piperacillin/tazobactam 240–300 mg/kg/d div q6–8h, or cefepime 150 mg/kg/d div q8h; with/without gentamicin 6–7.5 mg/kg/d div q8h; and vancomycin 40 mg/kg/d div q8h	Pathogens that cause hospital-acquired pneumonia often have multidrug resistance. Cultures are critical. Empirical therapy is often based on prior colonization and hospital epidemiology

Other bacterial pneumonias of established etiology	<i>Chlamydia pneumoniae</i> (TWAR), <i>C. psittaci</i> , or <i>C. trachomatis</i>	A macrolide <i>or</i> doxycycline (patients >7 y); ampicillin for <i>C. trachomatis</i>	
Legionnaires' disease	<i>Legionella pneumophila</i> <i>M. pneumoniae</i>	A macrolide and rifampin A macrolide <i>or</i> doxycycline	
Heart infections			
Endocarditis			Regimens not well defined in children; consider vancomycin <i>and</i> gentamicin for echocardiogram-positive endocarditis, pending culture results; combination provides bactericidal activity against most strains of streptococci, enterococci, and staphylococci (including MRSA)
	Viridans streptococcus	Fully susceptible to penicillin: penicillin G 200,000 U/kg/d IV div q4–6h × 30 d; <i>or</i> penicillin G <i>and</i> gentamicin 6–7.5 mg/kg/d IM, IV div q8h × 14 d; <i>or</i> ceftriaxone 50 mg/kg/d IV, IM q24h 30 d	Tolerant to penicillin: penicillin G 200,000–300,000 U/kg/d IV div q4–6h <i>and</i> gentamicin 6–7.5 mg/kg/d IM, IV div q8h; <i>or</i> vancomycin 40–60 mg/kg/d IV div q8h; × 4–6 wk Follow echocardiogram for resolution of vegetation
	<i>Enterococcus</i>	Ampicillin 200 mg/kg/d IV, IM div q6h <i>and</i> gentamicin 6–7.5 mg/kg/d IV div q8h; <i>or</i> vancomycin 40 mg/kg/d IV div q8h <i>and</i> gentamicin 6–7.5 mg/kg/d IV div q8h; × 4–6 wk	Combined treatment used for synergistic bactericidal activity. Use susceptibility results to guide therapy
	<i>S. aureus</i> (consider community-acquired or hospital-acquired MRSA), <i>S. epidermidis</i>	Vancomycin 40 mg/kg/d IV div q8h. For susceptible strains: nafcillin <i>or</i> oxacillin 150 mg/kg/d IV div q6h; × 6 wk; <i>add</i> gentamicin <i>or</i> rifampin for slow clinical <i>or</i> microbiologic response (at least for the first 2 wk of therapy)	Surgery may be necessary in acute phase; avoid cephalosporins because of conflicting data on efficacy. Consider continuing therapy at end of 6 wk if vegetations persist on echocardiogram. Consult an infectious disease specialist for prosthetic valve endocarditis

