به نام خدا

آنتی بیوتیکهای شایع

دکتر آقابالایی

متخصص بیماریهای عفونی

بخش عفونی بیمارستان امام خمینی

Quinolones

- Drugs: norfloxacin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin
- Mechanism of action:
  - Inhibit bacterial DNA synthesis by inhibiting DNA gyrase and topoisomerase IV → rapid cell death
  - Post antibiotic effect: lasts 1 to 2 hours, increases with increasing concentration
- Mechanism of resistance:
  - Chromosomal:
    - Alter target enzymes: DNA gyrase and topoisomerase IV
    - Decreased drug penetration: Pseudomonas, E. coli
  - Plasmid: seen in some K. pneumoniae and E. coli
  - Mutations in both target enzymes are needed to produce significant resistance

Members

Quinolones

- Nalidixic acid

Fluoroquinolones

First Generation

- Ciprofloxacin
- Norfloxacin
- Pefloxacin
- Ofloxacin

Fluoroquinolones

New Generations

- Lomefloxacin
- Levofloxacin
- Prulifoxacin

Second

- Sparfloxacin
- Gatifloxacin
- Gemifloxacin
- Moxifloxacin

Third

- Trovafloxacin
- Alatrofloxacin
- Finafloxacin

Fourth

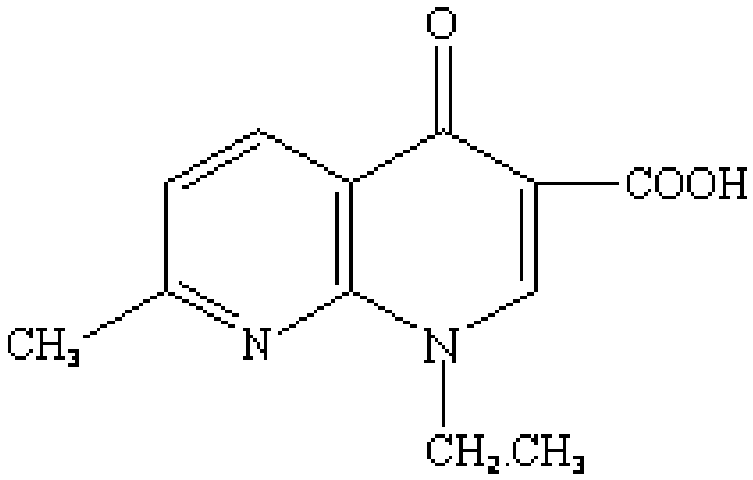
MAN Can SPOT Good Life

- Moxifloxacin
- Alatrofloxacin
- Norfloxacin
- Ciprofloxacin
- Sparfloxacin
- Pefloxacin
- Prulifoxacin
- Ofloxacin
- Trovafloxacin
- Gatifloxacin
- Gemifloxacin
- Lomefloxacin
- Levofloxacin

MAN Can
SPOT Good
Life

Quinolones

- Parent drug: nalidixic acid



Classification

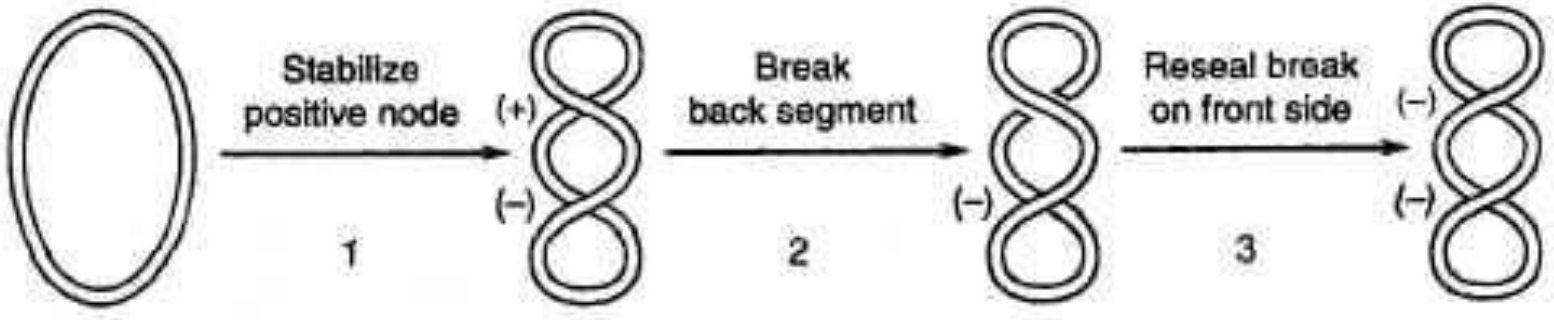
- Quinolones (1st generation)
  - Highly protein bound
  - Mostly used in UTIs
- Fluoroquinolones (2nd, 3rd and 4th generation)
  - Modified 1st generation quinolones
  - Not highly protein bound
  - Wide distribution to urine and other tissues; limited CSF penetration.

Generation	Drug Names	Spectrum
1st	nalidixic acid cinoxacin	Gram- but not Pseudomonas species
2nd	norfloxacin ciprofloxacin enoxacin ofloxacin	Gram- (including Pseudomonas species), some Gram+ (S. aureus) and some atypicals
3rd	levofloxacin sparfloxacin moxifloxacin gemifloxacin	Same as 2nd generation with extended Gram+ and atypical coverage
4th	*trovafloxacin	Same as 3rd generation with broad anaerobic coverage

