Cephalosporins

Cephalosporins are safe and reliable and have a broad spectrum of activity. The cephalosporins act by essentially the same mechanism as the penicillins and have similar pharmacologic properties. The primary therapeutic use of the cephalosporins is

- for gram-negative infections
- for patients who cannot tolerate the less expensive penicillins.

More than 20 cephalosporins are available. They are classified into four "generation,"

•First-generation compounds have excellent activity against Gram-positive organisms and some activity against Gram-negative ones. Many of them are potentially nephrotoxic.

• Second-generation drugs retain Gram-positive activity but have extended Gram-negative activity. Cephamycins (e.g. cefoxitin).

•Third-generation agents further improve anti- Gram-negative cover. For some (e.g. ceftazidime), this is extended to include Pseudomonas spp. Cefotaxime and ceftriaxone have excellent Gram-negative activity and retain good activity against Strep. pneumoniae and β-haemolytic streptococci. Ceftriaxone is administered once daily, and is therefore a suitable agent for outpatient antimicrobial therapy.

•Fourth-generation agents have an extremely broad spectrum of activity, including Pseudomonas spp., Staph. aureus and streptococci.

Adverse Effects

- Diarrhea
- abdominal cramping
- nausea
- fatigue
- rash, pruritus
- pain at injection sites
- oral or vaginal candidiasis
- pseudomembranous colitis
- nephrotoxicity
- anaphylaxis

Drug	Route and Adult Dose (max dose where indicated)
FIRST GENERATION	
cefadroxil (Duricef)	PO; 500 mg–1 g one to two times/day (max: 2 g/day)
cephalexin (Keflex)	PO; 250–500 mg qid nax: 12 g/day)
SECOND GENERATION	
cefaclor (Ceclor)	PO; 250–500 mg tid (max: 2 g/day)
cefotetan (Cefotan)	IV/IM; 1–2 g every 12 h (max: 6 g/day)
THIRD GENERATION	
cefdinir (Omnicef)	PO; 300 mg bid (max: 600 mg/day)
cefditoren (Spectracef)	PO; 400 mg bid for 10 days (max: 800 mg/day)
cefixime (Suprax)	PO; 400 mg/day or 200 mg bid (max: 800 mg/day)
cefotaxime (Claforan)	IV/IM; 1–2 g bid–tid (max: 12 g/day)
ceftizoxime (Cefizox)	IV/IM; 1–2 g every 8–12 h, up to 2 g every 4 h (max: 12 g/day)
ceftriaxone (Rocephin)	IV/IM; 1–2 g every 12–24 h (max: 4 g/day)
FOURTH AND FIFTH GENERATIONS	
cefepime (Maxipime)	IV/IM; 0.5–1 g every 12 h for 7–10 days (max: 6 g/day)
ceftaroline (Teflaro)	IV; 600 mg every 12 h for 5–14 days (max: 6 g/day)

Macrolides

Macrolides (erythromycin, clarithromycin and azithromycin). The macrolides inhibit protein synthesis by binding to the bacterial ribosome. At low doses, this inhibition produces a bacteriostatic effect. At higher doses, and in susceptible species, macrolides may be bacteriocidal.

Macrolides are used in Gram-positive infections in penicillin-allergic patients and in Mycoplasma and Chlamydia infections.

- Erythromycin is administered 6-hourly
- clarithromycin 12-hourly.
- The long intracellular half-life of azithromycin allows single-dose/.

Adverse effect

- Nausea, vomiting, diarrhea, abdominal cramping, dry skin or burning (topical route)
- Anaphylaxis, ototoxicity, pseudomembranous colitis,
- hepatotoxicity, superinfections, dysrhythmias, anemia

Drug	Route and Adult Dose (max dose where indicated)
azithromycin (Zithromax, Zmax)	PO; 500 mg for one dose, then 250 mg/day for 4 days
clarithromycin (Biaxin)	PO; 250–500 mg bid
erythromycin (E-Mycin, Erythrocin)	PO; 250–500 mg bid or 333 mg tid

Tetracyclines

Tetracyclines act by inhibiting bacterial protein synthesis by binding to the bacterial ribosome, the tetracyclines slow microbial growth and exert a bacteriostatic effect. The widespread use of tetracyclines in the 1950s and 1960s resulted in the emergence of a large number of resistant bacterial strains that now limit the therapeutic utility of tetracyclines.

TABLE 34.4 Tetracyclines	
Drug	Route and Adult Dose (max dose where indicated)
demeclocycline (Declomycin)	PO; 150 mg every 6 h or 300 mg every 12 h (max: 2.4 g/day)
doxycycline (Vibramycin, others)	PO/IV; 100 mg bid on day 1, then 100 mg/day (max: 200 mg/day)
minocycline (Minocin, others)	PO/IV; 200 mg as single dose followed by 100 mg bid
tetracycline (Sumycin, others)	PO; 250–500 mg bid–qid (max: 2 g/day)
tigecycline (Tygacil)	IV; 100 mg, followed by 50 mg every 12 h

Adverse effect

- Nausea, vomiting, abdominal cramping, flatulence, diarrhea,
- mild phototoxicity, rash, dizziness
- Anaphylaxis
- hepatotoxicity,
- exfoliative dermatitis,
- permanent teeth discoloration in children.

Aminoglycosides

The first aminoglycoside, streptomycin, was named after Streptomyces griseus, the soil organism from which it was isolated in 1942. Although more toxic than other antibiotic classes, aminoglycosides have important therapeutic applications for the treatment of aerobic gram-negative bacteria, mycobacteria, and some protozoans. Aminoglycosides are bacteriocidal(E. coli, Serratia, Proteus, Klebsiella, and Pseudomonas.) aminoglycoside act by inhibiting bacterial protein synthesis.

Drug	Route and Adult Dose (max dose where indicated)
amikacin	IV/IM; 5.0–7.5 mg/kg as a loading dose, then 7.5 mg/kg bid
gentamicin (Garamycin, others)	IV/IM; 1.5–2.0 mg/kg as a loading dose, then 1–2 mg/kg bid–tid
kanamycin	IV/IM; 5.0–7.5 mg/kg bid–tid
neomycin	PO; 4–12 g/day in divided doses
paromomycin (Humatin)	PO; 7.5–12.5 mg/kg in three doses
streptomycin	IM; 15 mg/kg up to 1 g as a single dose
tobramycin	IV/IM; 1 mg/kg tid (max: 5 mg/kg/day)

Adverse effect

- Pain or inflammation at the injection site,
- rash, fever,
- nausea,diarrhea,
- dizziness, tinnitus
- Anaphylaxis,
- neuropathy
- nephrotoxicity,
- irreversible ototoxicity.

Note: Loop diuretics taken with aminoglycosides increase the risk of ototoxicity.