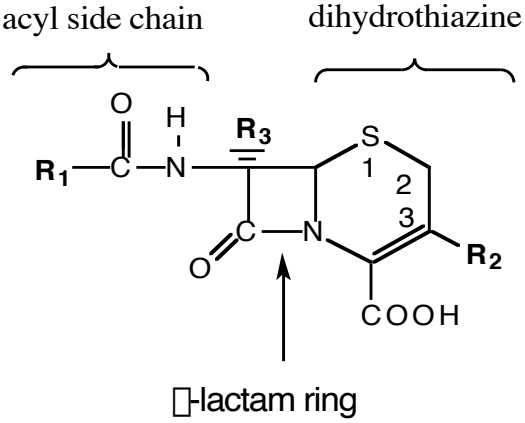
The Cephalosporins

I. CHEMISTRY AND MECHANISM OF ACTION

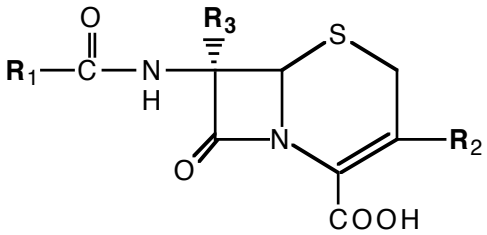
Cephalosporins are β-lactam antibiotics that differ from the penicillins in that the B ring is a 6-membered dihydrothiazine ring. Variations among the cephalosporins are made on either the acyl side chain at the 7-position to change antibacterial activity or at the 3-position to alter the pharmacokinetic profile. Cephalosporin C was first isolated in 1948 by Dr. Abraham from a fungus, *Cephalosporium acremonium*, collected in seawater near a sewage outlet in Sardinia by Professor Guiseppe Brotzu in 1945.

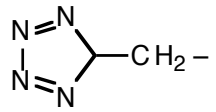
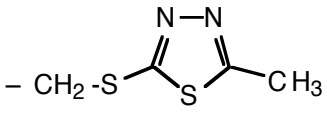
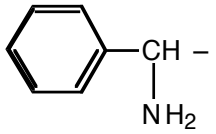
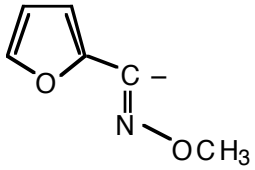
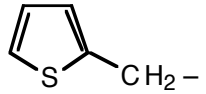
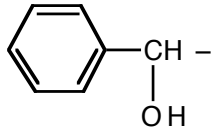
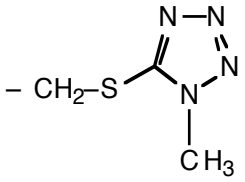
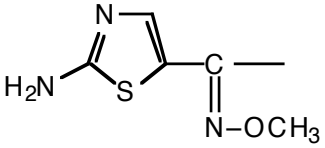
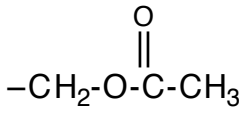
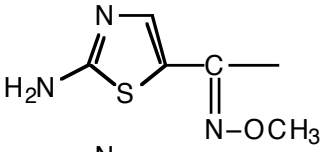
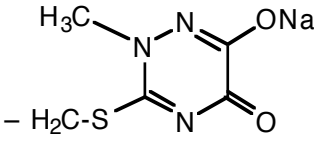
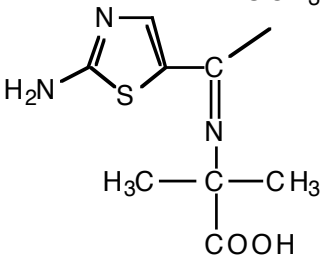
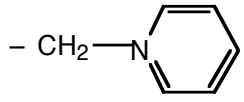


General structure of the Cephalosporins

- Similar mechanism of action to penicillins.
- Bind to penicillin binding proteins (transpeptidases, endopeptidases, and carboxypeptidases) and inhibit cell wall biosynthesis in both Gm + and Gm – bacteria.
- However, degree and extent of binding to different PBPs may be different for the cephalosporins than for penicillins. For example, cephalothin causes lysis of *Staph. aureus*, whereas cephalexin produces long filamentous forms in *E. coli*.
- In general, cephalosporins are less susceptible to β-lactamases compared to penicillins.

