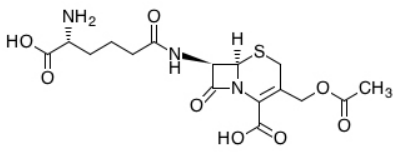
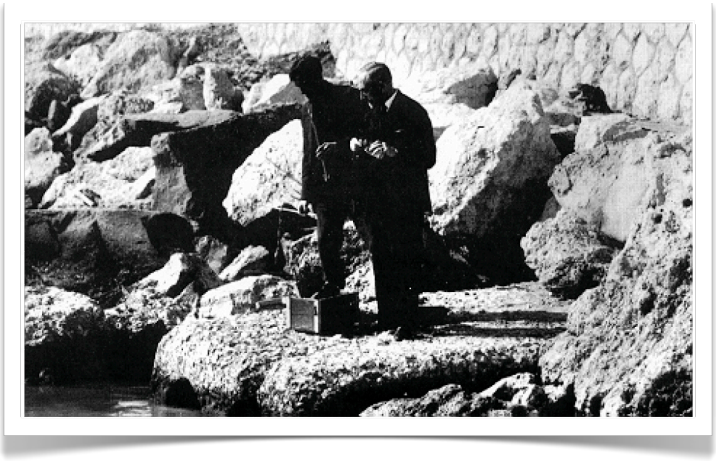
Cephalosporins



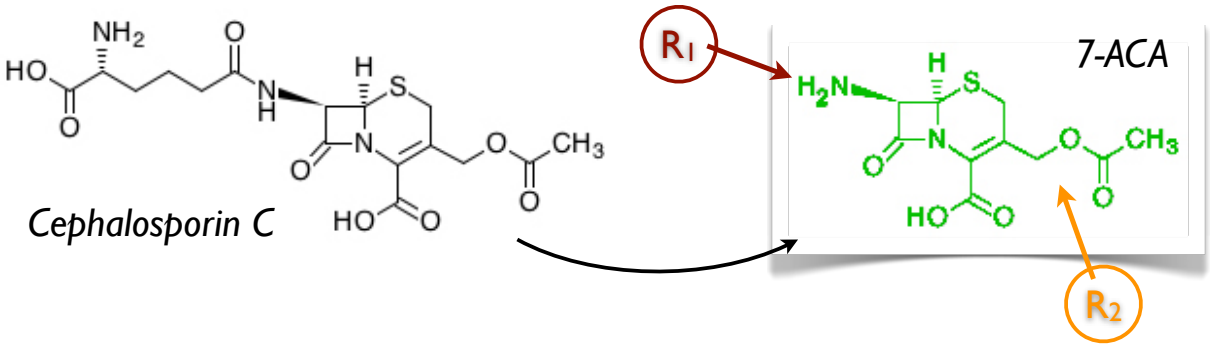
Cephalosporin C



- First isolated by Brotzu from *Cephalosporium acremonium* (a mold) from a sewage outfall (and popular swimming spot) in Sardinia. He noticed the *C. acremonium* cultures inhibited the growth of *Salmonella enterica (typhi)*, a Gram- bug that produces a penicillinase
- M.O.A. same as penicillins, to inhibit synthesis and maintenance of bacterial peptidoglycan

Semi-synthetic cephalosporins

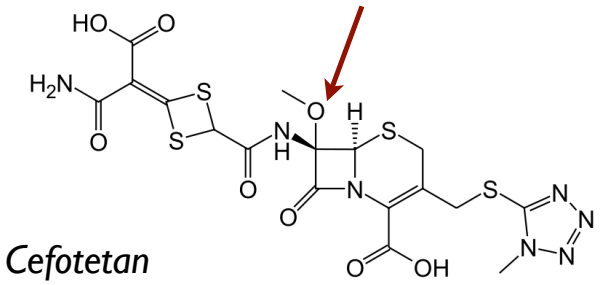
side chain(s)
affects activity, spectrum, etc.



Cephalosporin C

- Cephalosporin C had poor bioavailability, rapidly cleared
- All cephalosporins in use are of the semi-synthetic variety, no equivalents to Pen G and V in use.
- Cleave off natural sidechain to yield 7-aminocephalosporanic acid (7-ACA) core, which then could be synthetically substituted with other sidechains (R1, R2).
  - Alter the spectrum, stability, bioavailability, resistance to beta-lactamases
  - More modifications possible than w/ penicillins

Cephamycin general features



Cefotetan

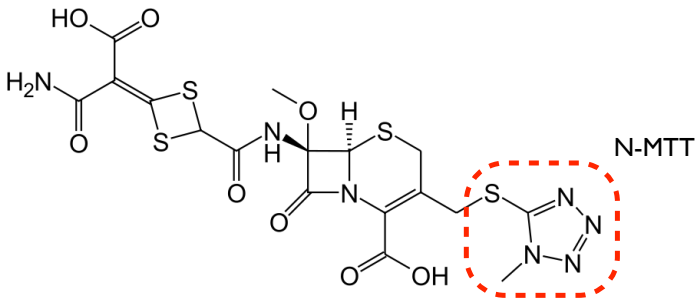
- Cephamycin beta-lactams + cephalosporins = cephems (but we will use "cephalosporin" to refer to both).
  - Originally isolated from *Streptomyces*; now semi-synthetic derivatives
  - Cephamycins have an O-methylated beta-lactam ring (→)
  - Good anaerobic activity

Cephalosporins general features

- Generally broader spectrum coverage than penicillins
  - Whereas original penicillins had primarily Gram+ coverage, most cephalosporins also cover some Gram-
  - Better resistance to beta-lactamases, but susceptible to AmpC, ESBL (if bug makes ESBL or AmpC, typically go to carbapenems instead).
- Cleared renally with ~5-30% metabolic breakdown, much active drug excreted in urine
- Low toxicity:
  - Lower allergenicity than penicillins though still some due to beta-lactam ring opening (10% cross-reactivity with penicillins)

Cephalosporins general features

- Other adverse drug reactions:
  - Some such as cefotetan has an N-methylthiotetrazole (N-MTT) moiety that is released as a metabolic byproduct. This can cause hypoprothrombinemia, which manifests as bleeding due to combination of effects: 1) altered gut flora changes vitamin K production, 2) direct interaction of N-MTT with prothrombin, 3) platelet dysfunction. First noted with moxalactam (2-3% fatalities; off market).
  - N-MTT also can inhibit aldehyde degydrogenase, giving rise to a disulfram-like reaction following alcohol consumption. Intense hang-over feeling, hyper-sensitivity to alcohol.



