

A decorative graphic on the left side of the slide, consisting of a dark green square, a gold square, and a vertical gold line.

First Generation Cephalosporins

Pharmacy 407

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Cephalosporium acremonium

Nucleus most useful was
Cephalosporin C



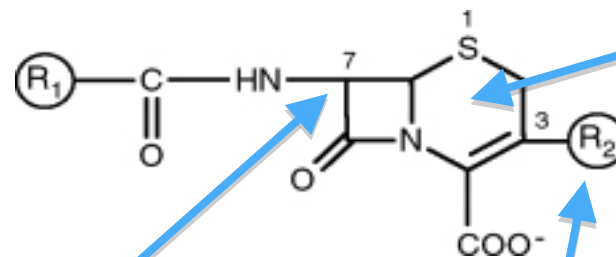
1st Generation Cephalosporins

Cephalosporin C Nucleus 7-aminocephalosporanic acid

They're good b/c wider
range of activity

they're active against
gram (-) rods which penicillin
does not cover

Affects activity
mostly



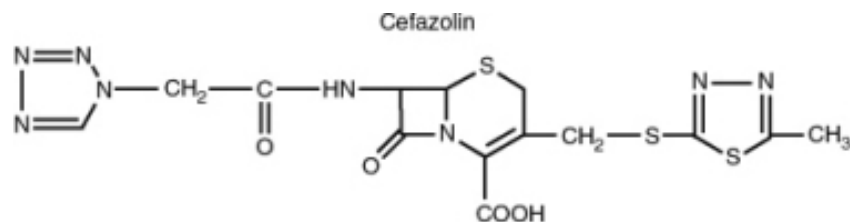
β -lactam
Ring

6 - membered
Dihydrothiazine
Ring

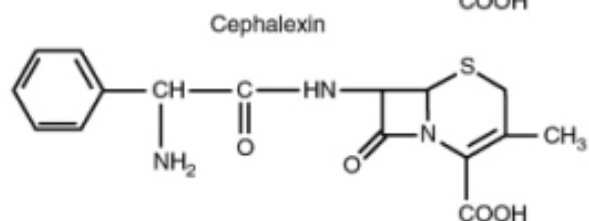
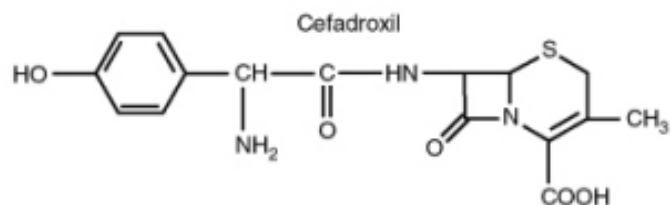
Affect PK

6-member ring
unlike 5-member
in penicillin

dihydrothiazine ring



Same side chain on C7 as penicillin



Injectable

Cephazolin

Cephalexin

Oral

Cefadroxil a lot like amoxicillin?

Cephalexin a lot like ampicillin?



1st Generation Cephalosporins

Parenteral

(Cephaloridine)

(Cephalothin) (Keflin®)

Cefazolin (Ancef®, Kefzol®)

Oral

Cephalexin (Keflex®)

Cefadroxil (Duricef®)



Parenteral 1st Generation (Parenteral)

(Cephaloridine)

➤ Interstitial Nephritis

Cephalothin
(Keflin)

- $t_{1/2}$ 0.6 hr
- q 4 - 6 h dosing
- Painful I.M.
- Best staphylococcal coverage