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Heart infections			
Endocarditis	Pneumococcus, gonococcus, group A strep	Penicillin G 150,000 U/kg/d IV div q4–6h × 30 d; alternatives: ceftriaxone or vancomycin	Ceftriaxone for gonococcus until susceptibilities known
Gastrointestinal infections			
Colitis, antibiotic-associated	<i>Clostridium difficile</i> toxin	Metronidazole 30 mg/kg/d PO div qid <i>or</i> vancomycin 40 mg/kg/d PO div qid × 7 d	Vancomycin PO may cause emergence of vancomycin-resistant enterococci in gut
Gastritis, peptic ulcer disease	<i>Helicobacter pylori</i>	Clarithromycin 7.5 mg/kg/dose 2–3 times each day <i>and</i> amoxicillin 40 mg/kg/dose (max 1 g) PO bid <i>and</i> omeprazole 0.6–0.7 mg/kg/dose PO qd 2 wk, followed by omeprazole alone × 2 wk	Most data from studies in adults; other regimens include bismuth, metronidazole, or other proton-pump inhibitors
Gastroenteritis			
	<i>Aeromonas</i>	TMP/SMZ as for shigellosis	Possible alternatives based on in vitro susceptibilities: fluoroquinolones, cefotaxime/ceftriaxone, cefepime
	<i>Campylobacter jejuni</i>	Erythromycin 40 mg/kg/d PO div qid × 5 d <i>or</i> azithromycin 10 mg/kg/d × 3 d	Alternatives: doxycycline and ciprofloxacin
Cholera	<i>Vibrio cholerae</i>	Doxycycline 4 mg/kg/d (max 200 mg/d) PO div bid	Ciprofloxacin; TMP/SMZ (if susceptible)
	<i>Escherichia coli</i> —a Note on <i>E. coli</i> and diarrheal disease: Antibiotic susceptibility of <i>E. coli</i> varies considerably from region to region in the world. For mild-to-moderate disease, TMP/SMX may be started as initial therapy. For severe disease, oral second- and third-generation cephalosporins (cefixime, cefuroxime, cefaclor, cefprozil, cefibuten, cefdinir, cefpodoxime) may be used. Cultures and antibiotic susceptibility testing are recommended for significant disease		
Enterotoxigenic (traveler's diarrhea)	<i>E. coli</i> (ST or LT toxin producing)	TMP/SMZ or cefixime 8 mg/kg/d PO qd × 5–7 d	Most illnesses brief and self-limited; alternative (for adults): ciprofloxacin

Enterohemorrhagic	O157:H7; STEC (shiga toxin-producing <i>E. coli</i>); associated with hemolytic-uremic syndrome	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	Injury to colonic mucosa may lead to invasive bacterial colitis
Salmonellosis Nontyphoid strains	<i>Salmonella</i>	Usually none for self-limited diarrhea. For persisting symptomatic infection: cefixime as for shigellosis; <i>or</i> for susceptible strains: amoxicillin 50 mg/kg/d PO div tid; <i>or</i> TMP/SMZ (8 mg/kg/d of TMP component) PO div bid; × 5–7 d	For severe colitis, a septic clinical picture, bacteremia, or compromised hosts: treat with ceftriaxone IV, IM
Typhoid fever	<i>S. typhi</i>	Ceftriaxone 50 mg/kg/d IV, IM q24h, or cefotaxime 150 mg/kg/d IV div q8h; ciprofloxacin 30 mg/kg/d IV, PO div bid; <i>or</i> azithromycin 12 mg/kg on day 1, followed by 6 mg/kg daily × 4 d	Ciprofloxacin or azithromycin for ceftriaxone-resistant strains; watch for relapse if ceftriaxone used
Shigellosis	<i>Shigella</i>	Cefixime 8 mg/kg/d PO qd; <i>or</i> azithromycin 12 mg/kg PO on day 1, followed by 6 mg/kg daily × 4 d; <i>or</i> ciprofloxacin 30 mg/kg/d PO div bid; <i>or</i> for susceptible strains: TMP/SMZ (8 mg/kg/d of TMP component) PO div bid; × 5 d	Ampicillin (not amoxicillin) when <i>Shigella</i> susceptible Avoid antiperistaltic drugs Treat to decrease communicability, even if symptoms resolving
	<i>Yersinia enterocolitica</i>	Antimicrobial therapy probably not of value for mild disease in normal hosts. Cefotaxime IV for TMP-SMZ IV for severe infection.	May mimic appendicitis. Limited clinical data exist on oral therapy; ciprofloxacin for adults
Perirectal abscess	<i>S. aureus</i> , enteric gram-negative bacilli, anaerobes	Clindamycin 30–40 mg/kg/d IV div q8h <i>and</i> gentamicin, cefotaxime, or ceftriaxone	<i>S. aureus</i> common, but may be mixed with coliforms, anaerobes; surgical drainage