Table 18. Structures of Representative Cephalosporins



Cephalosporin	R_1	R_2	R_3
Cefazolin			H
Cephalexin		CH_3	H
Cefuroxime		$-CH_2$-O-$CONH_2$	H
Cefoxitin		$-CH_2$-O-$CONH_2$	$-OCH_3$
Cefamandole			H
Cefotaxime			H
Ceftriaxone			H
Ceftazidime			H

II. CLASSIFICATION OF THE CEPHALOSPORINS

Table 19. Classification, Route of Administration, and Trade Names of Cephalosporins

Type and Generic Name	Route of Administration	Trade Names
First Generation		
Cefazolin	IM, IV	Ancef (Glaxo SK) Kefzol (Lilly)
Cephalothin	IM, IV	Keflin (Lilly)
Cephapirin	IM, IV	Cefadyl (Apothecon)
Cefadroxil	IV, PO	Duricef (Bristol-Myers Squibb)
Cephalexin	PO	Keflex & Keflet (Lilly) Cefanex (Apothecon)
Cephradine	PO	Velosef (Apothecon)
Second Generation		
Cefuroxime	IM, IV	Zinacef (Glaxo-SK), Kefurox (Lilly)
Cefamandole	IM, IV	Mandol (Lilly)
Cefoxitin	IM, IV	Mefoxin (Merck)
Cefonicid	IM, IV	Monocid (Glaxo-SK)
Cefotetan	IM, IV	Cefotan (Stuart)
Cefmetazole	IV	Zefazone (Pharmacia/Pfizer)
Cefuroxime axetil	PO	Ceftin (Glaxo-SK)
Cefaclor	PO	Ceclor (Lilly)
Cefdinir	PO	Omnicef (Pfizer)
Cefprozil	PO	Cefzil (Bristol-Myers Squibb)
Loracarbef	PO	Lorabid (Lilly)
Third Generation		
Cefotaxime	IM, IV	Claforan (Hoechst-Roussel)
Ceftizoxime	IM, IV	Cefizox (Fujisawa)
Ceftriaxone	IM, IV	Rocephin (Roche)
Ceftazidime	IM, IV	Fortaz & Ceptaz (Glaxo SK), Tazidime (Lilly), Tazicef (Glaxo SK)
Cefoperazone	IM, IV	Cefobid (Roerig)
Cefixime	PO	Suprax (Lederle)
Ceftibuten	PO	Cedax (Schering Plough)
Cefpodoxime axetil	PO	Vantin (Pharmacia/Pfizer)
Cefepime	IM, IV	Maxipime (Bristol-Myers Squibb)

III. MECHANISMS OF RESISTANCE (see Penicillin section III)

A. Production of β-lactamases (see penicillin section III)

1. In general, cephalosporins are much more resistant to β-lactamases

2. First and Second Generation cephalosporins are still susceptible to Richmond-Sykes Type I β-lactamases.

IV. SPECTRUM & USES

A. First Generation Cephalosporins - Spectrum

Prototype Drugs are CEFAZOLIN (for IV use) and CEPHALEXIN (oral use).

1. *Staph. aureus* - excellent activity against β-lactamase-producing strains
   Not effective against methicillin-resistant *Staph. aureus & epidermidis*

2. Streptococci - excellent activity versus *Streptococcus sp.*
   Not effective against penicillin-resistant *Strep. pneumoniae*

3. Other Gm + bacteria - excellent activity except for *Enterococcus sp.*

4. Moderate activity against gram negative bacteria.
   Caution: resistance may occur in all cases.

   Susceptible organisms include:

   E. coli
   Proteus mirabilis
   Indole + *Proteus sp.* (many strains resistant)
   Haemophilus influenzae (some strains resistant)
   Neisseria sp. (some gonococci resistant)

B. First Generation Cephalosporins - Uses

1. Upper respiratory tract infections due to *Staph.* and *Strep.*

2. Lower respiratory tract infections due to susceptible bacteria e.g. *Strep. pneumoniae* in penicillin-allergic patient (previous rash)

3. Uncomplicated urinary tract infections (Cephalexin)

4. Surgical prophylaxis for orthopedic and cardiovascular operations (cefazolin preferred because of longer half-life)

5. Staphylococcal infections of skin and skin structure

TABLE 20. COMMENTS ON INDIVIDUAL 1st GENERATION CEPHALOSPORINS

Cephalosporin	Comments
Cephalothin (Keflin)	Causes pain on IM admin. Short half-life (0.5 h). 1st generation ceph. with least susceptibility to staphylococcal β-lactamase
Cefazolin (Kefzol, Ancef)	Longer half-life (1.8h). Highly protein bound. Well tolerated.
Cephapirin (Cefadyl)	Very similar activity to cephalothin. Short half-life.
Cephalexin (Keflex)	Oral agent. Less active against Staphylococci. 90% excreted in urine.
Cefadroxil	Serum and urine concentrations more sustained than with cephalexin, with similar activity. May use qd or bid for UTIs.
Cephradine (Velosef)	Identical activity to cephalexin. Available PO and IV/IM. Nearly complete bioavailability.

C. Second Generation Cephalosporins – Spectrum

Prototype drug is CEFUROXIME (IV) and CEFUROXIME AXETIL (oral). CEFOXITIN has good activity vs. anaerobes.

1. Expanded activity against gram negative bacilli. Still have excellent activity against gram positive (*Staph*. and *Strep*.) bacteria.

Activity for Gram negative bacteria

Neisseria sp. (some gonococci resistant)
H. influenzae (including some ampicillin-resistant strains)
Moraxella catarrhalis (some resistance esp. to cefaclor)
E. coli
Proteus mirabilis
Indole + Proteus (some strains resistant)
Morganella morganii (some strains resistant)
Klebsiella pneumoniae
Serratia sp. (many strains resistant)

2. Anaerobic infections - CEFOXITIN & CEFOTETAN only

Moderate activity against *Bacteroides fragilis* group.
Good activity for other *Bacteroides sp., Peptostreptococcus, Fusobacterium, Clostridium sp*.