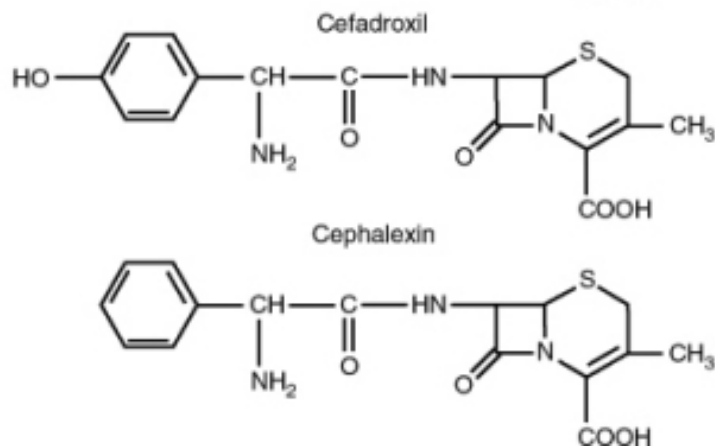
used more
often

Cefazolin
(Ancef, Kefzol)

- $t_{1/2}$ 1.5 hr
- q8h dosing
- less painful I.M.
- Better Gram negative activity

First Generation Cephalosporins (Oral)

Cephalexin (Keflex)



Cefadroxil (Duricef)

- $t_{1/2}$ 0.9 hr
- q6h dosing
- acid stable, take ^{may} with food
- least expensive
- ---

- $t_{1/2}$ 1.5 hr
- q12 h dosing
- acid stable, take with food
- most expensive



Spectrum of Activity

- Increased stability to β -lactamases produced by Staphylococci (MSSA, MSSE)
- Not active against MRSA
- Moderately active against Streptococci (*poor activity against PRSP*) penicillin resistant strep pneumo?
- **Not** active against enterococci
- **Not** active against *M. pneumoniae*, *C. pneumoniae* or Legionella
- Poor activity against Listeria

A decorative graphic consisting of overlapping gold and dark green squares with a thin gold crosshair.

Spectrum of Activity

Relative to ampicillin

- Improved activity against MSSA
- Reduced activity against *S. pneumoniae*
- *Reduced activity against Enterococci*
- *Reduced activity against Listeria*

- ? similar activity against *H. influenzae*
- Improved activity against *E. coli*, *Proteus mirabilis*, *K. pneumoniae* (Cefazolin)



Spectrum of Activity

Comparative Cephalosporin Activity

- Cephalothin better gram positive activity
- Cefazolin better gram negative activity
- Cephalexin most similar to Cephalothin

Gram (+)



Major Clinical Uses

- Surgical Prophylaxis
 - (does not cover *B. fragilis*) (*metronidazole* is added to Cefazolin for coverage of *B.fragilis*)

- Skin and Soft Tissue Infections

A decorative graphic consisting of overlapping squares in gold, dark green, and light green, with a thin gold crosshair.

Hypersensitivity

- most common problem with cephalosporins
- most often a maculopapular rash, but anaphylaxis and urticaria reported (0.0001 - 0.1%)
- Cross-sensitivity with penicillin - reports in the 1960s
 - Problems
 - ❑ patients not proven to be penicillin allergic
 - ❑ Initial cephalosporin compounds contained traces of penicillin
 - ❑ 1st generation cephalosporin more structurally similar to penicillin due to R1 side chain
 - ❑ (will address further following lectures on all cephalosporins)



Nephrotoxicity

- most common with cephaloridine (interstitial nephritis)(now not used)
- rarely cause significant renal toxicity alone
- interstitial nephritis with cephalothin (↑ 60 yrs)
- synergistic nephrotoxicity with cephalothin and aminoglycosides reported
- nephrotoxicity rare, mild, reversible with cefazolin



Other Adverse Effects

initially
organism may
appear to be
sensitive

- ❑ **Thrombophlebitis** - with all I.V. (dilute)

- ❑ **Diarrhea** - more frequent with ↑ biliary excretion

- ❑ **β-lactamase induction (SPICE)**

w/ SPICE organisms mostly -- they induce beta-lactamases

- ❑ **Neutropenia** - rare but reported

- ❑ **Elevated liver enzymes** (transient)

- ❑ **Bleeding** - more common with (MTT) (cefotetan),
(moxalactam) anti-platelet effects -- methothiotetrozole groups

- ❑ **Positive Coombs Test**

- ❑ with large doses, hemolysis rare

more particularly with
ceftriaxone (3rd gen)
and other liver-metabolised
cephalosporins