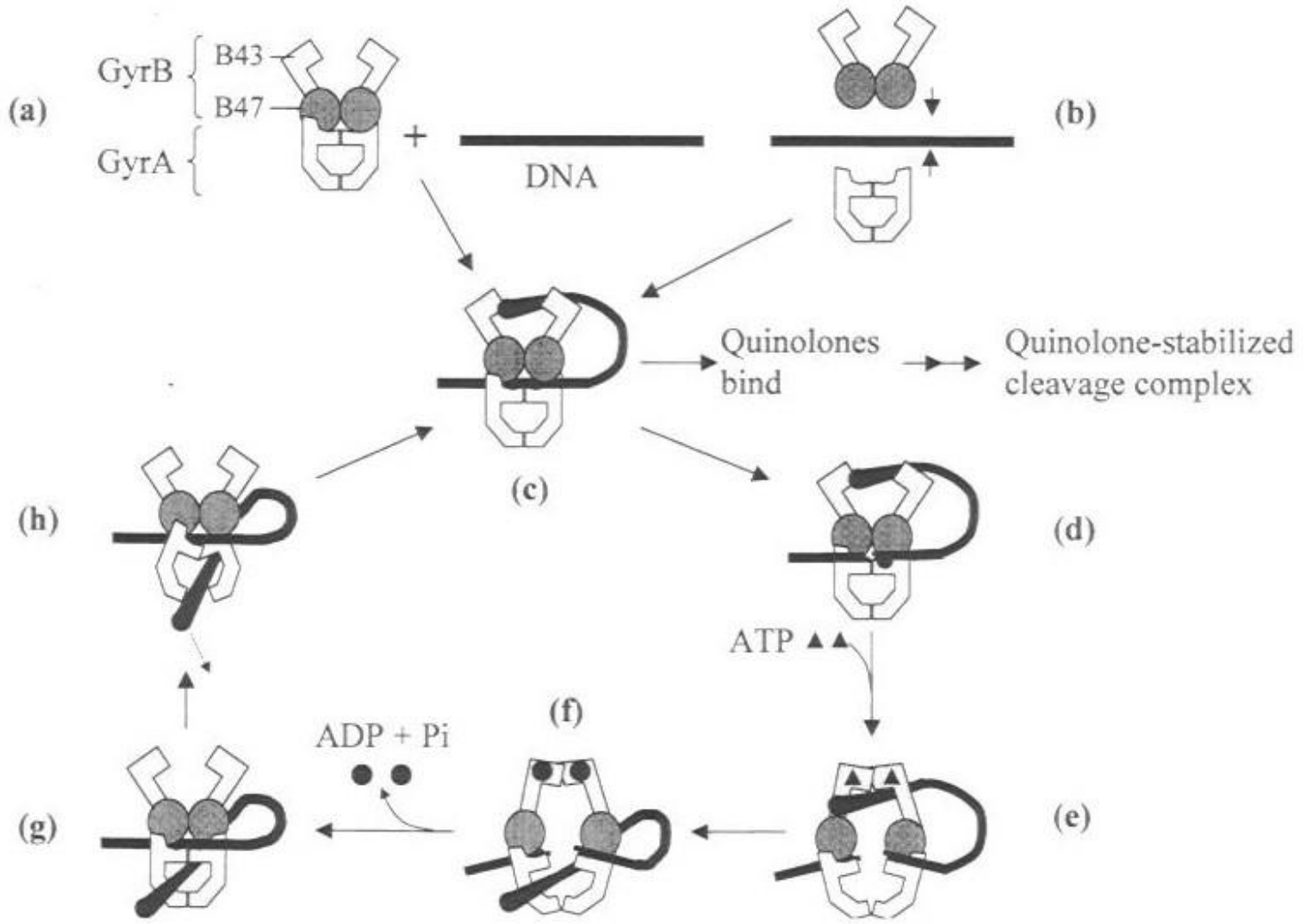
Mechanism of Action

- Dual MOA:
  1. Inhibition of bacterial DNA Gyrase (Topoisomerase II)
     1. Formation of quinolone-DNA-Gyrase complex
     2. Induced cleavage of DNA
  2. Inhibition of bacterial Topoisomerase IV
     1. Mechanism poorly understood

Mechanism of DNA Gyrase



Mechanism of Action



Quinolones

- [Conc] > serum:
  - Prostate tissue
  - Stool
  - Bile
  - Lung
  - Neutrophils
  - Macrophages
  - Kidneys
- [Conc] < serum:
  - Prostatic tissue fluid
  - Bone
  - CSF

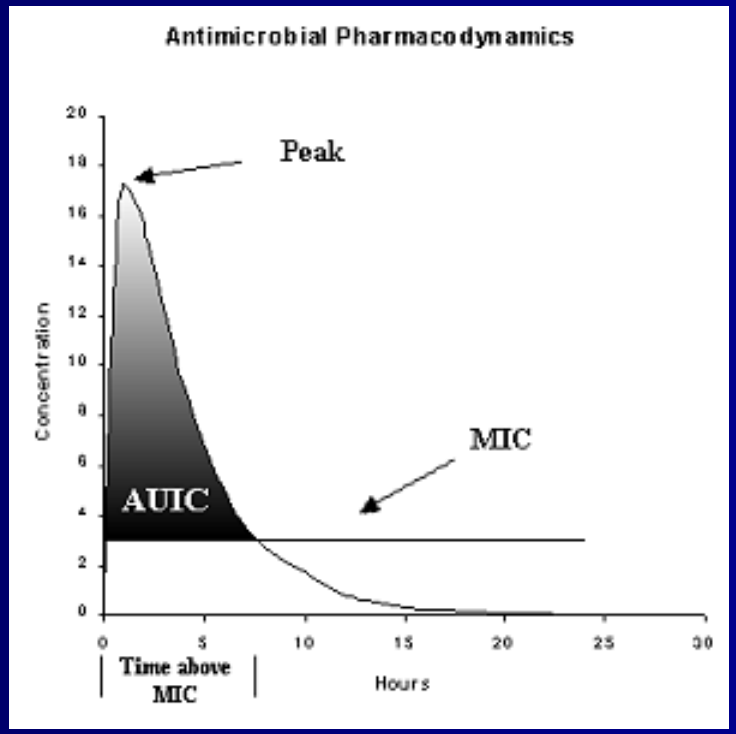
Quinolones

- Drug interactions:
  - ↓ absorption: Al3+, Mg2+, and Ca2+ antacids
  - CYP450 inhibition potential drug interactions for ciprofloxacin
    - (Ex) can increase warfarin exposure (real changes in INR are rare, but monitor)
- Adverse effects:
  - GI: Nausea, vomiting
  - CNS: HA, dizziness, confusion, insomnia, delerium, hallucinations, seizure (rare)
  - Cardiovascular: Torsades de pointes (rare)
  - Musculoskeletal: Rupture of tendon (rare)
  - Neurologic: Polyneuropathy (rare)