D. Second Generation Cephalosporins – Uses

1. Community-acquired pneumonia - Cefuroxime is widely used for empiric therapy. Has activity vs. many ampicillin-resistant *H. influenzae* strains.

2. Skin and soft tissue infection

3. Urinary tract infections

4. Upper respiratory tract infections (otitis media, sinusitis). Some resistance to *H. influenzae* to cefaclor (20-30%).

5. Mixed aerobic & anaerobic infections - Cefoxitin & Cefotetan. Resistance to *B. fragilis* is increasing.

6. Surgical prophylaxis - Cefoxitin or cefotetan are widely used in cases where mixed aerobic & anaerobic infections may occur, esp. intra-abdominal, colo-rectal, and gynecologic operations. For cardiovascular and orthopedic procedures, cefuroxime and others may be used, but cefazolin is cheaper and appears to work well.

TABLE 21A. COMMENTS ON INDIVIDUAL 2ND GENERATION CEPHALOSPORINS FOR PARENTERAL USE

Cephalosporin	Comments
Cefuroxime (Zinacef)	Protoype drug. Short half-life,
Cefoxitin (Mefoxin)	Activity vs. anaerobes because of -OCH3 group on A ring. Resistant to *Bacteroides* β-lactamases. Short half-life
Cefotetan (Cefotan)	Has anaerobic activity like cefoxitin. Long half-life. Give b.i.d.
Cefonicid (Monocid)	Long half-life (4-5 h). Similar spectrum to cefuroxime
Cefmetazole (Zefazone)	Me-too. Has anaerobic activity.

TABLE 21B. COMMENTS ON INDIVIDUAL 2ND GENERATION CEPHALOSPORINS FOR ORAL USE

Cephalosporin	Comments
Cefuroxime axetil (Ceftin)	Reasonably well absorbed (F = 35-45%). Better antimicrobial activity than cefaclor. Taste is fair. Recently became available as a liquid. BID dosing.
Cefaclor (Ceclor)	Long experience. Widely used. Resistance to both *H. influenzae & Moraxella catarrhalis* for otitis media. Shorter half-life but still can use either t.i.d. or even b.i.d. Good taste. Generally well tolerated (some rash, serum-sickness). Moderate cost, available as generic.
Cefdinir (Omnicef)	Approved late 1997. Good gram positive activity. Dosed QD or BID. Poor bioavailability. Good taste. Best selling oral cephalosporin in Japan. Some diarrhea. Expensive
Cefprozil (Cefzil)	Longer half-life than cefaclor (80 min). BID dosing. Only moderate activity vs. *H. influenzae*. Improved activity vs. *Moraxella catarrhalis*. Eosinophilia (2%). Increase in liver function tests (2%). Less diarrhea. Good taste. Expensive.
Loracarbef (Lorabid)	Carbacephem (C instead of S). BID dosing. High bioavailability (>90%). Basically a me-too. Expensive.

E. Third Generation Cephalosporins - Spectrum

Prototype drugs are CEFOTAXIME (IV) and CEFIXIME (oral). CEFTAZIDIME (for *Pseudomonas aeruginosa*.).

Further expansion of Gm negative spectrum to include hard to treat organisms such as *Enterobacter, Serratia, and Pseudomonas*. In addition to better Gm negative spectrum, this group has improved pharmacokinetic properties (longer half-lives) that allow once daily dosing with some agents. In general, activity toward Gm + bacteria is reduced. These are specialty antibiotics that should be reserved for specific uses.

Enterobacteriaciae that are almost always sensitive (>95% sensitive)

E. coli
Proteus mirabilis (indole –)
Proteus vulgaris (indole +)
Klebsiella pneumoniae

Gram negative bacilli that are generally sensitive (>75% sensitive)

Morganella morganii
Providencia retgerri
Citrobacter freundii
Serratia marcescens
Pseudomonas aeruginosa (Ceftazidime only)

Gram negative bacilli that are sometimes sensitive (<75% sensitive)

Enterobacter
Stenotrophomonas (Xanthomonas) maltophilia (Cefoperazone & Ceftazidime only)
Acinetobacter

Note: investigational agents cefepime & cefpirome are promising for these bacteria

Bacteria that are resistant

Listeria monocytogenes
Pseudomonas cepacia
Enterococcus sp. (investigational agents cefpiramide & cefpirome are active)

F. Third Generation Cephalosporins - Uses

1. Gram negative septicemia & other serious Gm – infections

2. *Pseudomonas aeruginosa* infections (Ceftazidime - 90% effective)

3. Gram negative meningitis - Cefotaxime, Ceftriaxone, Cefepime. For empiric therapy add vancomycin ± rifampin to cover resistant *Strep. pneumoniae*