Cefotetan

Cephalosporins general features

- Cephalosporin "generations": generally get broader, more Gm- coverage with later generations
  - Generation 1: Generally had better Gram+ than Gram- activity; susceptible to many Gram- beta-lactamases
    - Examples: Cephalexin, Cefazolin
  - Generation 2: Better resilience to Gram- beta-lactamases, Gram- coverage
    - Examples: Cefuroxime
  - Generation 3: More potent, better Gram- beta-lactamase stability, better penetration; pick up some anti-*Pseudomonal* activity, give up some Gram+ coverage
    - Examples: Cefpodoxime, Cefdinir, Cefixime, Cefotaxime, Ceftriaxone, Ceftazidime,
  - Generation 4: Very broad spectrum (Gm- and Gm+)
    - Example: Cefepime
  - Generation 5: MRSA and PRSP coverage
    - Example: Ceftaroline

Cephalosporins general features

- Some penetrate to the CNS:
  - *Cefuroxime*
  - *Cefotaxime*
  - *Ceftazidime*
  - *Ceftriaxone*

<u>underlined</u> are on UW formulary

Oral cephalosporins

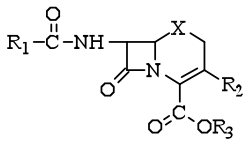
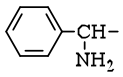
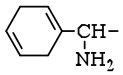
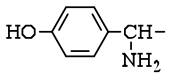
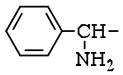
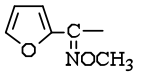
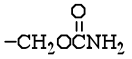
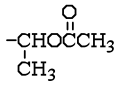
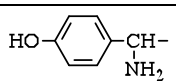
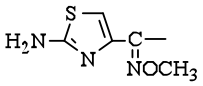
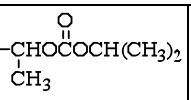
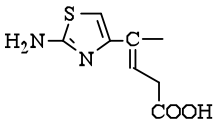
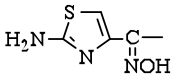
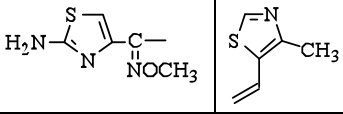


Table - Oral Cephalosporins

generation	name	brand name	structure				dose
			R_1	R_2	R_3	X	
1	cephalexin	generic		$-CH_3$	—H	–S –	QID
1	cephradine	generic		$-CH_3$	—H	–S –	BID
1	cefadroxil	generic		$-CH_3$	—H	–S –	BID
2	cefaclor	generic		–Cl	—H	–S –	TID
2	cefuroxime axetil	generic				–S –	BID
2	cefprozil	generic		$-CH=CHCH_3$	—H	–S –	BID

Courtesy Prof. Gary Elmer

Oral cephalosporins (cont.)

3	cefpodoxime proxetil	generic		$-CH_2OCH_3$		$-CH_2-$	BID
3	ceftibutin	Cedax®			—H	—S—	qd
3	cefdinir	generic		$-CH=CH_2$	—H	—S—	BID
3	cefditoren pivoxil	generic			$-CH_2OCOC(CH_3)_3$	—S—	BID
3	cefixime	Suprax®	----	----	----	----	qd

Courtesy Prof. Gary Elmer

Parenteral cephalosporins/cephamycins

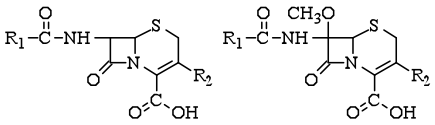
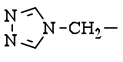
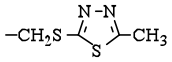
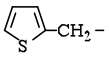
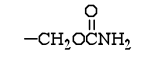
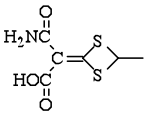
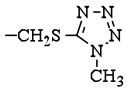
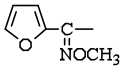
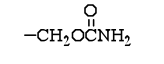
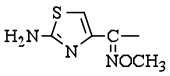
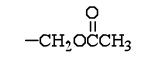
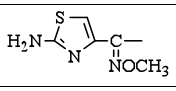
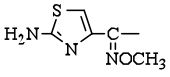
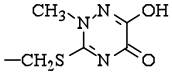
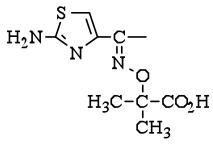
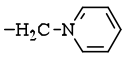
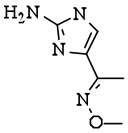


Table - Parenteral Cephalosporins and Cephamycins Cephalosporin *Cephamycin

generation	name	brand name	structure		dose
			R_1	R_2	
1	cefazolin	generic			TID
2	cefoxitin*	generic			QID
2	cefotetan*	generic			BID
2	cefuroxime	generic			TID
3	cefotaxime	generic			TID
3	ceftizoxime	Cefizox®		—H	TID
3	ceftriaxone	generic			qd

Courtesy Prof. Gary Elmer

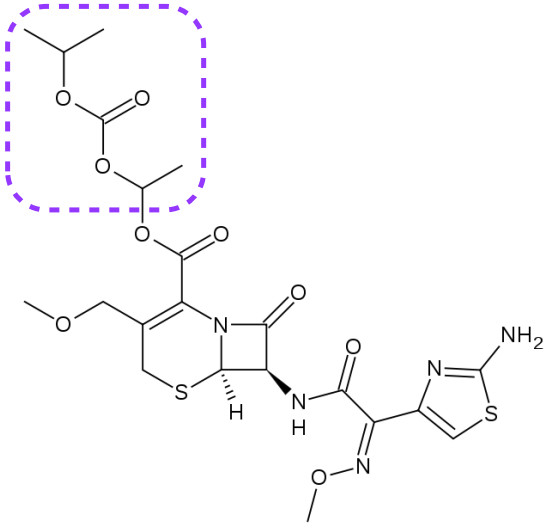
Parenteral cephalosporins/cephamycins (cont.)