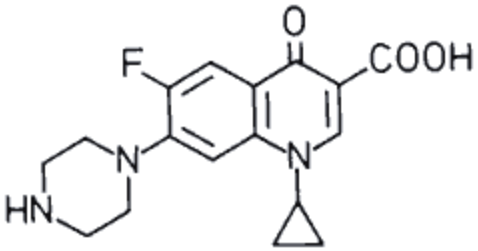
Quinolones PK/PD

- Bactericidal antibiotics
- Show both time-dependent and a combination of time-dependent and concentration dependent killing

Time-Dependent vs. Concentration-Dependent Killing



Ciprofloxacin



- **Administration [Usual Dosage]:** IV, PO [500 – 750 mg q 8-12h]
- **Spectrum:** Gram- aerobic rods, and Legionella pneumophila, and other atypicals. Poor activity against Strep. pneumoniae.
- **Indications:**
  - -- Nosocomial pneumonia
  - -- Intra-abdominal infections
  - – Uncomplicated/complicated UTI
  - – Anthrax exposure and prophylaxis
- **Unique Qualities:**
  - – Binds divalent cations (i.e. Ca & Mg) which decreases absorption
  - -- Increased effects of warfarin
- **ADRs**
  - – QTC prolongation, torsades de pointes, arrhythmias
  - – Nausea, GI upset
  - – Interstitial nephritis

First generation FQs

Ciprofloxacin-

- Long Post Antibiotic Effect (PAE)
- Less active at acidic pH
- Interacts with food and calcium
- High tissue penetrability (Except BBB)
- High conc. in urine and bile
- CNS side effects are common,
- Tendonitis and tendon rupture

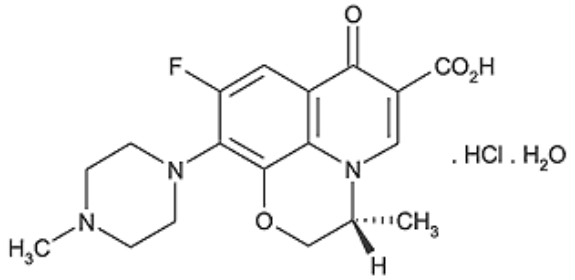
Drug Interaction-

- Inhibition of metabolism of other drug,
- Chelation
- QT interval prolongation

USES- (Extended spectrum)

- CNSI, MFI, OI, ENTI, RTI, GITI, UTI, PID, STDs, SBI
- Nosocomial Infections
- Septicaemia
- Tuberculosis- MDR TB and XDR TB
- Typhoid
  - Treatment 2 weeks
  - Prevention of carrier state 2 months
  - Other drugs-
    - Other FQs
    - Cephalosporins ,**Ceftriaxone (Fastest)**
    - Chloramphenicol
    - Cotrimoxazole
    - Ampicillin

Levofloxacin

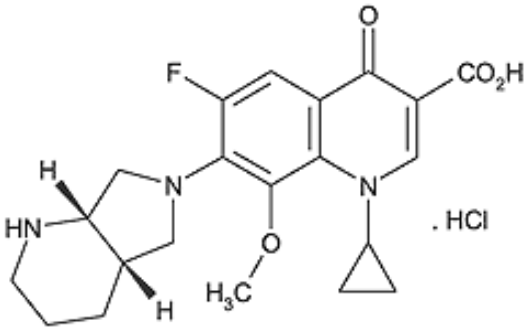


- **Brand Name:** Levaquin®, Quixin®
- **Administration [Usual Dosage]:** IV, PO and ophthalmic [500-750 mg q24h]
- **Spectrum:** Gram-, Gram+ (S. aureus including MRSA & S. pneumoniae) and Legionella pneumophila, atypical resp. pathogens, Mycobacterium tuberculosis
- **Indications:**
  - Chronic bronchitis and CAP
  - -- Nosocomial pneumonia
  - SSTIs
  - Intra-abdominal infections

- **Unique Qualities:**
  - Binds divalent cations (i.e. Ca & Mg) which decreases absorption

  ADRs
  - Blood glucose disturbances in DM patients
  - QTC prolongation, torsades de pointes, arrhythmias
  - Nausea, GI upset
  - Interstitial nephritis

Moxifloxacin



- **Brand Name:** Avelox®, Vigamox®
- **Administration [Usual Dosage]:** IV, PO and ophthalmic [400mg q24h]
- **Spectrum:** Gram-, Gram+ (S. aureus including MRSA & S. pneumoniae) & atypicals (L. pneumophila, C pneumonia & M. pneumoniae), Mycobacterium tuberculosis, gram-negative anaerobes
- **Indications:**
  - Chronic bronchitis
  - CAP
  - Bacterial conjuctivitis
  - Sinusitis
- **Unique Qualities:**
  - Binds divalent cations (i.e. Ca & Mg) which decreases absorption
  - Safety and efficacy not established in patients <18 y.o.
- **ADRs**
  - Blood glucose disturbances in DM patients
  - QTC prolongation, torsades de pointes, arrhythmias
  - Nausea, GI upset
  - Interstitial nephritis

Resistance Mechanisms

- Mutations that enhance antibiotic efflux capability
- Bacterial chromosomal mutations for genes that encode for bacterial DNA gyrase and Topo IV
- Mutations in outer membrane porins (Gram-)