4. Gonorrhea - Single shot of Ceftriaxone is drug of choice. Oral cefixime and ceftibuten are also OK.

5. Complicated urinary tract infections, pyelonephritis

6. Osteomyelitis - Ceftriaxone in home health care situations

7. Lyme disease - ceftriaxone in home health care situations

<u>Inappropriate Uses</u> (yet widely prescribed)

1. Surgical prophylaxis (use 1st or 2nd generation agents)

2. Otitis media, URIs - Cefixime (Suprax), ceftibuten have poor Gm + activity

3. Uncomplicated UTIs

TABLE 22. COMMENTS ON INDIVIDUAL THIRD GENERATION CEPHALOSPORINS

Cephalosporin	Comments
Ceftriaxone (Rocephin)	Most potent against *Neisseria*. Long half-life of 8 h allows bid or daily dosing. Good for home health care problems. CNS penetration is adequate. Best-selling of all IV cephalosporins.
Cefotaxime (Claforan)	Long experience. Excellent spectrum except for *Pseudomonas*. Reliable CNS penetration. Active desacetyl metabolite may increase activity towards anaerobes and extend duration of action.
Ceftizoxime (Cefizox)	Activity similar to cefotaxime. Less reliable CNS penetration.
Cefixime (Suprax)	First oral 3rd gen. agent. Activity similar to cefotaxime, but poorer Gm + activity than 1st and 2nd generation agents. Long half-life (4 h). Can give once a day. Good taste. Expensive.
Cefpodoxime axetil (Vantin)	Somewhat longer half-life (2 h). BID dosing. Highly active vs. *H. flu* and *M. cat*. Better activity vs. *Staph.* and *Strep*. than cefixime and ceftibuten. (some consider this a 2nd generation agent). Some diarrhea. Poor taste. Expensive.
Ceftibuten (Cedax)	High bioavailability (~90%). Half-life of 2.6 h, but may give once a day. Poor activity vs. *Staph.* and Group B *Strep*. Me-too of cefixime. Expensive.
Cefoperazone (Cefobid)	Some *Pseudomonas* activity (60%). Less active vs aerobic Gm negative bacteria than others. Low CNS penetration. High biliary excretion. Bleeding problems - Give with Vit K.
Ceftazidime (Fortaz)	Most active against *Pseudomonas*. Virtually no Gm + activity. CNS penetration is adequate to treat meningitis.
Cefepime (Maxipime)	Approved in 1996. Better activity vs.*Citrobacter*, *Enterobacter, Acinetobacter, & Serratia* than cefotaxime. Reasonable activity vs. *Pseudomonas* (ceftazidime slightly better). Decent Gm + activity. Marketed as 4th generation cephalosporin.
Cefpirome	Investigational. Better activity vs. *Enterococcus, Enterobacter, Citrobacter, Acinetobacter, & Serratia*

IV. ABSORPTION, DISPOSITION, AND METABOLISM

TABLE 23. PHARMACOKINETIC PROPERTIES OF THE CEPHALOSPORINS

Drug	Half-life (min)	Half-life in ESRD (hrs)	% Protein Bound	% Unchanged in Urine	Mean Peak Serum Level (μg/ml) 1g IV dose or 1g PO dose	CSF Penetration (inflamed meninges) (μg/ml)
1st Generation						
Cephalexin	50-80	19-22	10	>90		
Cefadroxil	78-96	20-25	20	>90	24-35 (p.o.)	
Cephradine	48-80	8-15	8-17	>90	86	
Cephalothin	30-50	3-15	70	68-70	30	
Cephapirin	24-36	1.8-4	54	68-70	73	
Cefazolin	90-120	3-7	80-86	80-96	185	
2nd Generation						
Cefuroxime	80	16-22	33-50	66-100	100	0.1-17
Cefamandole	30-60	8-11	70	65-85	139	
Cefoxitin	40-60	20	73	85-99	64-110	
Cefonicid	270	11	98	95-99	221	low
Cefmetazole	72		65	85		
Cefotetan	180-276	13-35	88-90	51-81	158	
Oral agents						
Cefaclor	35-54	2-3	25	60-85	23-25	
Cefdinir	100-120	17	60-70	15-30	2.0[c]	
Cefprozil	78	5.2-5.9	36	60		
Loracarbef	60	32	25	>90		
3rd Generation						
Cefixime	180-240	11.5	65	50	3.7[a]	
Ceftibuten	160	22.3	60-64	80-90	8.6-13.9[b]	
Cefpodoxime	120	9.8	21-29	29-33	3.8[a]	
Cefoperazone	102-156	1.3-2.9	82-93	20-30	75-153	0-11.5
Cefotaxime	60	3-11	30-40	20-36	42-102	5.6-44.3
Ceftizoxime	84-114	25-30	30	80	60-87	4.6 (.5-29)
Ceftriaxone	348-522	15.7	85-95	33-67	151	1.2-39
Ceftazidime	114-120	14-30	<10-17	80-90	69-90	9.8
Cefepime	114-144		16-19	>85%	29.6	

a = after 400 mg p.o. dose
b = after 200 mg p.o. dose
c = after 300 mg p.o. dose

A. Individual Pharmacokinetic Observations

1. First Generation Cephalosporins

i. Cephalothin & Cephapirin have short half-lives. Cefazolin has longest half-life but also has the highest protein binding (lower free levels).

ii. Must reduce dose or give less often or both in renal failure.

