

They're 70 (اعتماد 10%)

البديل الاول ال penicillin

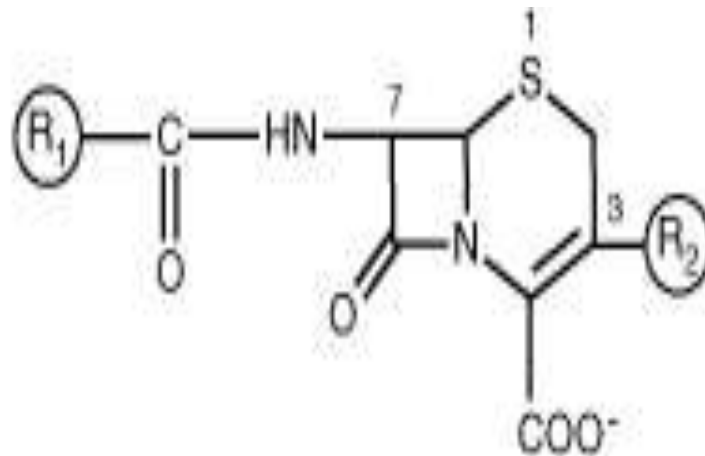
# Cephalosporins → الناس التي حكتها انهم 10% منهم حساسية من البنسلين

- Are also  $\beta$ -lactam antibiotics isolated from a strain of *Streptomyces*.
- There are a large number available for clinical use, variously termed "first- second- third- fourth generations.
- They are bactericidal and work in the same way as the penicillins.
- Resistance is due to <sup>①</sup>  $\beta$ -lactamases, <sup>②</sup> permeability mutants and <sup>③</sup> mutations to the target proteins.

\* Extended spectrum  $\beta$ -lactamase = include the Cephalosporins (Resistant)  
(ESBL) ↓

# Cephalosporins

- **Bicyclic ring structure**
  - **beta-lactam ring (in common with penicillins)**
  - **6 membered sulfur containing dihydrothiazine ring**
- **Changes in side chain R groups gives changes in spectrum of activity, pharmacokinetics, etc.**



# Cephalosporins

Skin infection

## 1st gen

- Cefadroxil *Oral*
- Cefazolin *injectable (IV) prophylactic before surgery*
- Cephalexin *Oral* *One gram, one hour before a surgery*
- Cephalothin *Oral*

حدي (الجلد)  
الجلد القفيفة

except abdominal area  
Frageus  
under diaphragm

↑ Gram negativity

## 2nd gen

- Cefaclor
- Cefoxitin
- Cefuroxime

يستعمل  
فريجيلس

بريتاني  
بدا لك

Augmentin  
المزيج  
في شفا بران

كل يوم نفس السوائل ليس آخر واحد  
أمنه وانه قد يسهل الـ pneumonia  
أقل مقاومة لآله

↑ gram negativity  
↓ gram positivity

## 3rd gen

- Cefnidir *Orally*
- Cefixime
- Cefotaxime
- Ceftazidime *the only one that treat Superbugs*
- Ceftibuten
- Ceftriaxone

دواء من غيب،  
↑ penetration  
All gram +ve and -ve  
except P. Aeruginosa

↑ penetration في meningitis

اسم لثاني دوسوفين

## 4th gen

### Cefepime

(Cefamax) ↓

Active on all -ve & +ve  
+ P. aeruginosa  
but not MRSA

← معلوم من شفا  
4th gen عند

+ 5th gen

# Cephalosporins clinical uses

- Some cephalosporins are given orally, eg. cephalexin, but most are administered intramuscularly or intravenously.
- Cephalosporins are second choice antibiotics for many infections including Gram-positive cocci such as *Staphylococcus*, *Streptococcus* and *Pneumococcus*, and Gram-positive rods such as *Clostridium*.
- They are first choice agents against Gram-negative rods of the *Enterobacteriaceae* such as *E. coli*, *Enterobacter* and *Klebsiella*.

# 1st generation

- Act as penicillin G, but they are resistant to the staphylococcal penicillinase.

have good activity against gram-positive bacteria and relatively modest activity against gram-negative microorganisms.

Most gram-positive cocci (with the exception of enterococci, methicillin-resistant *S. aureus*, and *S. epidermidis*) are susceptible.