3	ceftazidime	generic			TID
4	cefepime	generic			BID

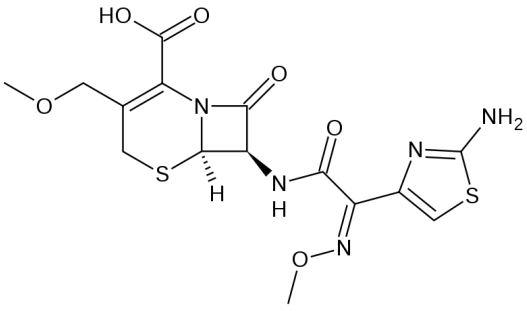
Courtesy Prof. Gary Elmer

Some oral cephalosporins are prodrugs

- Examples: Cefpodoxime, Cefuroxime, Ceftizoxime, Cefditoren,, Cefetamet, Cefditoren
  - Metabolized to active drug by intestinal mucosal tissue
  - Sometimes aids in better absorption; e.g. crossing membranes
  - Sometimes aids in better solubility



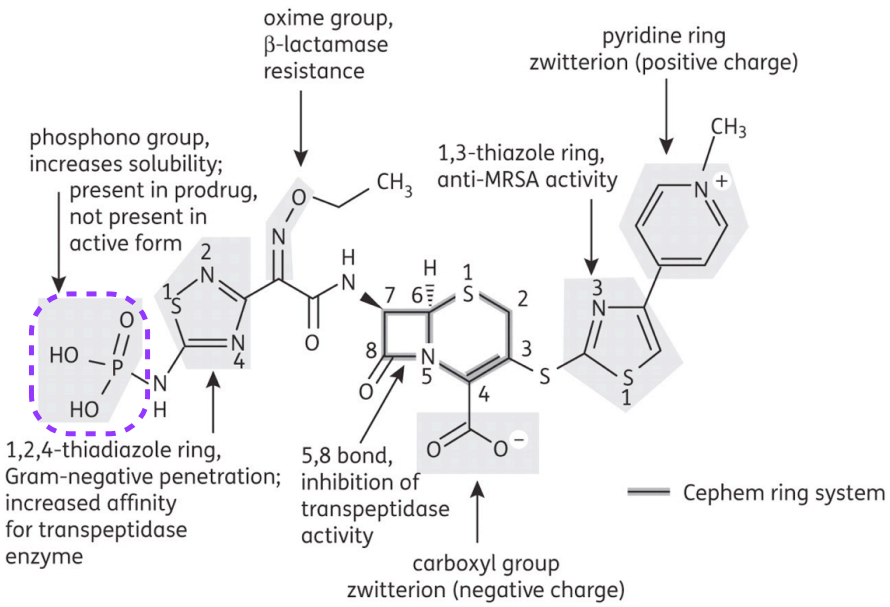
cefpodoxime proxetil



cefpodoxime

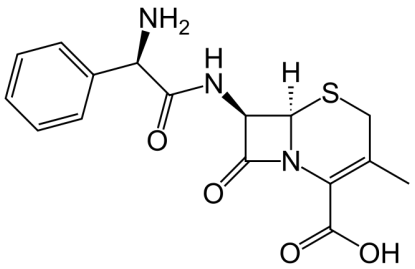
Some parenteral cephalosporins are prodrugs

◉ Anatomy of a cephalosporin: ceftaroline (a gen-5 ceph)



Laudano JB, J. Antimicrob. Chemother. 2011;66:iii11-iii18

Cephalexin (Gen1, PO)



◉ Keflex ® (Eli Lilly), and generics

◉ Up to 90% excreted unmodified in urine.

◉ Indications:

- ◉ Skin infections: *S. aureus* (*MSSA* even w/ penicillinase, not *MRSA*), *S. pyogenes*
- ◉ Respiratory infections: *S. pneumoniae* (not PRSP), *S. pyogenes*
- ◉ Otitis media: *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*
  - ◉ *H. influenzae* and *M. catarrhalis* may have resistance due to beta-lactamases
- ◉ Urogenital: *E. coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*
- ◉ Bone: *S. aureus*, *P. mirabilis*

Cephalexin (Gen1, PO)

Indicated spectrum for cephalexin (Gen1, oral):

Aerobic gram-positive microorganisms:

Staphylococcus aureus (including penicillinase-producing strains)
Streptococcus pneumoniae (only penicillin-sensitive strains)
Streptococcus pyogenes

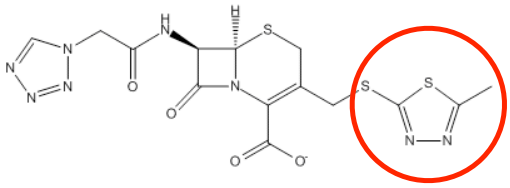
Resistant Gm+ bacteria, not covered:

MRSA
PRSP
Most strains of *enterococci* (*E. faecalis*) are resistant to cephalosporins, including Cephalexin.
Enterobacter spp.
Morganella morganii
Proteus vulgaris
Pseudomonas spp.
Acinetobacter calcoaceticus

Aerobic gram-negative microorganisms:

Escherichia coli
Haemophilus influenzae
Klebsiella pneumoniae
Moraxella catarrhalis
Proteus mirabilis

Cefazolin (Gen1, Parenteral IV/IM)



N-MTD
(N-methylthiodiazole)

- Ancef ® (GSKB), and generics
- Up to 80% excreted unmodified in urine.
- For Gm+ *Staphylococci* including *Staph. aureus* (not *MRSA*), *Streptococci* including *Strep. pyogenes, Strep. pneumoniae* (not *PRSP*)
  - Respiratory tract infections (*Staph., Strep.*)
  - Uncomplicated skin infections
  - Bone and joint
- Some Gram- coverage: *E. coli*, *H.* influenzae (some resistance), P. *mirabilis,*
  - Urogenitial
- Like N-MTT, N-MTD sidechain, potential for bleeding and disulfram-like alcohol side effects
  - Co-administration with parenteral vitamin K may counter bleeding