Norfloxacin –

- ✓Less potent,
- ✓Primarily used for UTI and GIT infections,

Ofloxacin-

- ✓Highly active against Mycobacterium leprae

Pefloxacin –

- ✓Methylated derivative of Norfloxacin,
- ✓Oral bioavailability is 100%

Second Generation FQs

- **Lomefloxacin –**
  - Once a day dose
- **Levofloxacin –**
  - Levo-isomer of Ofloxacin,
  - Oral absorption is **100%**
  - Single daily dose
  - ***Minimal drug interactions***

➢Sparfloxacin –

- Enhanced action against Chlamydia,
- ***Maximum half life and Plasma Protein Binding***
- Second line Anti-tubercular drug
- MAC in AIDS, Leprosy
- **No interaction** with Theophylline and Warfarin,
- Photoxicity
- Single daily dose,
- **May prolong Q-T interval** (Avoid with Cisapride, TCAs, Phenothiazines, Anti-arrhythemics, Hypokalemia)

- **Gatifloxacin –**
  - ***Prolongs Q-T interval,***
  - ***Unexpected Hypo or Hyperglycemia*** in Diabetes mellitus patients. (***Withdrawn***)

- **Moxifloxacin** –
  - **Most potent FQ against M. tuberculosis.**
  - Can prolong Q-T interval,
  - Phototoxic

- **Trovafloxacin –**
  - Hepatotoxic (Reserved and maximum of 15 days Tt.)
- **Alatrofloxacin -** Prodrug of Trovafloxacin
- **Finafloxacin, Prulifoxacin, Gemifloxacin**

Elimination of Fluoroquinolones

Renal

- Norfloxacin
- Ofloxacin
- Ciprofloxacin
- Lomefloxacin
- Levofloxacin
- Gatifloxacin

Hepatic

- Pefloxacin
- Moxifloxacin
- Trovafloxacin
- Sparfloxacin
- Gemifloxacin

Fluoroquinolones safe in renal failure

Pefloxacin
Moxifloxacin
Trovafloxacin

Miscellaneous points about Quinolones

- No FQs effective against spirochaetes
- Ofloxacin and Pefloxacin are effective against M. leprae
- Moxifloxacin is the only FQ **NOT** used in UTI as its concentration is poor in urine

- **Levofloxacin, Moxifloxacin, Gemifloxacin, Gatifloxacin, Sparfloxacin** have good activity against S. pneumonia and also called **Respiratory FQs.** They also have good activity against anaerobes

- Chronic Prostatitis Tt. Ciprofloxacin for 1 to 2 months

- Gonorrhea- Tt. Single dose Ciprofloxacin 500mg

- Chlamydia trachomatis- Ciprofloxacin one week or single dose Azithromycin

TABLE 10–1 Indications for Fluoroquinolones

Indication	Cipro	Levo	Moxi	Gemi
CAP, sinusitis, AECB	–	+	+	+
UTI	+	+	–	?
Intra-abdominal infection	+	+	+	?
Systemic Gram-negative infections	+	+	+	?
Skin/soft tissue infection	–	+	+	+
Pseudomonas infections (+/– beta-lactam)	+	+	–	–
Treatment/prophylaxis in bioterrorism scenarios (active vs. anthrax, plague, tularemia)	+	+	?	?

+ = approved/studied/makes sense for this indication.

? = should work, no clinical data.

– = suboptimal.

Dermatologic: Photosensitivity is often seen. Patients should avoid the sun or use sunscreen while taking fluoroquinolones.

Developmental: Because of toxicities seen in juvenile beagle dogs, fluoroquinolones are contraindicated in pregnant women and relatively contraindicated in children, although experience with use in children suggests they may be used.

Important Facts

Important Facts

While ciprofloxacin and levofloxacin have activity against pseudomonas, MICs are typically higher than with other susceptible organisms (e,g., E.coil). Thus, when using these drugs to treat documented or possible Pseudomonas infections, give them at higher, antipseudomonal doses: 400 mg IV q8h or 750 mgPO mg PO q12 h for ciprofloxacin; 750 mg IV/ PO daily for Levofloxacin.

Bioavailability of all fluoroquinolones is 80-100%, so oral dose= IVdose (except ciprofloxacin: PO =~ 1.25 times IV dose). Levofloxacin and ciprofloxacin are the only drugs that are well- absorbed and active against Pseudomonas, but resistance to them is unfortunately common for this pathogen. Susceptibility testing is a must.

Fluoroquinolones chelate cations, and their oral bioavailability is significantly oral bioavailability is significantly decreased when administered with calcium, iron, antacids, milk, or multivitamins. Separate these agents by at least 2 hours or have your patient take a week off of the supplements, if possible. Administration with tube feedings is also problematic. This problem is unique to the oral formulations- IV forms avoid it.

Most Fluoroquinolones are cleared renally and require dose reduction in renal dysfunction. Moxifloxacin is the exception; because it is not excreted into the urine, it is also not approved for treatment of UTIs.

Gemifloxacin has dual elimination, and its utility in treating UTIs is not established, though it does require dose adjustment in renal failure. It is probably best to avoid using gemifloxacin for UTIs until there is evidence that supports its use.

The FDA mandates a boxed warning to all fluoroquinolone packing inserts regarding the possibility of tendon rupture. Important note: in 2016, FDA required the addition of a warning for all systemic fluoroquinolones that their risks out weigh their benefits for most cases of sinusitis, bronchitis, and uncomplicated UTIs unless other options are not available. This is due to the possibility of rare but serious adverse effects, including those listed above.

What Thay're Goods for

What Thay're Goods for

Not everything, despite the temptation. Remember, the longer you want to be able to use these drugs, the more restraint should be exercised now.