2. Second Generation Cephalosporins

    i. Pharmacokinetic properties relatively similar. Cefonicid & Cefotetan have longer half-lives such that dosing may be on a once a day basis (Cefonicid) or b.i.d. (Cefotetan). This should result in some cost savings. However, both drugs are highly protein bound - lower free levels, lower CSF levels.

    ii. Oral agents similar, but urinary excretion of cefpodoxime is lower.

    iii. Must reduce dose or give less often or both in renal failure, except for cefpodoxime.

3. Third Generation Cephalosporins

    i. Ceftriaxone has long half-life (7-9 hrs). Used once daily. Single dose treatment for gonorrhea. Good for home health care situations. Chronic dosing may result in formation of biliary sludge.

    ii. Cefoperazone is mainly excreted in the bile. Advantage in renal failure. Useful for treatment of infections of biliary tract.

    iii. Must reduce dose or give less often or both in renal failure, especially for cefotaxime, ceftizoxime, cefepime, and ceftazidime.

    iii. Cefoperazone & ceftriaxone highly protein bound. Cefoperazone should not be used for meningitis. Ceftriaxone CSF levels appear to be adequate, but lower than with cefotaxime.

V. ADVERSE REACTIONS

In general, Cephalosporins are very well tolerated and can be used freely. Some problems with individual agents are noted below.

A. HYPERSENSITIVITY REACTIONS (1-7%)

1. anaphylaxis (rare)

2. rash (maculopapular, urticarial) (1-3%)

3. serum sickness-like reaction, eosinophilia, + Coombs test - esp. with cefaclor

4. Some cross-sensitivity with penicillins (5-10%), perhaps as low as 1%.

B. Phlebitis, Pain on IM injection

1. Most common with cephalothin and cephapirin. Cefotaxime also.

C. Hypoprothombinemia - associated with methylthiotetrazole ring

- Common with cefoperazone, cefamandole, cefotetan, & moxolactam (discontinued).
- Occurs in 20-60% of patients.
- Give Vitamin K (menadione) as preventative. Less bleeding problems with cefotetan.
- Other cephs. may also cause bleeding due to reduction of gut flora.

D. GI complaints (5-10%)

- Diarrhea more common with cefixime, cefdinir, and cefoperazone.

E. Elevation of liver enzymes (5-10%)

F. Disulfiram-like reaction.

- Flushing, sweating, headache, tachycardia associated with alcohol ingestion.
- Associated wtih methylthiotetrazole-containing cephalosporins only. (cefoperazone, cefamandole, cefotetan)

G. Cholecystitis-like syndrome with Ceftriaxone (~20% with chronic dosing).

- Precipitation of ceftriaxone in bile leads to biliary sludge.
- May require surgery.
- Rarely with cefoperazone.

H. Displacement of bilirubin from albumin binding sites - theoretical problem in neonates.

- Occurs with ceftriaxone & cefoperazone.

VI. DRUG INTERACTIONS

TABLE 24. DRUG INTERACTIONS OF THE CEPHALOSPORINS

Precipitant Drug	Object Drug	Effect	Description
Cephalosporins with methylthioltetrazol group	Ethanol	↑	Alcoholic beverages taken with or up to 72 h after cefametazole, cefoperazone cefazolin, or cefotetan may produce a disulfiram-like rxn. Flushing, sweating, tachycardia
Cephalosporins	Aminoglycosides	↑	Nephrotoxicity of AGs may be potentiated with some cephs., especially cephalothin
Cephalosporins with methylthioltetrazol group	Anticoagulants	↑	Hypoprothrombinemic effects of anticoagulants are increased. Bleeding complications may occur. An additional problem is depletion of the gut flora resulting in decreased Vitamin K synthesis (problem with 2nd & 3rd gen. cephs)
Cephalosporins	Urine glucose testing	↑	May lead to false positives in diabetics taking cephalosporins
Probenicid	Cephalosporins	↑	Probenicid inhibits renal tubular secretion of cephalosporins that are primarily renally excreted.
Antacids	Cephalosporins	↓	Reduced absorption of ceclor CD, cefdivir, and cefpodoxime
H_2 antagonists	Cefpodoxine, Cefuroxine	↓	Reduced absorption of cefpodoxime and celuoxime

VII. PRODUCTS AND DOSING

Cefazolin sodium

Powder for Injection: 250 mg, 500 mg, 1g in vials and piggyback vials. 5g, 10g, 20 g in bulk vials. (Kefzol® - Lilly, Ancef® - Glaxo SK, + generics).
Injection: 500 mg & 1g in 5% Dextrose in water (premixed, frozen) (Ancef® - Glaxo SK)

Moderate to severe infections: 500 mg to 1 g every 6-8 hours
Pneumococcal pneumonia: 500 mg every 12 hours
Acute UTIs: 1g every 12 hours
Surgical prophylaxis: 1g IV or IM, 30-60 min prior to surgery, then 0.5-1 g IV or IM q 6-8 hours up to 24 h after surgery. For long surgical procedures (>2h) - give 0.5-1g IV as needed.

