pathogen, determination of its susceptibility profile, and establishment of the extent of the infection. Directed therapy generally allows the use of more targeted and narrower-spectrum antibacterial agents than does empirical therapy.

Information on epidemiology, exposures, and local antibacterial susceptibility patterns can help guide empirical therapy. When empirical treatment is clinically appropriate, care should be taken to obtain clinical specimens for microbiologic analysis before the initiation of therapy and to de-escalate therapy as new information is obtained about the patient's clinical condition and the causal pathogens. De-escalation to the point of directed therapy can limit unnecessary risks to the patient as well as the risk of emergence of antibacterial resistance.

SITE OF INFECTION

The site of infection is a consideration in antibacterial therapy, largely because of the differing abilities of drugs to penetrate and achieve adequate concentrations at particular body sites. For example, to be effective in the treatment of meningitis, an agent must (1) be able to cross the blood–brain barrier and reach adequate concentrations in the cerebrospinal fluid (CSF) and (2) be active against the relevant pathogen(s). Dexamethasone, administered with or 15–20 min before the first dose of an antibacterial drug, has been shown to improve outcomes in patients with acute bacterial meningitis, but its use may reduce penetration of some antibacterial agents, such as vancomycin, into the CSF. In this case, rifampin is added because its penetration is not reduced by dexamethasone. Infections at other sites where either pathogens are protected from normal host defenses or penetration of an antibacterial drug is suboptimal include osteomyelitis, prostatitis, intraocular infections, and abscesses. In such cases, consideration must be given to the mechanism of drug delivery (e.g., intravitreal injections) as well as to the role of interventions to drain, debride, or otherwise reduce the barriers to effective antibacterial therapy.

HOST FACTORS

Host factors, including immune function, pregnancy, allergies, age, renal and hepatic function, drug–drug interactions, comorbid conditions, and occupational or social exposures, should be considered.

Immune Dysfunction Patients with deficits in immune function that blunt the response to bacterial infection, including neutropenia, deficient humoral immunity, and asplenia (either surgical or functional), are all at increased risk of severe bacterial infection. Such patients should be treated aggressively and often broadly in the early stages of suspected infection pending results of microbiologic tests. For asplenic patients, treatment should include coverage of encapsulated organisms, particularly *S. pneumoniae*, that may cause rapidly life-threatening infection.

Pregnancy Pregnancy affects decisions regarding antibacterial therapy in two respects. First, pregnancy is associated with an increased risk of particular infections (e.g., those caused by *Listeria*). Second, the potential risks to the fetus that are posed by specific drugs must be considered. As for other drugs, the safety of the vast majority of antibacterial agents in pregnancy has not been established, and such agents are grouped in categories B and C by the U.S. Food and Drug Administration. Drugs in categories D and X are contraindicated in pregnancy or lactation due to established risks. The risks associated with antibacterial use in pregnancy and during lactation are summarized in Table 170-2.

Allergies Allergies to antibiotics are among the most common allergies reported, and an allergy history should be obtained whenever possible before therapy is chosen. A detailed allergy history can shed light on the type of reaction experienced previously and on whether rechallenge with the same or a related medication is advisable (and, if so, under what circumstances). Allergies to the penicillins are most common. Although as many as 10% of patients may report an allergy to penicillin, studies suggest that up to 90% of these patients could tolerate a penicillin or cephalosporin. Adverse effects (Table 170-3) should be distinguished from true allergies to ensure appropriate selection of antibacterial therapy.

Drug–Drug Interactions Patients commonly receive other drugs that may interact with antibacterial agents. A summary of the most common drug–drug interactions, by antibacterial class, is provided in Table 170-4.

Exposures Exposures, both occupational and social, may provide clues to likely pathogens. When relevant, inquiries about exposure to ill contacts, animals, insects, and water should be included in the history, along with sites of residence and travel.

Other Host Factors Age, renal and hepatic function, and comorbid conditions are all considerations in the choice of and schedule for therapy. Dose adjustments should be made accordingly. In patients with decreased or unreliable oral absorption, IV therapy may be preferred to ensure adequate blood levels of drug and delivery of the antibacterial agent to the site of infection.

DURATION OF THERAPY

Whether empirical or directed, the duration of therapy should be planned in most clinical situations. Guidelines that synthesize available literature and expert opinion provide recommendations on therapy duration that are based on infecting organism, organ system, and patient factors. For example, the American Heart Association has published guidelines endorsed by the Infectious Diseases Society of America (IDSA) on diagnosis, antibacterial therapy, and management of complications of infective endocarditis. Similar guidelines from the IDSA exist for bacterial meningitis, catheter-associated urinary tract infections, intraabdominal infections, community- and hospital-acquired pneumonia, and other infections.

FAILURE OF THERAPY

If a patient does not respond to therapy, investigations often should include the collection of additional specimens for microbiologic testing and imaging as indicated. Failure to respond can be the result of an antibacterial regimen that does not address the underlying causative organism, the development of resistance during therapy, or the existence of a focus of infection at a site poorly penetrated by systemic therapy. Some infections may also require surgical interventions for cure (e.g., large abscesses, myonecrosis). Fever due to allergic drug reactions can sometimes complicate assessment of the patient's response to antibacterial treatment.

EXPERT GUIDANCE

Selected websites with the most up-to-date information and guidance for the clinician include the following:

- Johns Hopkins ABX Guide (*www.hopkins-abxguide.org*)
- IDSA Practice Guidelines (*www.idsociety.org/IDSA_Practice_Guidelines/*)
- Center for Disease Dynamics, Economics and Policy Resistance Map (*www.cddep.org/map*)
- CDC Antibiotic/Antimicrobial Resistance (*www.cdc.gov/drugresistance/*)

CLINICAL USE OF ANTIBACTERIAL AGENTS

The clinical application of antibacterial therapy is guided by the spectrum of the agent and the suspected or known target pathogen. Infections for which specific antibacterial agents are among the drugs of choice are listed, along with associated pathogens and susceptibility data, in Table 170-5. Resistance rates of specific organisms are dynamic and should be taken into account in the approach to antibacterial therapy. While national resistance rates can serve as a reference, the most useful reference for the clinician is the most recent local laboratory antibiogram, which provides details on local resistance patterns, often on an annual or semiannual basis.

β-LACTAMS

The β-lactam class of antibiotics consists of penicillins, cephalosporins, carbapenems, and monobactams. The term *β-lactam* reflects the drugs' four-membered lactam ring, which is their core structure. The differing