Cefazolin (Gen1, Parenteral IV/IM)

Indicated spectrum for cefazolin (Gen1, parenteral):

Aerobic gram-positive microorganisms:

- *Staphylococcus aureus* (including penicillinase-producing strains)
- *Staph. epidermidis*
- *Strep. pneumoniae* (only penicillin-sensitive strains)
- *Strep. pyogenes*
- *Strep. agalactiae*

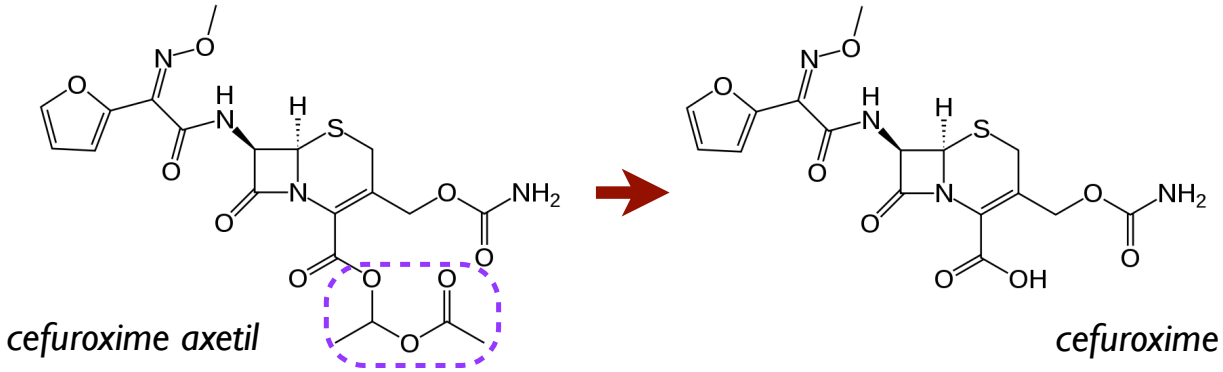
Resistant Gm+ bacteria, not covered:

- MRSA
- PRSP
- *Enterococci* (*E. faecalis*)

Aerobic gram-negative microorganisms:

- *Escherichia coli*
- *Proteus mirabilis*

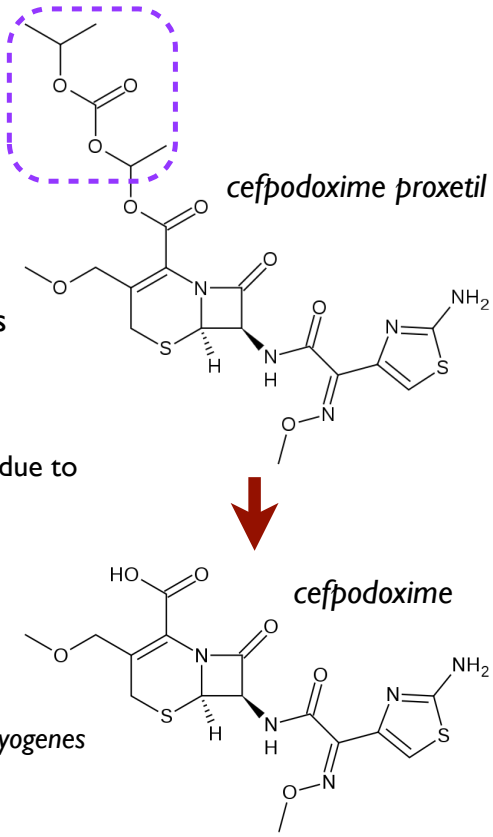
Cefuroxime axetil (Gen2, PO)



cefuroxime axetil *cefuroxime*

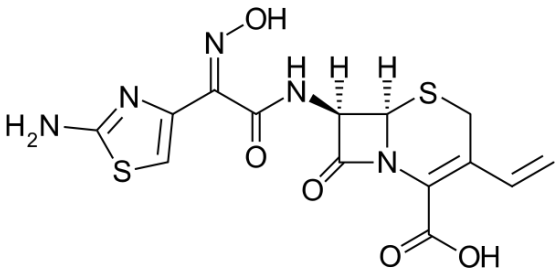
- Ceftin ® (GSKB) and generics
- Prodrug: cefuroxime axetil converted to cefuroxime (also IV, not as prodrug)
- Indications:
  - Pharyngitis, Tonsollitis, Otitis media, sinusitis, bronchitis (*H. flu*, *S. pneumo*, *M. cat*)
  - Skin infections (*S. pyogenes*, *MSSA*)
  - UTI (*E. coli, Klebsiella*)
  - *N. gonorrhoeae* including penicillinase-producing
  - Early Lyme disease *Borrelia Burgdorferi* (amoxicillin, doxycycline also)
- Penetrates to CNS: meningitis (*N. meningitidis*, *H. influenzae*, *S. pneumoniae*)

Cefpodoxime proxetil (Gen3, PO)



- Vantin ® (Pharmacia), and generics
- Prodrug
- Good Gram- and Gram+ coverage
  - not *Pseudomonas*, *Enterococci, B. fragilis*
- Indications: big for otitis media, pharyngitis, sinusitis
  - Community Acquired Pneumonia (CAP):
    - *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*
    - *H. influenzae* and *M. catarrhalis* may have resistance due to beta-lactamases
  - *N. gonorrhoeae*: single 200mg dose
  - UTI
  - Otitis media:
    - *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*
  - Uncomplicated skin infections: *S. aureus* (not MRSA), *S. pyogenes*

Cefdinir (Gen3, PO)



- Omnicef ® (Abbot) and generics
- Similar coverage to cefpodoxime, but tastes better (important for children)
- Best selling cephalosporin, often prescribed for AOM (acute otitis media) if infection not responding to amoxicillin