سفالوسپورینها

- سفالوسپورین ها به همراه پنی سیلین ها مهمترین آنتی بیوتیک هایی هستند که ساخت دیواره سلولی باکتری را مهار میکنند.
- این داروها را بتالاکتام می نامند که به دلیل وجود یک حلقه ۴ عضوی ست که در همه آنها مشترک است. سفالوسپورین ها به ۲ دسته وسیع الطیف و باریک طیف تقسیم میشوند.
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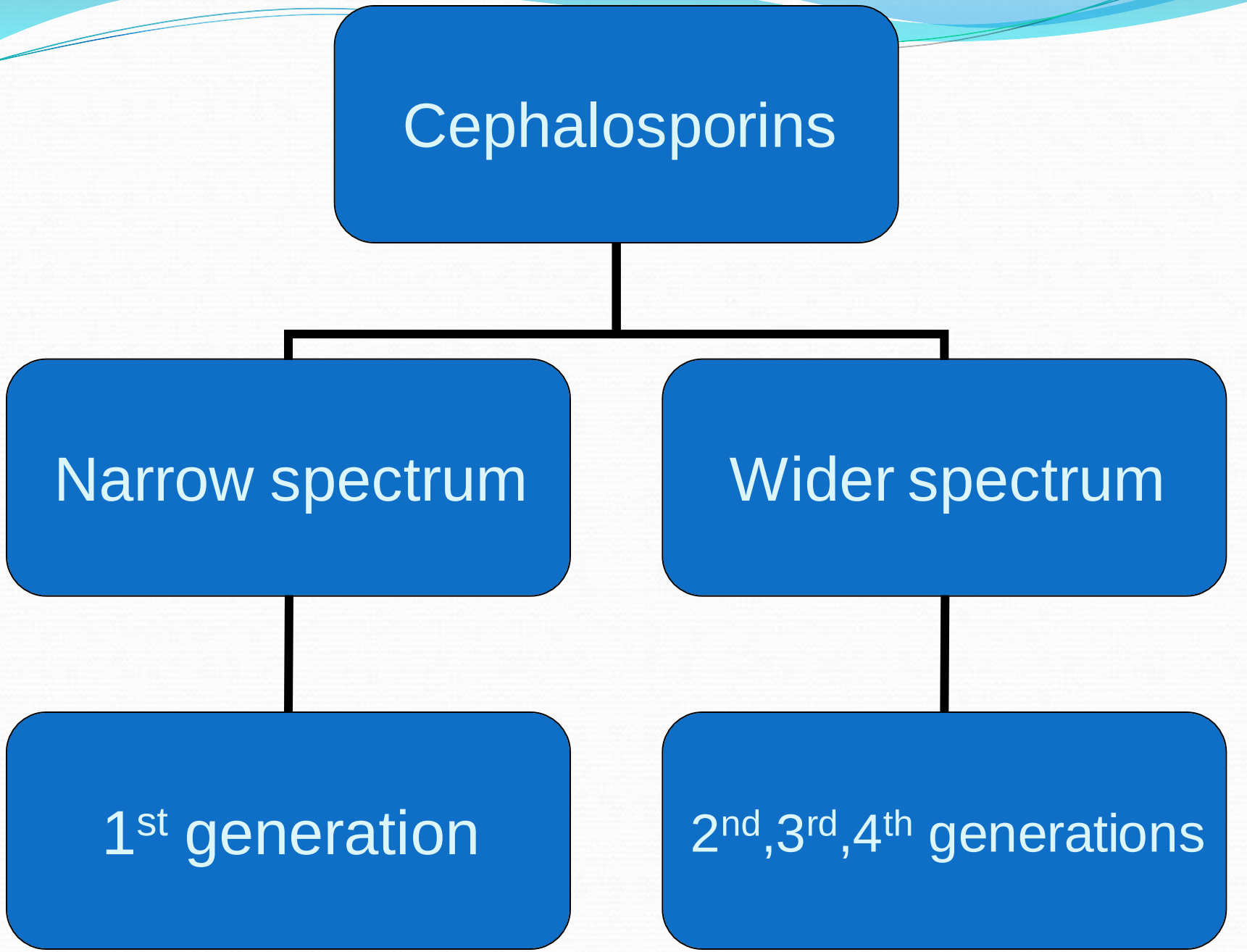
Cephalosporins
Narrow spectrum
Wider spectrum
1st generation
2nd,3rd,4th generations

طبقه بندی:

- سفالوسپورین ها مشتقات
- ۷-آمینوسفالوسپورانیک اسید هستند و حلقه بتا لاکتام دارند.
- فعالیت ضد باکتری آنها بسیار متفاوت است و بر اساس تقدم ورود به طب بالینی،داروهای نسل اول،دوم،سوم یا چهارم نامیده میشوند.

سفالوسپورین های نسل اول:

این گروه شامل:

سفادروکسیل

سفازولین

سفالکسین

سفالوتین

سفاپیرین

سفرادین

- این داروها در مقابل کوکسی های گرم مثبت،شامل پنوموکوکها،استرپتوکوکها و استافیلوکوکها بسیار موثر هستند.
- اگرچه سفالوسپورینهای نسل اول وسیع الطیف و نسبتا غیر سمی هستند ولی ندرتا به عنوان داروی انتخابی برای عفونتها به کار میروند.
- داروهای خوراکی برای درمان عفونتهای ادراری و ضایعات خفیف استافی،سلولیت یا آبسه های بافت نرم به کار میروند.
- با این حال نباید به سفالوسپورین های خوراکی در درمان عفونتهای خطرناک سیستمیک اعتماد کرد.

سفالوسپورین های نسل دوم:

- داروهای این گروه عبارتند از:
- سفاکلور
- سفامندول
- سفونیسید
- سفپروزیل
- لوراکاربف
- سفوروکسیم
- سفورانید
- سفامایسینها: سفمتازول-سفوتتان-سفوکسیتین

- به طور کلی این نسل در برابر میکروبهایی که به داروهای نسل اول حساس هستند، فعال میباشند. اما پوشش گسترده تری نسبت به باکتری های گرم منفی دارند.
- تمامی سفالوسپورین های نسل دوم در مقابل باکتریهای گرم مثبت کمتر از داروهای نسل اول موثرند.