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
Gastrointestinal infections			
Peritonitis			
Primary	Pneumococcus	Ceftriaxone 50 mg/kg/d q24h or cefotaxime 150 mg/kg/d div q8h; if penicillin-susceptible, penicillin G 150,000 U/kg/d IV div q6h; × 7–10 d	Other antibiotics according to culture and susceptibility tests
Secondary to bowel perforation or appendicitis	Enteric gram-negative bacilli, <i>Bacteroides</i> , <i>Enterococcus</i>	Meropenem 60 mg/kg/d IV div q8h or imipenem 60 mg/kg/d IV div q6h; <i>or</i> clindamycin 30 mg/kg/d IV, IM div q8h <i>and</i> ampicillin 150 mg/kg/d div q8h and gentamicin 6–7.5 mg/kg/d IV, IM div q8h; × ≥10 d	Many other regimens claimed to be effective for intra-abdominal infection based on limited data. No published data on oral convalescent therapy
Secondary to peritoneal dialysis	Check culture	Antibiotic added to dialysate in concentrations approximating those attained in serum for systemic disease (eg, 8 g/mL for gentamicin; 50 g/mL for vancomycin)	Selection of antibiotic based on organism isolated from peritoneal fluid; systemic antibiotics if there is accompanying bacteremia
Urinary tract infections			
<i>Note:</i> Antibiotic susceptibility profiles of <i>E. coli</i> vary considerably. For mild-to-moderate disease, TMP/SMZ may be started as initial therapy. For severe disease, obtain cultures and begin oral second- and third-generation cephalosporins (cefuroxime, cefaclor, cefprozil, cefixime, ceftibuten, cefdinir, cefpodoxime). Antibiotic susceptibility testing helps direct therapy			
Acute cystitis	<i>E. coli</i> most common; also caused by <i>Klebsiella</i> , other enteric gram-negative bacilli	TMP/SMZ (8 mg/kg/d of TMP component) PO div bid for mild-to-moderate disease, <i>or</i> cefixime 8 mg/kg/d PO qd OR (for patients >18 yr) ciprofloxacin 500 mg PO bid × 7–10 d	Alternative: amoxicillin 30 mg/kg/d PO div tid if susceptible. Follow-up culture after 36–48 h treatment if still symptomatic. Ceftibuten should be equivalent to cefixime in treatment of urinary tract infection

Acute pyelonephritis	See Acute cystitis	Ceftriaxone 50 mg/kg/d IV, IM q24h <i>or</i> gentamicin 5–6 mg/kg/d IV, IM div q8h <i>or</i> given as a single dose q24h; switch to oral therapy after clinical response. If organisms resistant to amoxicillin and TMP/SMZ, an oral second- or third-generation cephalosporin should be effective; × 10 d total therapy	Parenteral therapy if sepsis suspected; If bacteremia documented, and infant is <2–3 mo of age, R/O meningitis and treat 14 d IV <i>or</i> IM
Prophylaxis for recurrent UTI		TMP/SMZ (2 mg/kg TMP component) PO qd <i>OR</i> nitrofurantoin 1–2 mg/kg PO qd at bedtime	Prophylaxis for patients with reflux or frequent infections; resistance eventually develops to any antibiotic used
CNS infections			
Abscess, brain	Respiratory tract flora, skin flora, or bowel flora, depending on the pathogenesis of infection in a particular child	Until etiology established: meropenem 120 mg/kg/d div q8h; <i>or</i> nafcillin 150–200 mg/kg/d IV div q6h <i>and</i> cefotaxime 200–300 mg/kg/d IV div q6h <i>or</i> ceftriaxone 100 mg/kg/d IV div q24h <i>and</i> metronidazole 30 mg/kg/d IV, div q8h; × 7–10 d after successful drainage; longer therapy if no surgery (3–6 wk)	Surgery; anaerobes common. If CA-MRSA suspected <i>based</i> on skin lesions or other foci of staphylococci, <i>add</i> vancomycin pending culture results. If secondary to chronic otitis, use cefepime or meropenem for anti- <i>Pseudomonas</i> activity. Follow abscess size with CT scans
Meningitis, bacterial			