Relative tastiness of cephalosporins

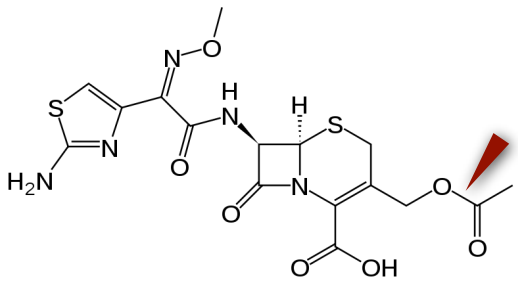
TABLE 2
Taste Ratings for Oral Cephalosporin Suspensions*

Antibiotic	Rating
Loracarbef	++++
Cefdinir	++++
Cefixime	+++
Cephalexin	+++
Cefaclor	+++
Amoxicillin†	+++
Trimethoprim-sulfamethoxazole†	++
Cefprozil	++
Amoxicillin/clavulanate†	++
Cefpodoxime	+
Cefuroxime axetil	+

* Data modified from references 9-11
† Comparative commonly prescribed agent in pediatric patients
++++, best overall taste; +++ above average; ++, below average; + poorly palatable

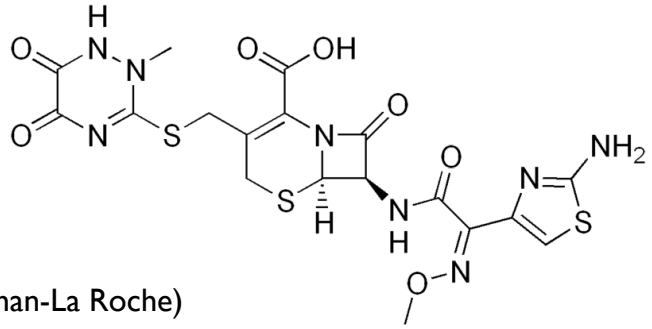
National Foundation for Infectious Diseases
http://www.nfid.org/pdf/pediatric_archive/cephalosporinsupdate.pdf

Cefotaxime (Gen3, Parenteral IV/IM)



- Claforan® (Sanofi Aventis)
- Cefotaxime becomes deacetylated, resulting desacetylcefotaxime also active
- Broad spectrum; Gram-, Gram+
  - Activity against PRSP, but used in combination with other antimicrobials
  - Notable Gm+ exceptions: *Enterococci*
  - Notable Gm- exceptions: *Pseudomonas*
- Lower respiratory tract infections, bone and joints, skin, urogenital infection, septicemia
- Intra-abdominal including use as pre-surgery prophylaxis
- Penetrates to CNS: meningitis

Ceftriaxone (Gen3, Parenteral IV/IM)



- Rocephin ® (Hoffman-La Roche)
- Broad spectrum; Gram-, Gram+
  - Can be used for Penicillin-resistant *Strep. Pneumoniae* (PRSP)
  - Highly active against *N. gonorrhoeae*: 250mg single IM dose
  - Some activity against *Pseudomonas aeruginosa*, but not the most potent
- Very long half-life ~6-8h (vs *e.g.* 1h for cefotaxime); less frequent dosing
- Penetrates the CNS
- Often used in combination w/ aminoglycoside or macrolide
  - *E.g.* w/ azithromycin for *Chlamydia tracomatis*
- Do not co-administer or dilute with calcium-containing compounds/solutions
  - *Ceftriaxone* precipitates with calcium

Ceftriaxone (Gen3, Parenteral IV/IM)

Aerobic gram-negative microorganisms:

Acinetobacter calcoaceticus
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Haemophilus influenzae (including ampicillin-resistant and beta-lactamase producing strains)
Haemophilus parainfluenzae
Klebsiella oxytoca
Klebsiella pneumoniae
Moraxella catarrhalis (including beta-lactamase producing strains)
Morganella morganii
Neisseria gonorrhoeae (including penicillinase- and nonpenicillinase-producing strains)
Neisseria meningitidis
Proteus mirabilis
Proteus vulgaris
Serratia marcescens
Pseudomonas aeruginosa

Aerobic gram-positive microorganisms:

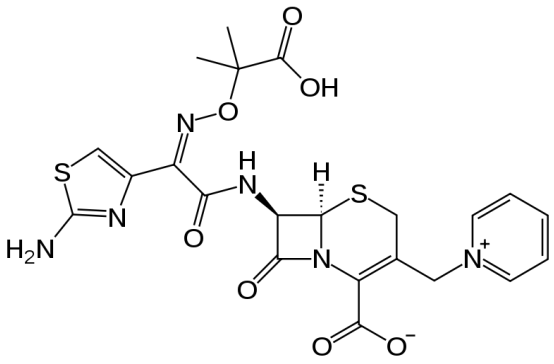
Staphylococcus aureus (including penicillinase-producing strains, not MRSA)
Staphylococcus epidermidis
Streptococcus pneumoniae (active for PRSP)
Streptococcus pyogenes
Viridans group streptococci

NOTE: MRSA resistant to most cephalosporins, including ceftriaxone. Most strains of Group D streptococci and enterococci, eg, *Enterococcus faecalis*, are resistant.

Anaerobic microorganisms:

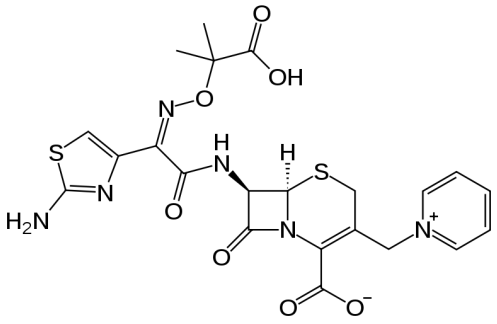
Bacteroides fragilis
Clostridium species (NOTE: Most strains of *Clostridium difficile* are resistant)
Peptostreptococcus species

Ceftazidime (Gen3, Parenteral IV/IM)



- Fortum ® (GSK)
- Broad spectrum; Gram-, some Gram+
  - Activity against *Pseudomonas aeruginosa*, ~85-90% sensitive (only ~68% for CF patients)
  - Poorer against Gm+, not generally used
- CNS penetration in meningitis