Cephalexin monohydrate

Capsules: 250 mg, 500 mg (Keflex® - Dista, + generics)
Tablets: 250 mg, 500 mg, 1 g (Keflet® - Dista)
Oral Suspension: 125 mg/5ml and 250 mg/5ml (Keflex® - Dista)
Pediatric Oral Suspension: 100mg per ml (5 mg/drop) (Keflex® - Dista)

Cephalexin HCl monohydrate

Tablets: 250 mg & 500 mg (Keftab® - Dista) Note: this formulation has a more rapid dissolution.

Adults: Usual dose is 250 mg q 6 h. May give up to 4 g/day for serious infections
Streptococcal pharyngitis, skin & skin structure infections, &cystitis: 500 mg q 12 h
Children: 25-50 mg/kg/day in divided doses.
Strep. pharyngitis and skin infections: give every 12 hours.
Otitis media: 75-100 mg/kg/day in 4 divided doses.

Cefadroxil
Capsules: 500 mg (Duricef® - Brisol-Myers Squibb, + generics)
Tablets: 1 g (Duricef® - Mead Johnson, Ultracef® - Bristol, + generics)
Oral suspension: 125 mg, 250 mg, & 500 mg per 5 ml - orange-pineapple flavor (Duricef® - Bristol-Myers Squibb)

Adults: 1g/day in single or 2 divided doses. For complicated UTIs - 2 g/d in 2 divided doses.
Children: 30 mg/kg/day in divided doses q 12 h.

Cephradine
Capsules: 250 mg, 500 mg (Velosef® - Bristol-Myers Squibb)
Tablets: 250 mg, 500 mg, 1 g (Velosef® - Bristol-Myers Squibb)
Oral Suspension: 125 mg/5ml and 250 mg/5ml reconstituted. Fruit flavor. (Velosef® - Bristol-Myers Squibb)
Powder for Injection: 250 mg, 500 mg, & 1g in vials. 2g in 100 ml infusion bottles.

Adults: *Mild infections* : 250 - 500 mg q 6 h or 500 mg q 12 h.
Lobar pneumonia: 500 mg q 6 h or 1 g q 12h. *UTIs:* 500 mg -1 g q 12 h.
Children: 50-100 mg/kg/day in equally divided doses q 6 h or q 12h.

Cephalothin
Injection: 1g or 2g in 5% Dextrose (premixed, frozen) in 50 ml single dose Viaflex Plus® containers (Baxter)
Powder for Injection: 1 g or 2 g in vials (1g/10 ml) or piggyback vials (1g/100 ml) (Keflin® Neutral - Lilly, + generics). 20 g in 200 ml vials (Keflin® Neutral - Lilly).

Adults: 500 mg - 1 g q 4-6 h
Infants & children: 100 mg/kg in divided doses q 4-6 h

Cephapirin
Powder for Injection: 1 g in vials and piggyback vials (Cefadyl® - Apothecon)

Adults: 500 mg - 1 g q 4-6 h
Children: 40-80 mg/kg/day administered in 4 equally divided doses.

SECOND GENERATION CEPHALOSPORINS

Cefuroxime sodium and Cefuroxime axetil
Tablets (as axetil): 125 mg, 250 mg, and 500 mg (Ceftin® - Glaxo SK)
Powder for Injection (as sodium): 750 mg and 1.5 g in vials, Faspak and ADD-Vantage vials. 7.5 g in bulk packages (Kefurox® - Lilly, Zinacef® - Glaxo SK, + generics). 2.4 mEq Na/g.
Injection: 750 mg and 1.5 g in 50 ml (premixed, frozen).

Oral Suspension: 125 and 250 mg per 5ml Tutti-frutti flavor (Ceftin®-Glaxo SK)

Adults: 250-500 mg twice daily. *UTIs:* 125 mg twice daily *Gonorrhea:* 1 g in single dose
Infants and Children: 125 mg twice daily.
Otitis media: <2 yrs - 125 mg b.i.d., >2 yrs - 250 mg b.i.d. Note: crushed tablet has strong bitter taste.

Absorption is enhanced when given with food.

