

They're 70, (١٥٪٠٧٠)

البىيل الـ ٧٠ لل penicillin

"Cephalosporins"

النام المـ ١٥٪٠ جـ ١٥٪٠ من البـ ٧٠

- Are also β -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.

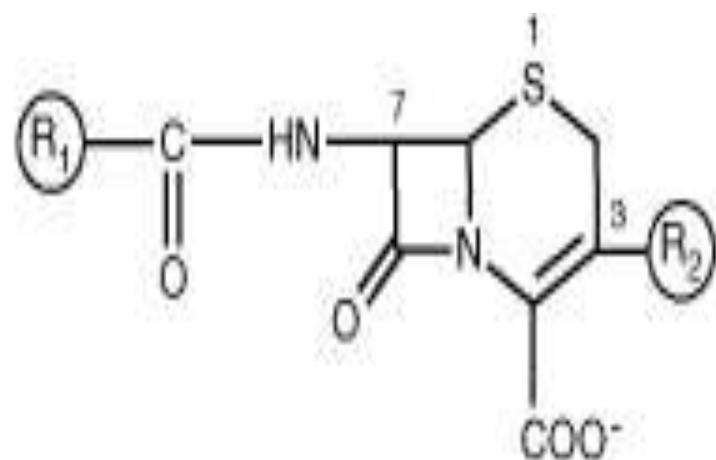
- Resistance is due to ① β -lactamases, ② permeability mutants and ③ mutations to the target proteins.

* Extended spectrum β -lactamase :- include the Cephalosporins (Resistant)

(ESBL) ↴

Cephalosporins

- Bicyclic ring structure
 - beta-lactam ring (in common with penicillins)
 - 6 membered sulfur containing dihidrothiazine 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)
prophylacti
 - Cephalexin Oral
one gram before
 - Cephalothin Oral

الجلد العظيم

except abdominal area
Under dia phragm

كلام (قص) السوطة ليس آخر دافع
تمتن دافعه في نهاد pneumonia
كل متوجه لجهة

↑ Gram negativity

- ## 2nd gen

 - Cefaclor
 - Cefoxitin
 - Cefuroxime

الكلام (السؤال) ينبع من المفهوم المأمور (المأمور) \rightarrow المفهوم المأمور ينبع من المفهوم المأمور

↑ نوکیه دار و دارای اکسیجین پریوریتی هست

3rd gen

- Cefnidir orally
 - Cefixime
 - Cefotaxime
 - Ceftazidime → one that treat superbug
 - Ceftibuten
 - Ceftriaxone

لعلاج هذه meningitis \rightarrow Penetrating

4th gen

Cefepime

(Cefamax) ↗

Active on all +ve, +ve
 +P. aerigenes

+ 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.

ال抵抗ى المقاوم لـ penicillins
penicilline Resistant

First Generation Cephalosporins

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

Gram-positive

لـ اعـنـ افـمـ مـدـ الـ حـلـ لـ بـسـتـ مـلـ
Skin infection Strep + staph S. aureus & cellulitis

pen-susc *S. pneumoniae*

Group A/B/C/Gstreptococci

viridans streptococci



↳ 4 generations are not active against Enterococcus

Gram-negative

E. coli

K. pneumoniae

P. mirabilis

Skin Soft tissue infections : العـلـمـ الـفـلـمـ بـلـ كـلـ
3rd generation

Cellulitis درـجـةـ 3 : اـفـلـيـنـ
Hypersensitivity toward the penicillin, what antibiotic
will you prescribe ?! 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.

Strep + Staph ① + 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.

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 *Enterbacter erogenes*. 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 A typical type

Second Generation Cephalosporins

Gram negativity

الكل في دائرة ← Spectrum of Activity

”جیٹس“ Cephuroxime ۱۵۰۰ مل

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.

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, tonsilitis ...

لَعْلَ مَا يَتَعَذَّبُنَا الْيَوْمَ،
يَكُونُ سَبَبًا فِي ابْتِسَامَةِ طَفْلٍ
مَتَّلِّمٍ غَدَرًا ..

الدكتور كمال سليمان: Spectrum Al

Streptococcus pyogenes | *Haemophilus coryzae*
S. pneumoniae | *H. influenzae*

Second Generation Cephalosporins

Spectrum of Activity

البعض
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 II Jun

Hypersensitivity ~~possible~~



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

ceftriaxone → يضر بـ تـرـتـبـ بـأـماـكـنـ مـخـلـفـةـ (Hyperbilirubin)
في أجسام متعلق بعد اكمال خواصه

مابوچنه له ولود غرم اهل

من العنوان العنوان .

لـ 38 عـ 15 جـ 1 جـ 1

دلو انوله ~~باعي~~ من اسبسو 42 J 288 ~~ل~~ سف Ceftriaxone ~~ل~~ سف

cefotaxime ؟

• (جواب ۴۲) نیوکریکی دیجیتالیز = پردازش

Ceftriaxone dis?

• Jeel S; Cefotaxime in liver failure due to S. aureus

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

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

- 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 β -lactamases; poor inducer of extended-spectrum β -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,

لأنه لا يرتبط بـ Penicillin binding protein

برغم ذلك فهو قادر على إنتاج إنزيم
يسعى لـ MRSA (Cefepime)
Cefamax (Cefazolin)

(Only Vancomycin)

it's not a good inducer for (ESBL)
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)