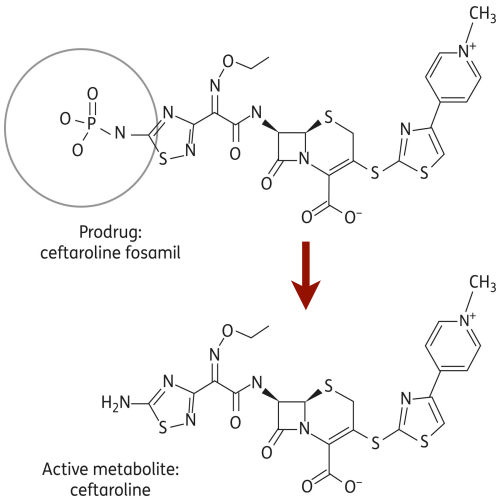
Cefepime (Gen4, Parenteral IV/IM)



- Maxipime ® (Elan)
- Even more resistant to beta-lactamases binds tightly to PBPs
- Better penetration of Gram- outer membranes
- Broad spectrum: Gram- and Gram+
  - Activity against PRSP
  - *Pseudomonas aeruginosa* coverage (90% sensitive for non-CF patients, only 50% for CF)
  - *Enterobacteriaceae*
  - Not anaerobes
- Empiric therapy: used to suppress infection, then switch to another cephalosporin
  - Does not induce the expression of chromosomal beta-lactamases;
- FDA precaution for neurotoxicity (encephalopathy, myoclonus, seizures)

Ceftaroline fosamil (Gen5, Parenteral IV/IM)

- Teflaro® (Cerexa, Forest Labs); FDA approved fall, 2010.
- *Ceftaroline fosamil* prodrug becomes dephosphonated in the blood to *ceftaroline*
- Similar spectrum to ceftriaxone, but gain increased Gram+ coverage including *MRSA* and *PRSP* due to increased affinity for *MRSA*'s PBP2a and pen. resistant *S. pneumoniae*'s PBP2x, which confers resistance to most beta-lactams.
  - *MRSA and VRSA*
  - *PRSP*
  - *H. influenzae*
  - *M. catarrhalis*
  - *S. pyogenes*
  - *S. viridans* group
  - *E. faecalis*
  - *K. pneumoniae*
  - *Shigella*
  - NOT for *P. aeruginosa,* beta-lactamase (ESBL, AmpC) producing *Enterobacteriaceae*, *Bacteriodes*, *C. difficile*
- Indicated uses
  - Skin infection
  - Community associated pneumonia (CAP)



Ceftaroline fosamil (Gen5, Parenteral IV/IM)

Table 1. *In vitro* activity of ceftaroline against common Gram-positive and Gram-negative bacteria[25]

Organism (number of isolates)	MIC (mg/L) range	50%	90%
Gram-positive			
Staphylococcus aureus			
MSSA (102)	0.03–0.5	0.25	0.25
MRSA (105)	0.5–2	0.5	1
vancomycin reduced susceptibility (47)	0.25–2	1	2
linezolid non-susceptible (13)	0.5–2	1	2
Streptococcus pyogenes (102)	≤0.008–0.015	≤0.008	≤0.008
Streptococcus agalactiae (104)	≤0.008–0.03	0.015	0.03
Enterococcus faecalis			
vancomycin susceptible (102)	0.25–16	2	4
vancomycin resistant (108)	0.5–16	4	8
Streptococcus pneumoniae			
penicillin susceptible (MIC ≤ 0.06 mg/L) (102)	≤0.008–0.06	≤0.008	0.03
penicillin intermediate (MIC 0.12–1 mg/L) (102)	≤0.008–0.12	0.03	0.06
penicillin resistant (MIC ≥ 2 mg/L) (100)	0.03–0.5	0.12	0.25
penicillin high-level resistant (MIC ≥ 8 mg/L) (40)	0.06–0.5	0.25	0.5
levofloxacin non-susceptible (53)	≤0.008–0.5	0.015	0.12
multidrug resistant (≥2 classes) (127)	≤0.008–0.5	0.12	0.25
Gram-negative			
Escherichia coli			
ceftazidime susceptible (102)	0.015–8	0.12	0.25
Klebsiella pneumoniae			
ceftazidime susceptible (102)	0.015–1	0.06	0.5
Haemophilus influenzae			
β-lactamase negative (110)	≤0.008–0.25	≤0.008	0.015
β-lactamase positive (101)	≤0.008–0.12	≤0.008	0.03
Pseudomonas aeruginosa (101)	4 to >16	>16	>16
Acinetobacter baumannii (101)	2 to >16	>16	>16

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Ceftaroline fosamil (Gen5, Parenteral IV/IM)

Table 2. Activity of ceftaroline and comparator agents against Gram-positive clinical isolates of skin pathogens from US and European medical centres in 2008[26]

Organism	Antimicrobial agent	MIC (mg/L) range	MIC (mg/L) 50%	MIC (mg/L) 90%	Susceptible (%)
Staphylococcus aureus					
methicillin susceptible (1554)	ceftaroline	≤0.008–1	0.25	0.25	—
	ceftriaxone	1–32	4	4	99.7
	vancomycin	0.25–2	1	1	100
	linezolid	0.25–2	2	2	100
methicillin resistant (1237)	ceftaroline	0.25–2	1	1	—
	ceftriaxone	1 to >32	32	>32	0
	vancomycin	0.25–2	1	1	100
	linezolid	0.25–2	2	2	100
Coagulase-negative staphylococci					
all isolates (641)	ceftaroline	≤0.008–4	0.25	1	—
	ceftriaxone	≤0.25 to >32	16	>32	25.3
	vancomycin	≤0.12–4	2	2	100
	linezolid	0.12 to >8	1	1	99.2
Enterococcus faecalis					
all isolates (613)	ceftaroline	0.12 to >16	2	8	—
	ceftriaxone	1 to >32	>32	>32	—
	vancomycin	0.5 to >16	1	2	95.6
	linezolid	0.25–2	1	2	100
β-Haemolytic streptococci					
all isolates (596)	ceftaroline	≤0.008–0.06	≤0.008	0.015	—
	ceftriaxone	≤0.25	≤0.25	≤0.25	100
	vancomycin	0.25–1	0.5	0.5	100
	linezolid	0.5–2	1	1	100
Viridans group streptococci					
all isolates (190)	ceftaroline	≤0.008–1	0.03	0.06	—
	ceftriaxone	≤0.25–16	≤0.25	0.5	93.7
	vancomycin	0.25–1	0.5	0.5	100
	linezolid	0.25–2	1	1	100
penicillin non-susceptible (42)	ceftaroline	≤0.008–1	0.03	0.5	—
	ceftriaxone	≤0.25–16	≤0.25	8	71.4
	vancomycin	0.25–0.5	0.5	0.5	100
	linezolid	0.5–1	0.5	1	100

