If a patient fails to respond to one of the category 1 or category 2 drugs (Table 201-2), consideration should be given to alternative therapy and to determination of the resistance patterns among *Bacteroides* isolates.

INFECTIONS AT SPECIFIC SITES

In clinical situations, specific regimens must be tailored to the initial site of infection. The duration of therapy also depends on the infection site; the reader is referred to specific chapters on sites of infection for recommendations.

Infections above the diaphragm usually reflect the orodental microbiota, which does not include the *B. fragilis* group. β-Lactamase production has been reported in anaerobic strains that are usually isolated from infections originating above the diaphragm. Up to 60% of clinical isolates classified as *Prevotella* or *Porphyromonas* species, non–*B. fragilis* species of *Bacteroides*, or *Fusobacterium* species reportedly produce β-lactamase; thus all β-lactam drugs (penicillins and cephalosporins) are poor options. Because most of these infections have a mixed etiology that includes microaerophilic and aerobic streptococci, antibiotics that cover both aerobic and anaerobic bacteria are recommended. The recommended regimens include clindamycin, a β-lactam/β-lactamase inhibitor combination, or metronidazole in combination with a drug active against microaerophilic and aerobic streptococci.

Bronchoscopy in lung abscess is indicated only to rule out airway obstruction and does not enhance drainage; in any event, it should be delayed until the antimicrobial regimen has begun to affect the disease process so that the procedure does not spread the infection. Surgery is almost never indicated because of the danger of spilling the abscess contents into the lungs.

Chloramphenicol has been used successfully against anaerobic CNS infections at doses of 30–60 mg/kg per day, with the exact dose depending on the severity of illness. However, penicillin G and metronidazole also cross the blood–brain barrier and are bactericidal for many anaerobic organisms.

Anaerobic infections arising below the diaphragm (e.g., colonic and intraabdominal infections) must be treated specifically with agents active against *Bacteroides* species (Table 201-2). In intraabdominal sepsis **(Chap. 159)**, the use of antibiotics effective against penicillin-resistant anaerobes has clearly reduced the incidence of postoperative infections and serious infectious complications. Specifically, a drug from category 1 (Table 201-2) must be included for broad-spectrum coverage. Single agents suitable for this purpose include the carbapenems, cefoxitin, and β-lactam/β-lactamase inhibitor combinations. A two-drug regimen is an alternative, with one drug active against coliforms and the other against anaerobes (e.g., a third-generation cephalosporin or a quinolone with metronidazole). In addition, if the clinician suspects that gram-positive facultative organisms such as enterococci are involved, therapeutic regimens should include ampicillin or vancomycin. Although clindamycin and cefotetan were previously considered acceptable options for intraabdominal infections involving anaerobes, these drugs are no longer recommended because of escalating rates of resistance in the *B. fragilis* group. Ampicillin/sulbactam is not recommended because of high rates of resistance among community-acquired strains of *E. coli* rather than because of resistance in anaerobic bacteria.

A meta-analysis of 40 randomized or quasi-randomized controlled trials of 16 antibiotic regimens for secondary peritonitis showed equivalent clinical success for all regimens.

Cases of anaerobic osteomyelitis in which a mixed flora is isolated from a bone biopsy specimen should be treated with a regimen that covers all isolates. When an anaerobic organism is recognized as a major or sole pathogen infecting a joint, the duration of treatment should be similar to that used for arthritis caused by aerobic bacteria **(Chap. 157)**. Therapy includes the management of underlying disease states, the administration of appropriate antimicrobial agents, temporary joint immobilization, percutaneous drainage of effusions, and (usually) the removal of infected prostheses or internal fixation devices. Surgical drainage and debridement procedures such as sequestrectomy are essential for the removal of necrotic tissue that can sustain anaerobic infections.

The outcome of anaerobic bacteremia is significantly better in patients either initially given or switched to appropriate therapy on the basis of known antibiotic susceptibilities.

FAILURE OF THERAPY

Anaerobic infections that fail to respond to treatment or that relapse should be reassessed. Consideration should be given to additional surgical drainage or debridement. Superinfections with resistant gram-negative facultative or aerobic bacteria should be ruled out. The possibility of drug resistance must be entertained; if resistance is involved, repeat cultures may yield the pathogen.

SUPPORTIVE MEASURES

Other supportive measures in the management of anaerobic infections include careful attention to fluid and electrolyte balance (since extensive local edema may lead to hypoalbuminemia), hemodynamic support for septic shock, immobilization of infected extremities, maintenance of adequate nutrition during chronic infections by parenteral hyperalimentation, relief of pain, and anticoagulation for thrombophlebitis. For patients with severe anaerobic infections of soft tissues, hyperbaric oxygen therapy is advocated by some experts, but its value has not been proven in controlled trials.

SECTION 8 MYCOBACTERIAL DISEASES

202 Tuberculosis

Mario C. Raviglione

Tuberculosis (TB), which is caused by bacteria of the *Mycobacterium tuberculosis* complex, is one of the oldest diseases known to affect humans and a major cause of death worldwide. Recent population genomic studies suggest that *M. tuberculosis* may have emerged ~70,000 years ago in Africa and subsequently disseminated along with anatomically modern humans, expanding globally during the Neolithic Age as human density started to increase. Progenitors of *M. tuberculosis* are likely to have affected prehominids. This disease most often affects the lungs, although other organs are involved in up to one-third of cases. If properly treated, TB caused by drug-susceptible strains is curable in the vast majority of cases. If untreated, the disease may be fatal within 5 years in 50–65% of cases. Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary TB.

ETIOLOGIC AGENT

Mycobacteria belong to the family Mycobacteriaceae and the order Actinomycetales. Of the pathogenic species belonging to the *M. tuberculosis* complex, which comprises eight distinct subgroups, the most common and important agent of human disease is *M. tuberculosis*. The