- داروهای نسل دوم خوراکی علیه هموفیلوس آنفولانزا موثر هستند و عمدتا برای درمان سینوزیت،اوتیت یا عفونتهای دستگاه تنفس تحتانی که این ارگانیسم در آنها نقش دارد به کار میروند.
- به علت فعالیت آنها علیه بی هوازیها، سفوکسیتین، سفوتتان یا سفمتازول در عفونتهای بی هوازی مخلوط چوت پریتونیت یا دیورتیکولیت مفید هستند.

- سفوروکسیم برای درمان پنومونی اکتسابی از جامعه استفاده میشود

- سفوروکسیم تنها داروی نسل دوم است که از سد خونی-مغزی عبور میکند اما در درمان مننژیت نباید به کار رود.

سفالوسپورین های نسل سوم:

- داروهای نسل سوم عبارتند از:
- سفوپرازون
- سفوتاکسیم
- سفتازیدیم
- سفتی زوکسیم
- سفتریاکسون
- سفیکسیم
- سفپودوکسیم پروگزتیل
- سفتی بوتن
- موگزالاکتام

- مهمترین خصوصیت این داروها به جز سفوپرازون فعالیت وسیع آنها علیه باکتریهای گرم منفی و قدرت نفوذ برخی از آنها در دستگاه عصبی مرکزی است.

- سفالوسپورینهای نسل سوم به منظور درمان طیف گسترده ای از عفونتهای خطرناک ایجاد شده به وسیله ارگانیسمهای مقاوم به اکثر داروهای دیگر به کار میروند.

- به دلیل نفوذ این داروها به دستگاه عصبی مرکزی میتوانند در درمان مننژیتهای ناشی از پنوموکوکها، مننگوکوکها، هموفیلوس آنفولانزا و باسیلهای گرم منفی روده ای، اما نه لیستریا مونوسیتوژن به کار روند.

- اندیکاسیونهای بالقوه دیگر عبارتند از درمان تجربی سپسیس با علت ناشناخته در افراد بدون نقص ایمنی یا دچار کمبود ایمنی، و در درمان عفونتهایی که برای آنها سفالوسپورین کمتریت سمیت دارویی را داشته باشد.

- در بیماران دچار نقص ایمنی، تب و نوتروپنی، سفالوسپورینهای نسل سوم غالبا به همراه یک آمینوگلیکوزید به کار میروند.

سفالوسپورین های نسل چهارم:

- سفپیم
- سفپیرم

- سفپیم در برابر هیدرولیز به وسیله بتالاکتامازهای کروموزومی که بسیاری از نسل سومی ها را بی اثر میکند مقاوم است.
- فعالیت خوبی علیه اغلب سویه های استرپتوکوکی مقاوم به پنی سیلین دارد.

عوارض جانبی سفالوسپورین ها:

- الف) آلرژی
- ب)مسمومیت
- ج)عفونتهای اضافه شونده

TABLE 20-6 Potential Adverse Effects of Cephalosporins

Type	*Specific*	*Frequency*
Hypersensitivity	Rash	1-3%
	Urticaria	<1%
	Serum sickness	<1%
	Anaphylaxis	0.01%
Gastrointestinal	Diarrhea	1-19%
	Nausea, vomiting	1-6%
	Transient transaminase elevation	1-7%
	Biliary sludge	20-46%*
Hematologic	Eosinophilia	1-10%
	Neutropenia	<1%
	Thrombocytopenia	<1-3%
	Hypoprothrombinemia	<1%
	Impaired platelet aggregation	<1%
	Hemolytic anemia	<1%
Renal	Interstitial nephritis	<1%
Central nervous system	Seizures	<1%
False positive laboratory	Coombs positive	3%
	Glucosuria	Rare
	Serum creatinine	Rare
Other	Drug fever	Rare
	Disulfiram-like reaction†	Rare
	Superinfection	Rare
	Phlebitis	Rare

*Ceftriaxone.
†Cephalosporins with thiomethyl tetrazole ring (MTT) side chain.

TABLE 20-1 Classification of Parenteral and Oral Cephalosporins

Cephalosporins	*First Generation*	*Second Generation*	*Cephamycins*	*Third Generation*	*Fourth Generation*
Parenteral	Cefazolin (Ancef, Kefzol)	Cefamandole (Mandol)	Cefmetazole (Zefazone)	Cefoperazone (Cefobid)	Cefepime (Maxipime)
	Cephalothin (Keflin, Seffin)	Cefonicid (Monocid)	Cefotetan (Cefotan)	Cefotaxime (Claforan)	Cefpirome
	Cephapirin (Cefadyl)	Cefuroxime (Kefurox, Zinacef)	Cefoxitin (Mefoxin)	Ceftazidime (Fortaz)	
	Cephradine (Velosef)			Ceftizoxime (Cefizox)	
				Ceftriaxone (Rocephin)	
				Moxalactam	
Oral	Cefadroxil (Duricef, Ultracef)	Cefaclor (Ceclor)		Cefdinir (Omnicef)	
	Cephalexin (Keflex, Biocef, Keftab)	Cefprozil (Cefzil)		Cefditoren (Spectracef)	
	Cephradine (Velosef)	Cefuroxime-axetil (Ceftin)		Cefixime (Suprax)	
		Loracarbef (Lorabid)		Cefpodoxime (Vantin)	
				Ceftibuten (Cedax)	

TABLE 20-5 Dosing Adjustment of Cephalosporins in Patients with Renal Insufficiency