Notes

- Initial empirical therapy for suspected pneumococcal meningitis should be with vancomycin *plus* cefotaxime or ceftriaxone until susceptibility test results are available
- Dexamethasone (0.6 mg/kg/d IV div q6h × 2 d) as an adjunct to antibiotic therapy decreases hearing deficits and possibly other neurologic sequelae in *Haemophilus* meningitis and possibly other types. The first dose of dexamethasone preferably is given before or concurrent with the first dose of antibiotic. There is probably no benefit if given >1 h after the antibiotic is given

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Table 2 (continued)

Clinical diagnosis	Usual pathogen(s)	Therapy	Comments
CNS infections			
Empirical therapy		Cefotaxime 200–300 mg/kg/d IV div q6h <i>or</i> ceftriaxone 100 mg/kg/d IV div q24h. <i>Add</i> vancomycin 60 mg/kg/d IV div q8h if Gram stain suggests pneumococcus	Alternative: meropenem 120 mg/kg/d IV div q8h
	<i>H. influenzae</i> type b	Cefotaxime 200–300 mg/kg/d IV div q6h <i>or</i> ceftriaxone 100 mg/kg/d IV div q1224h; 10 d	Alternative: ampicillin 200–400 mg/kg/d IV div q6h (for β -lactamase-negative strains) <i>or</i> chloramphenicol 100 mg/kg/d IV div q6h
	Pneumococcus (<i>S. pneumoniae</i>)	When pneumococcus is suspected on culture, <i>add</i> vancomycin 60 mg/kg/d IV div q8h until susceptibility results are known. For penicillin-susceptible and cephalosporin-susceptible strains: penicillin G 250,000 U/kg/d IV div q4–6h, <i>or</i> ceftriaxone 100 mg/kg/d IV div q24h <i>or</i> cefotaxime 200–300 mg/kg/d IV div q6h; \times 10 d; for penicillin-resistant pneumococci: continue the combination of vancomycin and ceftriaxone IV	Some pneumococci may be resistant to penicillin, but susceptible to cefotaxime and ceftriaxone and may be treated with these antibiotics alone
	Meningococcus (<i>Neisseria meningitidis</i>)	Penicillin G 250,000 U/kg/d IV div q4h \times 7 d; <i>or</i> ceftriaxone 100 mg/kg/d IV div q24h, <i>or</i> cefotaxime 200 mg/kg/d IV div q6h	Rare strains are resistant to penicillin; meningococcal prophylaxis: rifampin 10 mg/kg PO, q12h \times 4 doses <i>or</i> ceftriaxone 125–250 mg IM once <i>or</i> ciproflaxin 500 mg PO once (adults)

Miscellaneous systemic infections

Bacteremia	Meningococcus; if unimmunized, pneumococcus and <i>H. influenzae</i> type b	Ceftriaxone 50 mg/kg/d IM, IV q24h, <i>or</i> cefotaxime 150 mg/kg/d IV, div q8h; Until afebrile 24 h (usually 2–5 d), then convalescent oral therapy	R/O meningitis, other focal infection; oral convalescent therapy (amoxicillin 75–100 mg/kg/d PO div tid) to complete 7 d (meningococcus) to 10 d (pneumococcus, <i>Haemophilus</i>)
Cat-scratch disease	<i>Bartonella henselae</i>	Supportive (aspiration of pus); azithromycin 12 mg/kg/d PO qd × 5 d shortens the duration of adenopathy	Aminoglycosides, rifampin, TMP/SMZ, ciprofloxacin, cefotaxime also may be effective. Azithromycin dose is that used for group A strep pharyngitis
Lyme disease	<i>Borrelia burgdorferi</i>	Early localized or early disseminated disease: doxycycline (patients >7 y) 4 mg/kg/d (max 200 mg/d) PO div bid <i>or</i> amoxicillin 50 mg/kg/d (max 1.5 g/d) PO div tid × 14–21 d Arthritis (no CNS infection): oral therapy as outlined above, for 28 d Bell's palsy: treat with oral therapy (doxycycline) × 21–28 d Neuroborreliosis: ceftriaxone IV, <i>or</i> cefotaxime IV <i>or</i> penicillin G IV × 14–21 d	Neurologic evaluation, including lumbar puncture, if there is clinical suspicion of CNS involvement; children who have persistent or recurrent joint swelling after recommended courses should repeat treatment with another 4-wk course of oral antibiotics or with a 2- to 4-wk course of ceftriaxone IV; guidelines available at http://www.journals.uchicago.edu/IDSA/guidelines/