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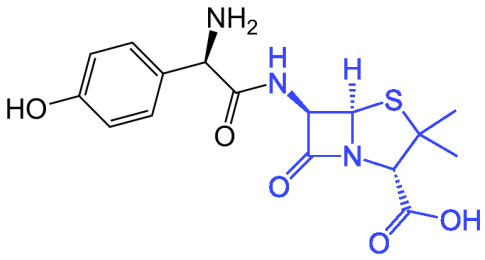
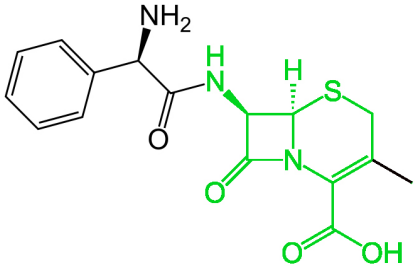
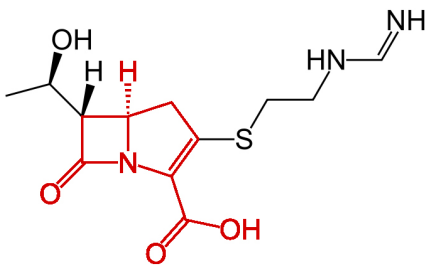
Beta-lactam antibiotics

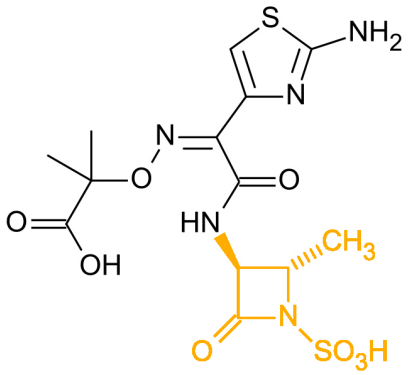
Amoxicillin (penicillin)



Cephalexin (cephalosporin)



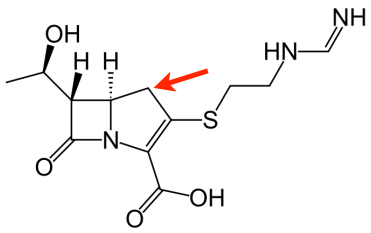




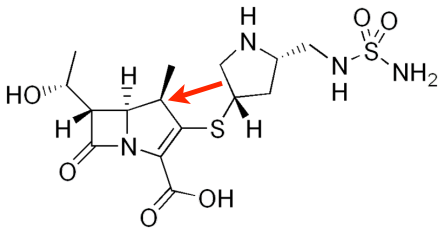
Imipenem (carbapenem)

Aztreonam (monobactam)

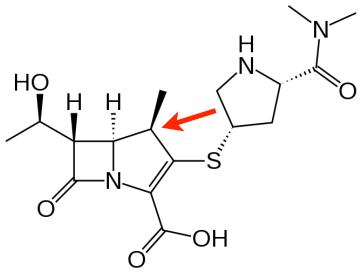
Beta-lactam antibiotics: Carbapenems



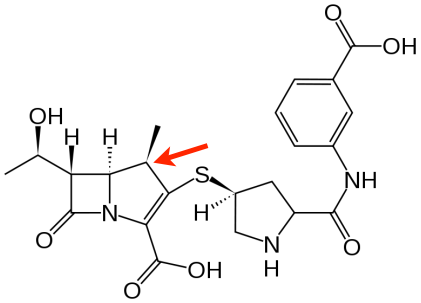
Imipenem



Doripenem



Meropenem



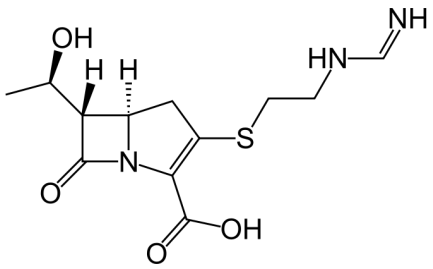
Ertapenem

- Carbon instead of sulfur in 5-membered ring (→)
- All are IV products, none oral

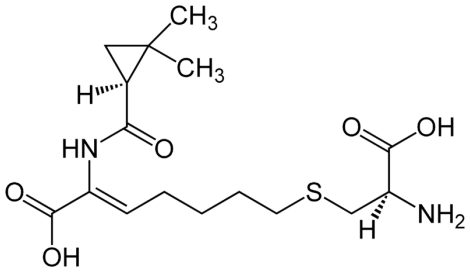
Carbapenems: general features

- Highly resistant to most beta-lactamases
  - Including to ESBLs and AmpC
  - Carbapenemases are emerging (KPC, VIM, NDM-1)
  - Induce expression of chromosomal beta-lactamases (though not degraded), thus switching to another beta-lactam after carbapenem not advised
- Extremely broad spectrum; broader than penicillins, cephalosporins
  - *Pseudomonas* coverage (not ertapenem), but MICs pretty high (all IV)
  - Not *MRSA*
  - Not *Enterococci*
- Reserved for last line use or complicated cases
  - Used for polymicrobial infections
  - If multi-drug resistance is evident
- Relatively low toxicity