Cephalosporin	Usual Adult Dosing Regimen	Dosing Regimen with Renal Insufficiency			Dosing Regimen with Dialysis	
		GFR < 10 mL/min	GFR 10-50 mL/min	GFR 50-90 mL/min	Hemodialysis	CAPD
First Generation						
Cefazolin	1 g q8h	0.5-1 g q24h	0.5-1 g q12h	NC	0.5-1 g after	0.5 g q12h
Cephalothin	1 g q4-6h	0.5 g q8h	0.5 g q6h	NC	0.5 g after	1 g q12h
Cephapirin	1 g q4-6h	0.5 g q8h	0.5 g q6h	NC	0.5 g after	1 g q12h
Cephradine	1 g q4-6h	0.5 g q8h	0.5 g q6h	NC	0.5 g after	1 g q12h
Second Generation						
Cefamandole	1 g q6h	1 g q12h	1 g q8h	NC	0.5 g after	1 g q12h
Cefonicid	1 g q24h	0.125 g q24h	0.5 g q24h	NC	None	0.125 g q24h
Cefuroxime	1.5 g q8h	0.75 g q24h	0.75 g q8-12h	NC	0.75 g after	0.75 g q24h
Cephamycins						
Cefmetazole	2 g q8-12h	1 g q24h	2 g q24h	NC	1 g after	1 g q24h
Cefotetan	2 g q12h	1 g q24h	2 g q24h	NC	1 g after	1 g q24h
Cefoxitin	2 g q6h	1 q q12h	2 g q12h	2 g q8h	1 g after	1 g q12h
Third Generation						
Cefoperazone	1 g q8h	NC	NC	NC	None	NC
Cefotaxime	2 g q8h	2 g q24h	2 g q12h	NC	1 g after	1 g q24h
Ceftazidime	2 g q8h	0.5 g q24h	2 g q24h	2 g q12h	1 g after	0.5 g q24h
Ceftizoxime	1 g q8h	0.5 g q24h	1 g q24h	NC	1 g after	0.5 g q24h
Ceftriaxone	1 g q24h	NC	NC	NC	None	NC
Moxalactam	1 g q8h	0.2 g q24h	0.35 g q24h	0.5 g q8h	1 g after	0.25 g q24h
Fourth Generation						
Cefepime	2 g q12h	0.5-1 g q24h	1 g q24h	NC	1 g after	0.5-1 g q24h
Oral—First Generation						
Cefadroxil	500 mg q12h	500 mg q24h	500 mg q24h	NC	500 mg after	500 mg q24h
Cephalexin	500 mg q6h	250 mg q12h	500 mg q12h	NC	500 mg after	500 mg q12h
Cephradine	500 mg q6h	250 mg q12h	250 mg q6h	NC	500 mg after	500 mg q12h
Oral—Second Generation						
Cefaclor	500 mg q8h	500 mg q12h	NC	NC	500 mg after	500 mg q12h
Cefprozil	500 mg q12h	250 mg q24h	500 mg q24h	NC	500 mg after	250 mg q24h
Cefuroxime (axetil)	500 mg q8h	500 mg q24h	500 mg q12h	NC	500 mg after	500 mg q24h
Loracarbef	400 mg q12h	200 mg q24h	200 mg q12h	NC	400 mg after	400 mg q24h
Oral—Third Generation						
Cefdinir	300 mg q12h	300 mg q24h	NC	NC	300 mg after	300 mg q24h
Cefditoren	400 mg q12h	200 mg q24h	200 mg q12h	NC	None	200 mg q24h
Cefixime	400 mg q24h	200 mg q24h	300 mg q24h	NC	300 mg after	200 mg q24h
Cefpodoxime	200 mg q12h	200 mg q24h	NC	NC	200 mg after	200 mg q24h
Ceftibuten	400 mg q24h	100 mg q24h	200 mg q24h	NC	300 mg after	100 mg q24h

CAPD, continuous ambulatory peritoneal dialysis; GFR, glomerular filtration rate; NC, no change.