Abbreviation: TMP/SMZ, trimethoprim/sulfamethoxazole.

* This table should be considered a rough guideline for the “usual” patient. Dosages recommended are for patients without renal or hepatic failure. Duration of treatment should be individualized. The periods recommended are based on common practice and general experience. Critical evaluations of duration of therapy have been carried out in only a few diseases. In general, a longer duration of therapy should be used (1) for tissues in which antibiotic concentrations may not be high (eg, abscess, bone), (2) when the organisms are less susceptible to antibiotic therapy, (3) when a relapse of infection is unacceptable (eg, CNS infections), or (4) when the host is immuno compromised in some way.

inating those of the child being treated. The simulation provides the physician with the percent of children who achieve a cure at each dose of antibiotic under consideration.

Although these simulations are now an integral part of drug development within the pharmaceutical industry, the US Food and Drug Administration, and the National Institutes of Health, these computer simulations are not yet available in most hospitals or clinics to help the clinicians on the frontlines. Experts involved in making recommendations for antibiotic therapy for infected children have access to published or presented data on Monte Carlo simulations, however, for an ever-increasing number of different antibiotic treatment regimens for many different pathogens causing specific infections.

Host

Host factors, such as patient age and underlying disease, are important considerations in selecting appropriate antibiotic therapy for suspected bacterial infections. Host factors influence the types of bacteria likely to be pathogenic and the anticipated pharmacokinetics and side-effect profiles of different antibiotics. Neonates, especially preterm infants, have immature immunity and disruption of their mucosal and skin barriers by the use of ventilators and deep indwelling catheters. Antibiotic dosing is complicated by pharmacokinetic profiles distinct from the pharmacokinetic profiles of older children. Because of a larger total body water content and higher proportion of extracellular fluid, neonates typically have a larger volume of distribution for certain antibiotics compared with older infants and children. Newborns also have impaired renal function, especially during the first few weeks of life [20–22]. The mg/kg doses for certain antibiotics in these neonates might need to be greater to compensate for the larger volume of distribution and given less frequently to compensate for delayed renal excretion.

Antibiotic adverse reactions

Safety is a major consideration in selection of an appropriate antibiotic for children. All antibiotics have potential side effects, and it is important for the clinician to be aware of how these might affect the patient. Each class of antibiotics has associated risks, and different antibiotics within the same class often have different rates of adverse events. The β -lactams have proved to be among the safest antibiotics for children. Macrolides, aminoglycosides, glycopeptides, sulfonamides, and quinolones all have documented toxicities; some of these antibiotics also have the potential to interfere with drug metabolism of other, concurrently prescribed medications.

Summary

Understanding of the microbiology of infectious pathogens and their mechanisms of resistance has grown tremendously in the past decades. Technologic advances have enabled clinicians to establish the genetic basis for many bacterial resistance phenotypes. The challenge continues: to choose safe and effective antimicrobial agents that are administered to children in a way that maximizes clinical and microbiologic cure, while minimizing adverse drug effects and the development of antibiotic resistance. Table 2 gives examples of infections commonly seen in children and what antibiotics are believed to be reasonable therapy based on the principles discussed in this article [22].

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