



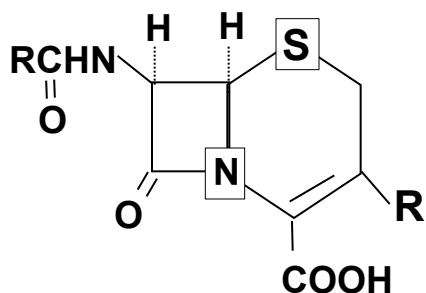
2nd Generation Cephalosporins and Cephameycins

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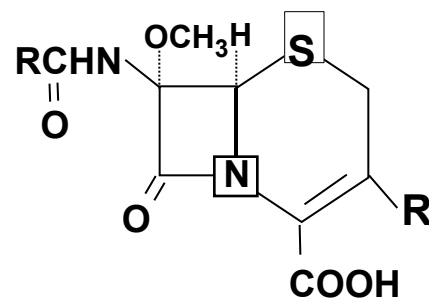
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2nd Generation Cephalosporins

Cephalosporin



Cephamycin



methoxy group at C7
really gives difference
in activity





'2nd Generation' Cephalosporins

2nd Gen Cephalosporins
Enhanced Activity against
H. influenzae very good for resp inf.

~~(Cefamandole*) (Mandel[®])~~
Cefuroxime (Zinacef[®])

Oral

Cefaclor (Ceclor[®]) (tid)
Cefuroxime axetil (Ceftin[®]) (bid)
Cefprozil (Cefzil[®]) (bid)
~~(Loracarbef (Lorabid[®]) (bid))~~

Cephameycins
Enhanced Activity
against *B. fragilis*

Cefoxitin (Mefoxin[®])

~~(Cefotetan*) (Cefotan[®])~~

~~(Cefmetazole*[®])~~

* Methylthiotetrazole group



Spectrum of Activity

- ❑ less activity than 1st generation cephalosporins against *S. aureus* and broader activity against gram negative organisms
- ❑ active against many cephalothin resistant *E. coli*, *Klebsiella*, *Proteus mirabilis*
- ❑ Cephalosporin group (cefuroxime) more active against ***H. influenzae*, *S. pneumoniae***
- ❑ Cephameycins (Cefoxitin group) more active against ***B. fragilis***
- ❑ **No activity** against Enterococci, Mycoplasma, Chlamydia or Legionella (as with all Cephalosporins)

Cefuroxime

- ❑ “Claim to fame” more resistant to β -lactamases produced by *H. influenzae*
- ❑ compared to 1st generation some improved activity against *E. coli*, Klebsiella, Enterobacter, Indole + Proteus
- ❑ improved binding to PBPs in *S. pneumoniae* compared to 1st generation cephalosporins
- ❑ results in good activity against sensitive & intermediate resistant *S. pneumoniae* (but not highly resistant)



Cefuroxime

- ❑ penetrates somewhat into C.S.F. (but failures reported in meningitis)
- ❑ does not have a methylthiotetrazole side chain
- ❑ $t_{1/2}$ 1.3 -1.5 hr

- ❑ Place in therapy - community acquired pneumonia
(with Doxycycline or a Macrolide)
to cover atypical organisms
- ❑ Dose 750 mg q8h



Cefuroxime axetil (Ceftin®)

- ❑ oral ester of cefuroxime
- ❑ hydrolyzed to cefuroxime after absorption
- ❑ 30 - 50% bioavailability (inc)
- ❑ (absorption increased with food)
- ❑ t_{1/2} 1.3 hours

- ❑ place in therapy - alternative otitis, sinusitis, CAP
- ❑ Dose 250 - 500 mg b.i.d.



Ceprozil (Cefzil®)

TASTES BETTER than cefuroxime

- ❑ Similar activity to cefuroxime
- ❑ Relatively good activity against *S. pneumoniae*
(*not as good as cefuroxime*)
- ❑ Good side effect profile
- ❑ Only available orally
- ❑ bid dosing



Cefaclor (Ceclor®)

- ❑ Reduced activity against penicillin intermediate resistant *S. pneumoniae* & resistant *S. pneumoniae*
- ❑ associated with a higher incidence of skin rashes in children
- ❑ associated with Serum sickness (0.05%) which is thought to be a direct cytotoxic effect

