Mechanism of Action

Aminoglycosides penetrate the cell walls of susceptible bacteria and bind irreversibly to 30S ribosomes, intracellular structures that synthesize proteins. As a result, the bacteria cannot synthesize the proteins necessary for their function and replication.

Indications for Use

The major clinical use of parenteral aminoglycosides is to treat serious systemic infections caused by susceptible aerobic gram-negative organisms. Many hospital-acquired infections are caused by gram-negative organisms. These infections have become more common with control of other types of infections, widespread use of antimicrobial drugs, and diseases (eg, acquired immunodeficiency syndrome [AIDS]) or treatments (eg, radical surgery and therapy with antineoplastic or immunosuppressive drugs) that lower host resistance. Although they can occur anywhere, infections due to gram-negative organisms commonly involve the respiratory and genitourinary tracts, skin, wounds, bowel, and bloodstream. Any infection with gram-negative organisms may be serious and potentially life threatening. Management is difficult because the organisms are in general less susceptible to antibacterial drugs, and drug-resistant strains develop rapidly. In pseudomonal infections, an aminoglycoside is often given concurrently with an antipseudomonal penicillin (eg, piperacillin) for synergistic therapeutic effects. The penicillin-induced breakdown of the bacterial cell wall makes it easier for the aminoglycoside to reach its site of action inside the bacterial cell. However, the drugs are chemically and physically incompatible. Therefore, they should not be mixed in a syringe or an IV fluid because the aminoglycoside will be deactivated.

A second clinical use is for treatment of tuberculosis. Streptomycin was often used before the development of isoniazid and rifampin. Now, it may be used for treatment of tuberculosis resistant to other antitubercular drugs. Multidrug-resistant strains of the tuberculosis organism, including strains resistant to both isoniazid and rifampin, are being identified with increasing frequency. This development is leading some authorities to recommend an aminoglycoside as part of a four- to six-drug regimen.

A third clinical use is for synergistic action when combined with ampicillin, penicillin G, or vancomycin in the treatment of enterococcal infections. Regimens for enterococcal infections, particularly meningitis or endocarditis, should include **gentamicin** in divided doses rather than once-daily dosing. Some enterococcal strains are resistant to gentamicin, however, and microbiology results should be reviewed for each patient.

A final clinical use is oral administration to suppress intestinal bacteria. Neomycin and kanamycin may be given before bowel surgery and to treat hepatic coma. In hepatic coma, intestinal bacteria produce ammonia, which enters the bloodstream and causes encephalopathy. Drug therapy to suppress intestinal bacteria decreases ammonia production. Paromomycin is used mainly in the treatment of intestinal amebiasis.

A few aminoglycosides are administered topically to the eye or to the skin. These are discussed in Chapters 65 and 66, respectively.

Contraindications to Use

Aminoglycosides are contraindicated in infections for which less toxic drugs are effective. The drugs are nephrotoxic and ototoxic and must be used very cautiously in the presence of renal impairment. Dosages are adjusted according to serum drug levels and creatinine clearance. The drugs must also be used cautiously in clients with myasthenia gravis and other neuromuscular disorders because muscle weakness may be increased.

FLUOROQUINOLONES

Fluoroquinolones are synthetic bactericidal drugs with activity against gram-negative and gram-positive organisms. They may allow oral ambulatory treatment of infections that previously required parenteral therapy and hospitalization. Most are given orally, after which they are well absorbed, achieve therapeutic concentrations in most body fluids, and are metabolized to some extent in the liver. The kidneys are the main route of elimination, with approximately 30% to 60% of an oral dose excreted unchanged in the urine. Dosage should be reduced in renal impairment.

Mechanism of Action

The drugs act by interfering with deoxyribonucleic acid (DNA) gyrase, an enzyme required for synthesis of bacterial DNA and therefore required for bacterial growth and replication.

Indications for Use

Fluoroquinolones are indicated for various infections caused by aerobic gram-negative and other microorganisms. Thus, they may be used to treat infections of the respiratory, genitourinary, and GI tracts as well as infections of bones, joints, skin, and soft tissues. Additional uses include treatment of gonorrhea, multidrug-resistant tuberculosis (see Chap. 38), *Mycobacterium avium* complex (MAC) infections in clients with AIDS, and fever in neutropenic cancer clients. Indications vary with individual drugs and are listed in Drugs at a Glance: Fluoroquinolones.

Contraindications to Use

Fluoroquinolones are contraindicated in clients who have experienced a hypersensitivity reaction and in children younger than 18 years of age, if other alternatives are available. Lim-