Cefaclor
Capsules (Pulvules): 250 mg and 500 mg (Ceclor® - Lilly)
Extended Release Tablets: 375 mg and 500 mg (Ceclor CD® - Lilly) –
Administer with food. Do not crush or chew
Powder for Oral Suspension: 125 mg, 187 mg, 250 mg, and 375 mg per 5 ml. Strawberry flavor. Suspension should be refrigerated after reconstitution. Discard after 14 days. (Ceclor® - Lilly)

Adults: 250 mg q 8 h. May go up to 500 mg q 8 h for severe infections. Ceclor CD - 375-500 mg BID
Children: 20 mg/kg/day in divided doses q 8 hours.
Otitis media & severe infections: 40 mg/kg/day in 2 or 3 divided doses. Maximum dose = 1 g/day

Cefoxitin
Powder for Injection: 1g and 2 g in vials, infusion bottles, and ADD-Vantage vials. 10 g in bulk bottles (Mefoxin® - Merck) Contains 2.3 mL Na/g.
Injection: 1 g and 2 g in 5% Dextrose in Water (premixed, frozen in 50 ml plastic containers)

Adults: 1-2 g q 6-8 h. *Gonorrhea:* 2 g IM + 1 g oral probenecid.
Surgery prophylaxis: 2 g IV or IM 30-60 min prior to surgery followed by 2 g q 6 h after 1st dose for no more than 24 hours (72 hrs for prosthetic arthroplasty).
Infants & Children: 80-160 mg/kg/day divided q 4-6 hrs. Do not exceed 12 g/day.
Prophylactic use: 30-40 mg/kg/day q 6 h.

Cefamandole naftate
Powder for Injection: 500 mg, 1 g, and 2 g in vials ADD-Vantage vials & Faspacks. 10g in 100 ml vials. (Mandol® - Lilly)

Adults: 500 mg to 1 g q 4-8 h. 500 mg q 6 h is adequate for pneumonia, skin & skin structure infections. Serious UTIs: 1 g q 8 h.
Infants & children (>3 mos. old): 50-100 mg/kg/day in equally divided doses

Cefmetazole
Powder for Injection: 1g and 2 g in vials (Zefazone® - Pharmacia/Pfizer)
Injection: 1g/50mL and 2g/50mL -store frozen. Do not refreeze if thawed.

Adults: 2 g IV q 6-12 h
Surgical prophylaxis: 1-2 g IV 30-60 min before surgery. Repeat 1 g dose at 8 and 16 h post-surgery.

Cefonicid
Powder for Injection: 500 mg in vials; 1 g in vials and piggyback vials; 10g in bulk vials (Monocid® - Glaxo-SK). Contains 3.7 mEq sodium/gm

Adults: 1 g q 24 hrs IV or by deep IM injection. May give up to 2 g per day if necessary (rare).
Surgical prophylaxis: 1g one hour prior to surgery. May give for 2 additional days to patients undergoing prosthetic arthroplasty or open heart surgery.

Cefotetan disodium
Powder for Injection: 1g in 10 & 100 ml vials, 2 g in 20 & 100 ml vials. 10 g in 100 ml vials. (Cefotan® - Zeneca). Contains 3.5 mEq sodium/gm
Injection: 1g and 2g in 50mL (premixed)

Adults: 1 or 2 g IV or IM q 12 h. *Prophylaxis:* 1 or 2 g IV dose 30-60 min prior to surgery

Cefpodoxime axetil
Tablets: 100 mg and 200 mg (Vantin® - Pharmacia/Pfizer)
Granules for suspension: 50 and 100 mg per 5 ml. Lemon creme flavor (Vantin® - Pharmacia/Pfizer)
Adults: 100-400 mg q 12 h for 7-14 days
Children (6 mos.-12 yrs). 10 mg/kg/day divided q 12 hr (maximum 400 mg/day).

Cefprozil
Tablets: 250 mg and 500 mg (as anhydrous) (Cefzil® - Bristol-Myers Squibb)
Powder for suspension: 125 mg and 250 mg per 5 ml. Bubble gum flavor. (Cefzil® - BMS)
Note: Refrigerate after reconstitution.

Adults: *URIs:* 500 mg q 24 h. *Lower respiratory tract infections:* 500 mg q 12 h.
Children (6 mos -12 yrs) : 15 mg/kg q 12 h for otitis media, 7.5 mg/kg for pharyngitis/tonsillitis.

Loracarbef
Capsules (Pulvules): 200 mg (Lorabid® - Lilly)
Powder for suspension: 200 mg per 5 ml. Strawberry bubble gum flavor. (Lorabid® - Lilly)

Adults: 200-400 mg q 12 h.
Infants and children (6 mos-12 yrs): 30 mg/kg/day q 12 h for otitis media. 15 mg/kg for pharyngitis/tonsillitis and impetigo.

THIRD GENERATION CEPHALOSPORINS

Cefotaxime
Powder for Injection: 1g and 2 g in vials, infusion bottles, & and ADD-Vantage vials. 10 g in bulk vials. (Claforan® - Aventis). Contains 2.2 mEq sodium/gm.
Injection: 1 g and 2 g in 50 ml (premixed, fozen) (Claforan® - Hoechst Marion Roussel)

Adults: 1-2 g q 8 h for moderate to severe infections. For life-threatening infections 2 g q 4 h
Gonorrhea: 1 g IM as single dose.
Children (1 mo. - 12 yrs): 50-180 mg/kg/day in 4-6 divided doses
Children (1-4 weeks): 50 mg/kg q 8 hrs.
Children (<1 week): 50 mg/kg q 12 h.