الدكتور حكيم انهم يشبهوا ال  
penicillinase Resistant  
penicillins

# First Generation Cephalosporins

Best activity against gram-positive aerobes,  
with limited activity against a few gram-  
negative aerobes

## Gram-positive

هون ما في  
Enterococcus

لأعني انهم ضد ال Strep + Staph  
Skin infection

& cellulitis

meth-susc *S. aureus*

↳ 4 generations are not  
active against Enterococcus

pen-susc *S. pneumoniae*

بس الخاص بـ Strep

Group A/B/C/G streptococci

viridans streptococci

## Gram-negative

*E. coli*

*K. pneumoniae*

*P. mirabilis*

Skin soft tissue infections : بالسلاية الناعمة

3rd generation

ليسا : حريف عند Cellulitis ، بس عند كمان  
Hypersensitivity toward the penicillin, what Antibiotic  
will you perscribe ?! 1st gen Cephalosporins.  
"Empirically" ←

- The first-generation cephalosporins are excellent agents for skin and soft tissue infections owing to *S. aureus* and *S. pyogenes*.



- A single dose of cefazolin just before surgery is the preferred prophylaxis for procedures in which skin flora are the likely pathogens.



زول: ليزوال الخطر  
 Strep + Staph <sup>①</sup> + ② it has a high penetration

One gram, one hour before the surgery

- For colorectal surgery, where prophylaxis for intestinal anaerobes is desired, the second-generation agents cefoxitin or cefotetan are preferred.

Colorectomy ← نستعمل القولون  
 this area: Under diaphragm is full of (Fragilis): Anaerobes under diaphragm ; we don't use cephazolin because you're not covering fragilis.  
 ↳ you'll prescribe a 2nd generation cephalosporin "Cefoxitin"

For cellulitis → it's preferred to prescribe the Orally taken 1st generation cephalosporins.

## Cephalosporins generations

**Second generation:** have greater activity against three additional gram-negative organism : *H influenzae*, *Neisseria*, and *Enterobacter aerogenes*. However, the activity against gram positive bacteria is weaker.

A subset of second-generation agents ( *cefoxitin*, *cefotetan*, and *cefmetazole* ) also is active against the *B. fragilis* group.

so can be used to treat mixed anaerobic infections such as peritonitis or diverticulitis. aerobic anaerobic

**Cefuroxime** is used to treat community-acquired pneumonia because it is active against beta-lactamase-producing *H influenzae* or *K pneumoniae* and penicillin-resistant pneumococci.

Because he's not susceptible  
toward the Atypical type

Cefuroxime يمكن استخدامه للبكتيريا البنية والبكتيريا اللاهوائية  
Empirically



# Second Generation Cephalosporins

Gram  
negativity

← هاد اللي زودنا فيه Spectrum of Activity

← سيتر / Cephuroxime "زينات"

## Gram-positive

meth-susc *S. aureus*

pen-susc *S. pneumoniae*

Group A/B/C/G strep

viridans streptococci

## Gram-negative

*E. coli*

*K. pneumoniae*

*P. mirabilis*

*H. influenzae*

*M. catarrhalis*

*Neisseria sp.*

"لعل ما يتعسنا اليوم،  
يكون سببا في ابتسامة طفل  
مئة سنة غداً"

You can use it as an alternative antibiotic for patients who have hypersensitivity toward penicillins, when they have an upper respiratory tract infection; pharyngitis, sinusitis, tonsillitis ....

ال Spectrum الـ الدكتور ركز عليه:

Streptococcus pyogenes | Moraxella catarrhalis  
Streptococcus pneumoniae | H. influenzae

# Second Generation Cephalosporins

## Spectrum of Activity

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The cephamycins (cefoxitin and cefotetan) are the only 2nd generation cephalosporins that have activity against anaerobes

### Anaerobes

*Bacteroides fragilis*

*Bacteroides fragilis* group

# *Third-generation cephalosporins*

- generally are less active than first-generation agents against gram-positive cocci,
- but they are much more active against the Enterobacteriaceae, including beta-lactamase-producing strains.
- A subset of third-generation agents (*ceftazidime* and *cefoperazone*) also is active against *P. aeruginosa*.

Ceftazidime: tazosyn ١١ ١١ ١١  
Hypersensitivity ١١ ١١ ١١ ١١ ١١



highly active toward gram-ve  
not active toward *S. pneumoniae*  
Active toward *P. aeruginosa*  
3rd ١١ ١١ ١١ ١١ ١١  
gen

طيف مولود عند صفار (Hyperbilirubin) ← يصير بترتيب بأماكن مختلفة في الجسم  
Ceftriaxone → متعلق بعدم اكتمال الخواكب

ما يتو صفح لمولود عمره أقل من 42 أسبوع (شهر)  
لبنول 38 أسبوع / لبسن شهر.

