the third generation. The second- and third-generation drugs are more active against gram-negative organisms because they are more resistant to the beta-lactamase enzymes (cephalosporinases) produced by some bacteria to inactivate cephalosporins.

Fourth-Generation Cephalosporins

Fourth-generation cephalosporins have a greater spectrum of antimicrobial activity and greater stability against breakdown by beta-lactamase enzymes compared with third-generation drugs. Cefepime is the first fourth-generation cephalosporin to be developed. It is active against both gram-positive and gram-negative organisms. With gram-positive organisms, it is active against streptococci and staphylococci (except for methicillin-resistant staphylococci). With gram-negative organisms, its activity against *Pseudomonas aeruginosa* is similar to that of ceftazidime and its activity against Enterobacteriaceae is greater than that of third-generation cephalosporins. Moreover, cefepime retains activity against strains of Enterobacteriaceae and *P. aeruginosa* that have acquired resistance to third-generation agents.

Indications for Use

Clinical indications for the use of cephalosporins include surgical prophylaxis and treatment of infections of the respiratory tract, skin and soft tissues, bones and joints, urinary tract, brain and spinal cord, and bloodstream (septicemia). In most infections with streptococci and staphylococci, penicillins are more effective and less expensive. In infections caused by methicillin-resistant *S. aureus*, cephalosporins are not clinically effective even if in vitro testing indicates susceptibility. Infections caused by *Neiserria gonorrhoeae*, once susceptible to penicillin, are now preferentially treated with a third-generation cephalosporin such as ceftriaxone. Cefepime is indicated for use in severe infections of the lower respiratory and urinary tracts, skin and soft tissue, female reproductive tract, and in febrile neutropenic clients. It may be used as monotherapy for all infections caused by susceptible organisms except *P. aeruginosa;* a combination of drugs should be used for serious pseudomonal infections.

Contraindications to Use

A major contraindication to the use of a cephalosporin is a previous severe anaphylactic reaction to a penicillin. Because cephalosporins are chemically similar to penicillins, there is a risk of cross-sensitivity. However, incidence of cross-sensitivity is low, especially in clients who have had delayed reactions (eg, skin rash) to penicillins. Another contraindication is cephalosporin allergy. Immediate allergic reactions with anaphylaxis, bronchospasm, and urticaria occur less often than delayed reactions with skin rash, drug fever, and eosinophilia.

CARBAPENEMS

Carbapenems are broad-spectrum, bactericidal, beta-lactam antimicrobials. Like other beta-lactam drugs, they inhibit synthesis of bacterial cell walls by binding with penicillin-binding proteins. The group consists of three drugs.

Imipenem/cilastatin (Primaxin) is given parenterally and distributed in most body fluids. Imipenem is rapidly broken down by an enzyme (dehydropeptidase) in renal tubules and therefore reaches only low concentrations in urine. Cilastatin was synthesized to inhibit the enzyme and reduce potential renal toxicity of the antibacterial agent. Recommended doses indicate the amount of imipenem; the solution contains an equivalent amount of cilastatin.

The drug is effective in infections caused by a wide range of bacteria, including penicillinase-producing staphylococci, *E. coli*, *Proteus* species, *Enterobacter–Klebsiella–Serratia* species, *P. aeruginosa*, and *Enterococcus faecalis*. Its main indication for use is treatment of infections caused by organisms resistant to other drugs. Adverse effects are similar to those of other beta-lactam antibiotics, including the risk of cross-sensitivity in clients with penicillin hypersensitivity. Central nervous system toxicity, including seizures, has been reported. Seizures are more likely in clients with a seizure disorder or when recommended doses are exceeded; however, they have occurred in other clients as well. To prepare the solution for IM injection, lidocaine, a local anesthetic, is added to decrease pain. This solution is contraindicated in people allergic to this type of local anesthetic or who have severe shock or heart block.

Meropenem (Merrem) has a broad spectrum of antibacterial activity and may be used as a single drug for empiric therapy before causative microorganisms are identified. It is effective against penicillin-susceptible staphylococci and *S. pneumoniae*, most gram-negative aerobes (eg, *E. coli*, *H. influenzae*, *Klebsiella pneumoniae*, *P. aeruginosa*), and some anaerobes, including *B. fragilis*. It is indicated for use in intra-abdominal infections and bacterial meningitis caused by susceptible organisms. Compared with imipenem, meropenem costs more and seems to offer no clinical advantages. Adverse effects are similar to those of imipenem.

Ertapenem (Invanz) also has a broad spectrum of antibacterial activity, although more limited than imipenem and meropenem. It is approved for complicated intra-abdominal, skin and skin structure, acute pelvic, and urinary tract infections. It can be used to treat community-acquired pneumonia caused by penicillin-susceptible *S. pneumoniae*. Unlike imipenem and meropenem, ertapenem does not have in vitro

How Can You Avoid This Medication Error?

Glen Rilley returns to your busy surgical unit with the following antibiotic order: Cefuroxime 1 g q12h. The antibiotic comes from the pharmacy labeled "ceftizoxime 1 g q12h (0900 & 2100). Infuse 50 cc over 30 minutes." You hook up the antibiotic and set the hour rate for 100 cc/hour.