some circumstances—penicillin, cephalosporins, or tetracyclines) suggests an anaerobic etiology.

TREATMENT ANAEROBIC INFECTIONS

Successful therapy for anaerobic infections requires the administration of a combination of appropriate antibiotics, surgical resection, debridement of devitalized tissues, and drainage either surgically or percutaneously (guided by an imaging technique such as CT, MRI, or ultrasound). Any anatomic breach must be closed promptly, closed spaces drained, tissue compartments decompressed, and an adequate blood supply established. Abscess cavities should be drained as soon as fluctuation or localization occurs.

ANTIBIOTIC THERAPY AND RESISTANCE

The antibiotics used to treat anaerobic infections should be active against both aerobic and anaerobic organisms because many of these infections are of mixed etiology. Antibiotic regimens can usually be selected empirically on the basis of the type of infection, the species of the organisms usually present in such cases, the results of Gram's staining, and a knowledge of antimicrobial resistance patterns (Chap. 170 and Table 201-2). Other factors influencing the selection of antibiotics include need for bactericidal activity and for penetration into certain organs (such as the brain), toxicity, and impact on the normal microbiota. Antibiotics active against clinically relevant anaerobes can be grouped into four categories based on their predicted activity (Table 201-2). Nearly all the drugs listed have toxic side effects, which are described in detail in Chap. 170.

Antibiotic susceptibility testing of anaerobic bacteria has been difficult and controversial. Because of the slow growth rate of many anaerobes, the lack of standardized testing methods and of clinically relevant standards for resistance, and the generally good results obtained with empirical therapy, there has been limited interest in testing these organisms for antibiotic susceptibility. However, one study of antibiotic-treated patients with *Bacteroides* isolates from blood found mortality rates of 45% among those whose isolates were deemed resistant to the agent used and 16% among those whose isolates were deemed sensitive. It is accepted that testing is important for patients with serious or prolonged infections or in cases in which antibiotics have not had an impact. Testing is also helpful in monitoring the activity of new drugs and recording current resistance patterns among anaerobic pathogens. The antibiotics with the greatest activity against nearly all anaerobic bacteria include carbapenems, β-lactam/β-lactamase inhibitor combinations, metronidazole, and chloramphenicol.

Antibiotic resistance in anaerobic bacteria is an increasing problem. Resistance rates vary with the institution and the geographic region. In recent years, the activity of clindamycin, cefoxitin, cefotetan, and moxifloxacin has decreased against *B. fragilis* and related strains (*B. distasonis, B. ovatus, B. thetaiotaomicron, B. uniformis, B. vulgatus*). Multidrug-resistant *B. fragilis* has recently been reported. Nearly all organisms in the *B. fragilis* group (>97%) are resistant to penicillin G. The cephamycins cefoxitin and cefotetan display greater activity against this group, but rates of resistance have increased, with current figures at ~10% in the United States and higher in Argentina (28%) and Europe (17%). Rates of resistance to β-lactam agents among anaerobes other than *Bacteroides* are lower but are highly variable. β-Lactam/β-lactamase inhibitor combinations such as ampicillin/sulbactam, ticarcillin/clavulanic acid, and piperacillin/tazobactam are usually good therapeutic options against β-lactamase-producing anaerobes, including the *B. fragilis* group. Although resistance rates reported from most countries are still low, several studies have documented nonsusceptibility to ampicillin/sulbactam in 0.5–3% of isolates in the United States, 3–10% in Europe, and 1–8% in Argentina. Recently, up to 48% of *B. fragilis* isolates in Taiwan were found to be nonsusceptible to ampicillin/sulbactam, and a significant increase in resistance to this combination was also identified among other *Bacteroides*, *Prevotella*, and *Fusobacterium* species.

Carbapenems (ertapenem, doripenem, meropenem, and imipenem) are equally active against anaerobes, with <1% of *B. fragilis* strains showing resistance in the United States and Europe. Higher rates of carbapenem nonsusceptibility are being reported from some countries (5% in Germany, 8% [to doripenem] in Canada, and 7–12% in Taiwan).

Metronidazole is active against gram-negative anaerobes, including the *B. fragilis* group; resistance, although rare (<1%), has been reported in both Europe and the United States. Resistance to metronidazole is more common among gram-positive anaerobes, including *P. acnes, Actinomyces* species, lactobacilli, and anaerobic streptococci. Clindamycin is active against many anaerobes. However, rates of resistance to clindamycin among the *B. fragilis* group have increased in the United States from 3% in 1982 to 16% in 1996 and 26% in 2000, with rates as high as 40–50% in some series. Resistance to clindamycin among non-*Bacteroides* anaerobes is much less common (<10%).

Tigecycline is active against some anaerobic bacteria, including *Peptostreptococcus*, *Propionibacterium*, *Prevotella*, *Fusobacterium*, and most *Bacteroides* species. Its efficacy for treatment of intraabdominal infections was comparable to that of imipenem in two phase 3 double-blind clinical trials. This drug is therefore recommended as single-agent treatment for complicated intraabdominal infections, but resistance (~6%) among *Bacteroides* and non-*Bacteroides* species has been reported.

Fluoroquinolones such as moxifloxacin have shown potential in the treatment of mixed aerobic-anaerobic infections. A survey in the United States found a 38% rate of resistance to moxifloxacin among the *B. fragilis* group; in Europe 14–30% of isolates were nonsusceptible to this drug, as were 7–25% of anaerobes isolated from blood cultures in Taiwan. Despite excellent in vitro activity against all clinically important anaerobes, chloramphenicol is less desirable than other active drugs for the treatment of anaerobic infection because of documented clinical failures.

TABLE 201-2 ANTIMICROBIAL THERAPY FOR INFECTIONS INVOLVING COMMONLY ENCOUNTERED ANAEROBIC GRAM-NEGATIVE RODS

Category 1 (Nearly Always Active)	Category 2 (Usually Active)	Category 3 (Variable Resistance)	Category 4 (Resistance)
Carbapenems (imipenem, meropenem, doripenem)	Tigecycline	Cephamycins (cefoxitin, cefotetan)	Aminoglycosides
Metronidazole[a]	High-dose antipseudomonal penicillins	Clindamycin	Monobactams
β-Lactam/β-lactamase inhibitor combination (ampicillin/sulbactam, ticarcillin/clavulanic acid, piperacillin/tazobactam)		Penicillins	Trimethoprim-sulfamethoxazole
Chloramphenicol[b]		Cephalosporins	
		Tetracycline	
		Vancomycin	
		Erythromycin	
		Moxifloxacin	

[a]Usually needs to be given in combination with aerobic bacterial coverage. For infections originating below the diaphragm, aerobic gram-negative coverage is essential. For infections from an oral source, aerobic gram-positive coverage is added. Metronidazole also is not active against *Actinomyces, Propionibacterium,* or other gram-positive non-spore-forming bacilli (e.g., *Eubacterium, Bifidobacterium*) and is unreliable against peptostreptococci. [b]Despite excellent in vitro activity against all clinically important anaerobes, this drug is less desirable than other active drugs because of documented clinical failures.