ولو انوله بباقي من أسبوع 28 ل 42  
لبسن وما بطن Ceftriaxone  
شد بعطيه Cefotaxime ؟

\* بالاختصاص : اذا المريفه حره أكثر من شهر (42 أسبوع) :  
أعطيه Ceftriaxone

لبس لو انه كبير عند Liver failure وبعطيه Cefotaxime في الطفل .

# Clinical uses

- The third-generation cephalosporins, with or without aminoglycosides, have been considered to be the drugs of choice for serious infections caused by *Klebsiella*, *Enterobacter*, *Proteus*, *Serratia*, and *Haemophilus* spp.
- They may be particularly useful in treating hospital-acquired infections,

although increasing levels of extended-spectrum beta-lactamases are reducing the clinical utility of this class of antibiotics.

# Clinical uses

- In neutropenic, febrile immunocompromised patients, third-generation cephalosporins are often used in combination with an aminoglycoside.
- Other potential indications include empirical therapy of sepsis of unknown cause in both the immunocompetent and the immunocompromised patient

# Third Generation Cephalosporins

## Spectrum of Activity

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### Gram-negative aerobes

*E. coli*, *K. pneumoniae*, *P. mirabilis*

*H. influenzae*, *M. catarrhalis*, *N. gonorrhoeae* (including beta-lactamase producing); *N. meningitidis*

*Citrobacter* sp., *Enterobacter* sp., *Acinetobacter* sp.

*Morganella morganii*, *Serratia marcescens*, *Providencia*

*Pseudomonas aeruginosa* (✓ ceftazidime and ~~cefoperazone~~)

# Clinical uses

- Ceftriaxone and cefotaxime

1. are used for the initial treatment of meningitis in nonimmunocompromised (**in combination with vancomycin**)

because of their antimicrobial activity, good penetration into CSF, and record of clinical success.

2. are the most active cephalosporins against penicillin-resistant strains of pneumococci and are recommended for empirical therapy of serious infections that may be caused by these strains.
3. Ceftriaxone is the therapy of choice for all forms of gonorrhea and for severe forms of **Lyme disease**.



# ***Fourth-generation cephalosporins***

- ***cefepime***, have an extended spectrum of activity compared with the third generation.
- The fourth-generation cephalosporins are indicated for the empirical treatment of nosocomial infections

particularly useful when gram-positive microorganisms, Enterobacteriaceae, and *Pseudomonas* all are potential etiologies.

# Fourth Generation Cephalosporins

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- 4th generation cephalosporins for 2 reasons
  - Extended spectrum of activity
    - ♦ gram-positives: similar to ceftriaxone
    - ♦ gram-negatives: similar to ceftazidime, including *Pseudomonas aeruginosa*; also covers beta-lactamase producing *Enterobacter* sp.
  - Stability against  $\beta$ -lactamases; poor inducer of extended-spectrum  $\beta$  -lactamases
- Only cefepime is currently available

# Clinical uses

- For example, cefepime has superior activity against nosocomial isolates of *Enterobacter*, *Citrobacter*, and *Serratia* spp. compared with ceftazidime and piperacillin (Jones *et al.*, 1998).
- Cross blood-brain barrier and are effective in meningitis.

MRSA: its mechanism of Resistant doesn't deal with all cell wall inhibitors,  
↓ لازم الدواء يرتبط بـ Penicillin binding protein

يتغير شكل هذين، في دواء من المضادات يرتبط

(Only Vancomycin)

MRSA

هذا (Cefepime) Cefamandole هو لم يتغير

it's not a good inducer for (ESBL) \* هو لم يتغير  
the chance of Resistance is lower

# Cephalosporins adverse effects

- Hypersensitivity, patient who has an anaphylactic response to penicillin should avoid cephalosporins.
- **N-methyl-thiotetrazole-containing cephalosporins**
- **cefamandole, cefotetan, cefditoren, cefoperazone, and only**
  - 1) A disulfiram-like effect: happened when some cephalosporins is indigested with alcohol, because of the blockade to the alcohol metabolism, which result in accumulation of acetaldehyde.
  - 2) Bleeding: some cephalosporins have an anti vitamin K effect, and may cause bleeding (hypoprothrombinemia )