Ceftriaxone
Powder for injection: 250 mg and 500 mg in vials, 1g and 2 g in vials, piggyback vials, and ADD-Vantage vials. 10 g in bulk containers. (Rocephin® - Roche). Contains 3.6 mEq sodium/gm.
Injection: 1 g and 2 g in 50 ml plastic containers (premixed, frozen). (Rocephin® - Roche)

Adults: 1-2 g once a day.
Gonorrhea (uncomplicated): 250 mg single IM dose plus doxycycline or erythromycin (if pregnant).
For children (<45kg) 125 mg IM once.
Surgical prophylaxis: Single 1 g dose 0.5-2 hours before surgery.
Children: 50-75 mg/kg/day (not to exceed 2 g) in divided doses q 12 h for serious infections.
Meningitis: 100 mg/kg/day (not to exceed 4 g) every 12 hour, with or without a loading dose of 75 mg/kg.

Ceftizoxime sodium
Powder for injection: 500 mg, 1 g, 2 g in 10ml or 20ml single dose fliptop vials and 100 ml piggyback vials. 10 g as pharmacy bulk package. (Cefizox® - Fujisawa).
Injection: 1 or 2 g in 50 ml of 5% Dextrose in water (premixed, frozen). Contains 2.6 mEq Na/g.

Adults: 1-2 g q 8-12 h IM or IV. For life-threatening infections 3-4 g q 8 h.
Uncomplicated UTIs: 500 mg q 12 h.
Children (≥6 mos): 50 mg/kg q 6-8 h.

Cefoperazone sodium
Powder for injection: 1 g and 2 g in vials and piggyback units. (Cefobid® - Pfizer).
Injection: 1 or 2 g in 50 ml (premixed, frozen). Contains 1.5 mEq sodium/gm.

Adults: 2-4 g/day in equally divided doses q 12 h. For severe infections 6-12 g/day.

Ceftazidime
Powder for Injection: 500 mg, 1 g, 2 g in vials, piggyback vials, *Faspak* and *ADD-Vantage* vials (1 and 2 g only). 6 g in bulk package or 100 ml vial. (Fortaz® - Glaxo SK, Tazicef® - Glaxo SK, Bristol-Myers Squibb, Tazidime® - Lilly). Contains 2.3 mEq sodium/gm.
Powder for Injection, L-arginine formulation: 1g, 2g vials - (Ceptaz®-Glaxo SK)
Injection: 1g or 2 g in 50 ml (premixed, frozen) - (Fortaz® - Glaxo SK), Tazicef (SKB/BMS)

Adults: 1g q 8-12 h. For life-threatening infections 2 g IV q 8 h.
Uncomplicated UTIs: 250 mg q 12 h. *Complicated UTIs:* 500 mg q 8-12 h.
Pseudomonal lung infections in cystic fibrosis patients: 30-50 mg/kg IV to a maximum of 6 g/day
Infants and children (1mo.-12 yrs): 30-50 mg/kg IV q 8 h to a maximum of 6 g/day.
Neonates ≤ 4 weeks: 30 mg/kg IV q 12 h.

Cefixime
Tablets: 200 mg and 400 mg (Suprax® - Lederle)
Powder for oral suspension: 100 mg per 5 ml. Strawberry flavor. (Suprax® - Lederle)
Note: suspension gives higher blood levels than tablets, so for otitis media use suspension.

Adults: 400 mg/day as single 400 mg tablet (for gonococcal infections) or 200 mg b.i.d.
Children: 8 mg/kg/day as single dose or 4 mg/kg q 12 h.

Ceftibuten
Capsules: 400 mg (Cedax® - Schering)
Powder for Oral Suspension: 90 mg and 180 mg per 5 ml. Cherry Flavor.
Note: Refrigerate suspension after reconstitution.

Adults: 400 mg/day
Children: 9 mg/kg per day for pharyngitis, tonsilitis or otitis media due to *Strep. pyogenes* and for otititis media due to *H. influenzae* and *M. catarrhalis* (note: not for *Strep. pneumoniae*).

Cefdinir
Capsules: 300 mg (Omnicef® - Pfizer)
Powder for Oral Suspension 125mg per 5mL: Strawberry flavor

Adults: 600 mg once daily or 300 mg BID – use BID dosing for pneumonia and skin infections.
Indications: Community-acquired pneumonia, acute exacerbation of chronic bronchits, acute bacterial sinusitis, pharyngitis and tonsillitis due to *Strep. pyogenes*, uncomplicated skin and skin structure infections.
Children: 14 mg/kg once daily or 7 mg/kg BID for otitis media, sinusitis, or pharyngitis due to *Strep. pyogenes*.

Cefepime HCl
Powder for Injection: 1 g and 2 g (Maxipime® - Dura)

Adults: 1 to 2 g q 12 h

Approved for febrile neutropenia and complicated intra-abdominal infections.
Uncomplicated and complicated urinary tract infections, moderate-to-severe pneumonia