TABLE 20-4 Pharmacokinetics of Cephalosporins

Cephalosporin	Adult Dose	Peak Serum Concentration (μg/mL)	Half-life (hr)	Serum Protein Binding (%)	Route of Excretion	Cerebrospinal Fluid Concentration Range (μg/mL)	Cerebrospinal Fluid Penetration (%)	Stability at Room Temperature (hr) or Oral Bioavailability (%)
First Generation								
Cefazolin	0.5-1 g q8h	193 (1 g)	1.9	74-86	R (65-100%)	<0.7	0-4	24
Cephalothin	0.5-2 g q4-6h	64 (1 g)	0.5-1.0	50-80	R (50-70%)	0.16-0.31	1	24
Cephapirin	0.5-2 g q4-6h	70 (1 g)	0.6	50-60	R (60-85%)	NA	NA	24
Cephradine	0.5-1 g q6h	50 (1 g)	0.7	8-17	R (75-100%)	NA	NA	2-10
Second Generation								
Cefamandole	0.5-2 g q6h	88 (1 g)	0.7-1.3	50-78	R (80%)	0.35-7.4	0-8.6	24
Cefonicid	0.5-1 g q24h	221 (1 g)	4.4	98	R (95%)	NA	NA	24
Cefuroxime	0.75-1.5 g q8h	39 (1 g)	1.2-1.8	33-50	R (70-100%)	0.35-22.5	11.6-13.7	24
Cephamycins								
Cefmetazole	2 g q8h	143 (2 g)	1.3-1.8	68	R (75-85%)	NA	NA	24
Cefotetan	1-2 g q12h	158 (2 g)	3.5	76-90	R (80%)	1.1-4.8	0.8-3.6	24
Cefoxitin	1-2 g q6h	110 (1 g)	0.8-1	41-79	R (90%)	1.2-22	0.8-35	24
Third Generation								
Cefoperazone	1-3 g q8-12h	153 (1 g)	1.6-2.1	90	H (80%) R (20%)	<0.8-119	2.5-5.9	12
Cefotaxime	1-2 g q12h	102 (1 g)	1-1.2	35-40	R (50-80%)	1-83	4-55	24
Ceftazidime	1-2 g q8-12h	107 (1 g)	1-2	17	R (80-90%)	1.4-30	14-45	24
Ceftizoxime	1-2 g q6-12h	113 (1 g)	1.4-1.7	31	R (70-100%)	<0.5-29	3-22.6	24
Ceftriaxone	1-2 g q12-24h	145 (1 g)	6.4	85-95	R (50%) H (40%)	2-20	1.5-7	72
Moxalactam	1-2 g q8h	70 (1 g)	2.2	50	R (67-88%)	0.8-39	12-69	24
Fourth Generation								
Cefepime	1-2 g q12h	79 (1 g)	2	16-19	R (85%)	5.7	11.8	24
Cefpirome	1-2 g q12h	80 (1 g)	2	10	R (90%)	0.8-4.2	5-67%	24
Oral—First Generation								
Cefadroxil	0.5-1 g q12h	15 (0.5 g)	1.3-1.6	20	R (90%)	NA	NA	80%
Cephalexin	0.5-1 g q6h	5.8 (250 mg)	0.5-1.2	6-15	R (80-100%)	NA	NA	90%
Cephradine	0.5-1g q6h	15 (0.5 g)	1-2	10-20	R (80-90%)	NA	NA	95%
Oral—Second Generation								
Cefaclor	250-500 mg q8h 375 mg q12h	6 (250 mg) 19.2 (400 mg)	0.5-1	25-50	R (50-80%)	NA	NA	50-90% FE
Cefprozil	500 mg q12h	9.3 (500 mg)	1.3	35-45	R (61%)	NA	NA	95%
Cefuroxime (axetil)	250-500 mg q12h	4.6 (250 mg)	1.2	33-50	R (66-100%)	NA	NA	52-68% FE
Loracarbef	200-400 mg q12h	8 (200 mg)	1.0	25	R (87%)	NA	NA	90%
Oral—Third Generation								
Cefdinir	300 mg q12h	2.9	1.5-1.7	60-73	R (18%)	NA	NA	25%
Cefditoren (pivoxil)	200-400 mg q12h	2.5 (200 mg)	0.8-1.6	88	R (16-22%)	NA	NA	17% FE
Cefixime	200-400 mg q12-24h	2.8 (200 mg)-4.5 (400 mg)	3-4	65-70	R (50%) H (5%)	NA	NA	40-50%
Cefpodoxime (proxetil)	200 mg q12h	2.2 (200 mg)	2.2-2.7	18-40	R (29-33%)	NA	NA	50-80% FE
Ceftibuten	400 mg q24h	15 (400 mg)	2.4	65-77	R (57%)	NA	NA	75-90%

FE, food enhances; H, hepatic; NA, not applicable; R, renal.

TABLE 20-7 Dosing Regimens of Cephalosporins in Adults and Children

Cephalosporin	Adults		Children
	Usual Dose	Severe Disease	Usual Dose
First Generation			
Cefazolin	0.5-1 g q8-12h	2 g q6-8h	12.5-33 mg/kg q6-8h
Cephalothin	0.5-1 g q6h	2 g q4-6h	20-25 mg/kg q6h
Cephapirin	0.5-1 g q6h	2 g q4-6h	10-20 mg/kg q6h
Cephradine	0.5-1 g q6h	2 g q4-6h	12.5-25 mg/kg q6h
Second Generation			
Cefamandole	1 g q6h	2 g q4h	12.5-25 mg/kg q4-6h
Cefonicid	1 g q24h	2 g q24h	50 mg/kg q24h
Cefuroxime	0.75-1.5 g q8h	1.5 g q8h	12.5-60 mg/kg q6-8h
Cephamycins			
Cefmetazole	1-2 g q8h	2 g q6h	Not recommended
Cefotetan	1-2 g q12h	2-3 g q12h	Not recommended
Cefoxitin	1-2 g q6h	2 g q4-6h	20-25 mg/kg q4-6h
Third Generation			
Cefoperazone	1-2 g q12h	2-4 g q8h	Not recommended
Cefotaxime	1 g q8-12h	2 g q4-8h	25-30 mg/kg q4-6h
Ceftazidime	1 g q8-12h	2 g q8h	30-50 mg/kg q8h
Ceftizoxime	1 g q8-12h	2 g q8-12h	50 mg/kg q6-8h
Ceftriaxone	1 g q24h	2 g q12-24h	50-100 mg/kg q24h
Moxalactam	1 g q8h	2 g q8h	Not recommended
Fourth Generation			
Cefepime	1 g q12h	2 g q8-12h	50 mg/kg q8h
Cefpirome	1 g q12h	2 g q12h	Not recommended
Oral—First Generation			
Cephalexin	250-500 mg qid	1 g qid	6.25-25 mg/kg qid
Cephradine	250-500 mg qid	500 mg qid	6.25-25 mg/kg qid
Cefadroxil	500 mg bid	1 g bid	15 mg/kg bid
Oral—Second Generation			
Cefaclor	250 mg tid or 375 mg bid	500 gm tid	8.3-16.7 mg/kg tid
Cefprozil	250-500 mg bid	500 mg bid	7.5-15 mg/kg bid
Cefuroxime (axetil)	250-500 mg bid	500 mg bid	10-15 mg/kg bid
Loracarbef	200 mg bid	400 mg bid	7.5-15 mg/kg bid
Oral—Third Generation			
Cefdinir	300 mg bid or 600 mg qd	300 mg bid or 600 mg qd	7 mg/kg bid or 14 mg/kg qd
Cefditoren	200-400 mg bid	400 mg bid	Not recommended
Cefixime	200 mg bid or 400 mg qd	400 mg bid	4 mg/kg bid or 8 mg/kg qd
Cefpodoxime	200-400 mg bid	400 mg bid	5 mg/kg bid
Ceftibuten	400 mg qd	400 mg qd	9 mg/kg qd


با تشکر از توجه شما