So much (-)'s --> shouldn't be used anymore

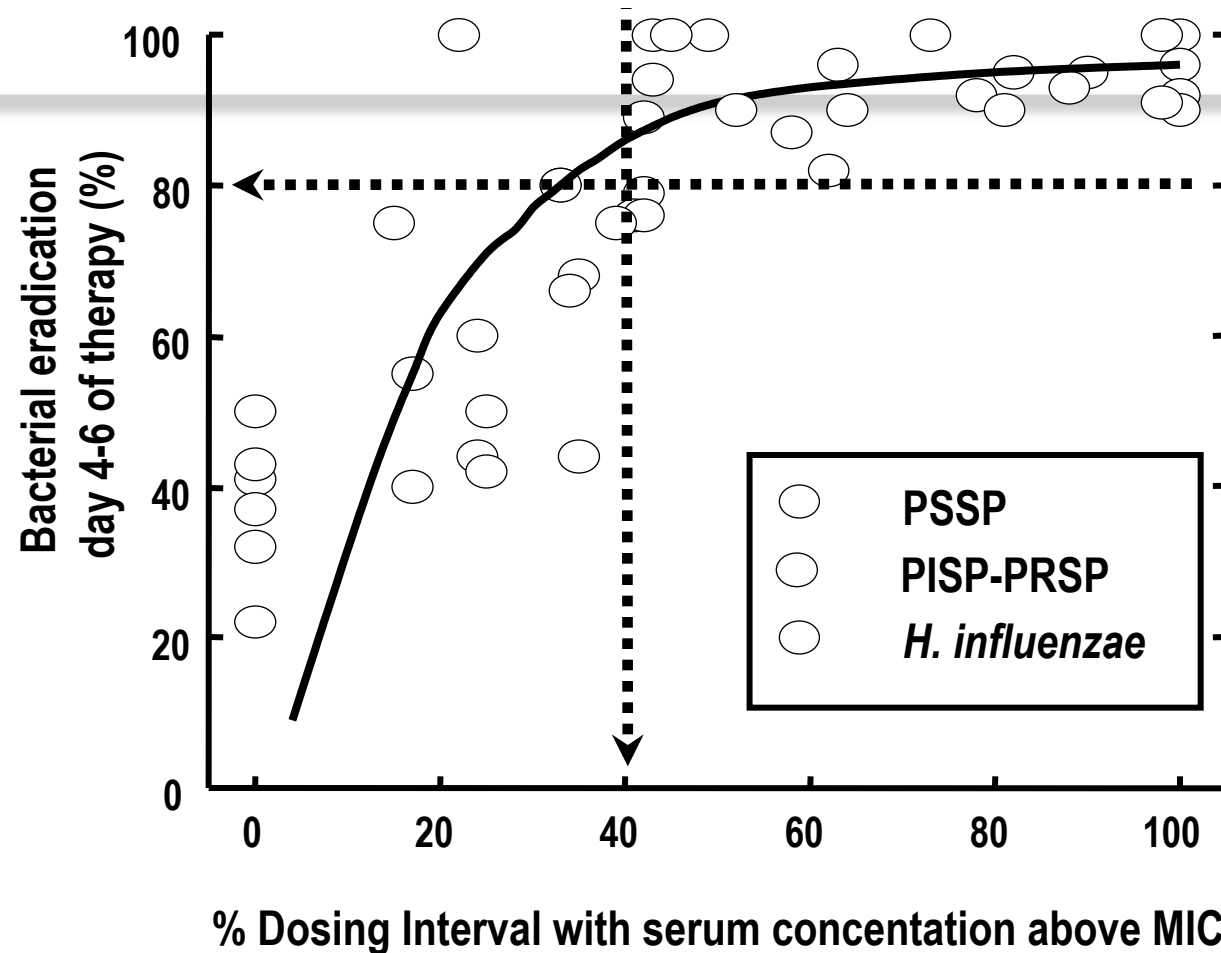


Relative Activity Against *S. pneumoniae*

- Ampicillin / Amoxicillin > Cefuroxime
> Cefprozil > Cefixime* ≥ Cefaclor* >
Cephalexin*
- Cefixime, cefaclor or cephalexin **not recommended**
if *S. pneumoniae* resistance suspected or in
treatment of otitis media



Relationship between $t > \text{MIC}$ and bacterial eradication with β -lactams in otitis media



Craig W., Andes D. *Pediatr Infect Dis J* 1996; **15**:255–259.

Dagan R. et al. studies

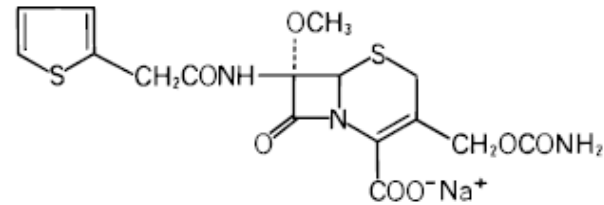
*Howie, V. *Clin Pediatr* 1972, **11**:205-214].



T > MIC for *S. pneumoniae* in Middle Ear Fluid

Antibiotic	Dose	Time > MIC (Intermediate resistance)	Time > MIC Resistant
Amoxicillin	13.3 mg/kg tid	55 - 80%	43 - 55%
Cefuroxime	15 mg/kg bid	40 - 56%	0 - 30%
Cefaclor	13.3 mg/kg tid	0 - 20%	0%

Cefoxitin



- ❑ cefamycin - methoxy group at C7
- ❑ more active than 1st generation and 2nd generation cephalosporins against *Bacteroides fragilis*
- ❑ more active than 1st generation against *E. coli*, *Klebsiella*, *Indole + & -Proteus*, and *Serratia*
- ❑ less active than cephalothin and cefuroxime against gram + and less active than cefuroxime against *H. influenzae*



Cefoxitin

- Role - abdominal or pelvic infections, surgical prophylaxis (if anaerobes), diabetic ulcerations
- $t_{1/2}$ **0.8 hr** Dose 2g q **6-8 h**
- In CHA - substitute Cefazolin plus metronidazole



Role for 2nd Generation

Cephalosporins / Cephameycins

2nd Generation Cephalosporins

- ❑ Community acquired pneumonia or acute exacerbation of chronic bronchitis
 - ❑ in patients with co-morbid illness - (COPD etc.)
- ❑ Alternative in otitis, sinusitis

Cephameycins (Cefoxitin)

- ❑ Surgical Prophylaxis (abdominal, gynecological)
- ❑ Intra-abdominal and Gynecological Infections
- ❑ Replaced by Cefazolin plus metronidazole in CHA