Carbapenems: Imipenem + Cilastatin



Imipenem



Cilastatin

- Primaxin ® (Merck)
- Combined with cilastatin because normally imipenem would be hydrolyzed by a renal dihydropeptidase enzyme (DHP-1). Cilastatin inhibits this enzyme.
  - Other carabapenems more stable, do not require DHP-1 inhibitor
- Impipenem unusual in that it actually also inhibits some beta-lactamases
- Risk for seizures (1.5-2%), thus not indicated for meningitis

Carbapenems: Imipenem + Cilastatin

- Indicated microbial spectra:

Gram-positive aerobes:

Enterococcus faecalis
(NOTE: Imipenem is inactive against Enterococcus faecium)
Staphylococcus aureus including penicillinase-producing strains
(NOTE: **not MRSA**.)
Staphylococcus epidermidis including penicillinase-producing strains
Streptococcus agalactiae (Group B streptococci)
Streptococcus pneumoniae
Streptococcus pyogenes

Gram-negative aerobes:

Acinetobacter spp.
Citrobacter spp.
Enterobacter spp.
Escherichia coli
Gardnerella vaginalis
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella spp.
Morganella morganii
Proteus vulgaris
Providencia rettgeri
Pseudomonas aeruginosa
(NOTE: Imipenem is inactive in vitro against Xanthomonas (Pseudomonas) maltophilia and some strains of P. cepacia.)
Serratia spp., including S. marcescens

Gram-positive anaerobes:

Bifidobacterium spp.
Clostridium spp.
Eubacterium spp.
Peptococcus spp.
Peptostreptococcus spp.
Propionibacterium spp.

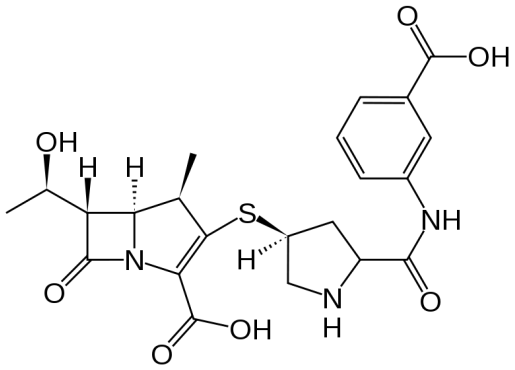
Gram-negative anaerobes:

Bacteroides spp., including B. fragilis
Fusobacterium spp.

Imipenem + Cilastatin: indicated uses

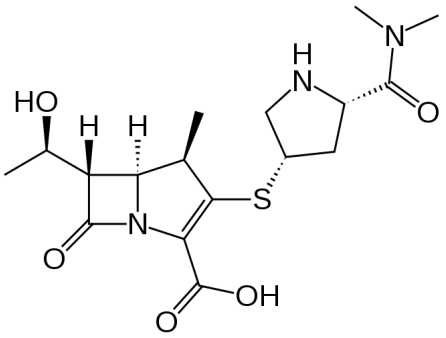
- Lower respiratory tract infections
- UTI, complicated and uncomplicated
- Intra-abdominal infections
- Gynecological infections
- Septicemia
- Bone and Joint infections
- Skin infections
- Endocarditis
- Polymicrobial infections

Carbapenems: Meropenem



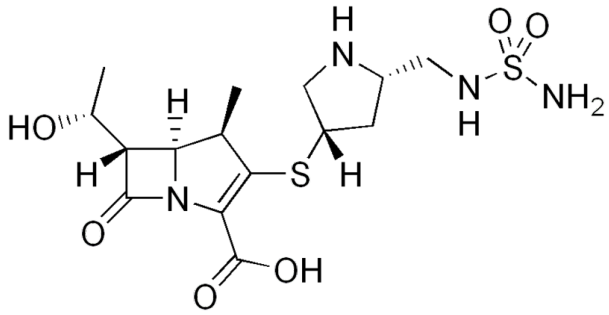
- Merrem ® (AstraZeneca)
- Lower seizure risk (0.4%) than imipenem. Inidicated use for meningitis caused by *S. pneumoniae, H. influenzae, N. meningiditis*
- Other indicated uses:
  - Intra-abdominal infections caused by *Strep. viridans, E. coli, Klebsiella pneumoniae, P. aeruginosa, B. fragilis*
  - Complicated skin infections (not MRSA)

Carbapenems: Ertapenem



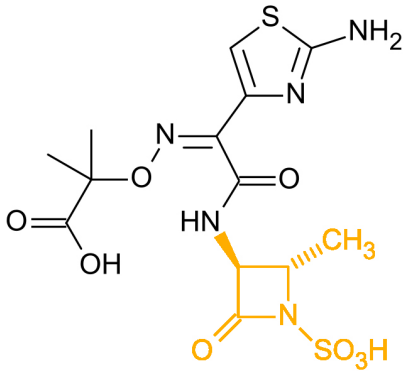
- Invanz ® (Merck)
- Possibly more susceptible to ESBL and AmpC than other carbapenems
- Very broad spectrum, thus good for polymicrobial infections
  - But not covering *PRSP*, not *MRSA*, not *Pseudomonas*
- Other indicated uses:
  - Complicated intra-abdominal infections
  - Complicated skin infections (not MRSA)
  - Complicated UTI
  - Pelvic infections
  - CAP (not involving PRSP)

Carbapenems: Doripenem



- Doxibax ® (Ortho-McNeil)
- Very good activity against Gram-, including *Pseudomonas* and anaerobes
- Other indicated uses:
  - Complicated intra-abdominal infections
  - Complicated skin infections (not MRSA)
  - Complicated UTI
  - Pelvic infections
  - CAP (not involving PRSP)

Monobactam: Aztreonam (IV, inhaled)



- Azactam® (Squibb), Cayston® (Gilead) and generics
- Natural product, but now produced synthetically
- Gram- spectrum, similar to aminoglycosides; (minimal Gram+ and anaerobe)
  - Activity against *Pseudomonas* (Cayston inhaled formulation: indicated for *P. aeruginosa* CF patient)
- Resistant to most beta-lactamases but not ESBL
- No penicillin allergy cross-reactivity