



# *PHARMACOLOGY*



**Sheets**



**Slides**

**Number: 16**

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**Subject: Cephalosporins**

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"This sheet is written according to section 1 recording"

## Cephalosporins

The most important thing in understanding cephalosporins is to understand the heterogeneity (الاختلاف) between the drugs, even in the same generation.

To recap what we have taken about Cephalosporins so far:

### 1st generation:

- Used to treat cellulites and anything related to skin and soft tissues, why? Because they cover strep & staph.
- 1- Cephalexin (oral tablet).
- 2- Cefazolin (injection): used as prophylactic drug before any surgery (expect when we go in, toward the anaerobes).

### 2nd generation:

- Here the heterogeneity starts, but the thing that gathers them together is: having good activity against gram +ve and some gram -ve (especially H-influenza) thus being suitable for treating upper respiratory tract infections as an alternative of Augmentin in patients who are allergic to penicillins. (In England **Cefuroxime** is the first choice in treating upper respiratory tract infections).
  - Cefoxitin & Cefotetan have good activity against anaerobes, thus used as prophylactic before the surgeries that include going in, toward the anaerobes (inside the abdomen).
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## Now let's start with the topic of this lecture :

In this lecture we are going to take only four different drugs, I'll mention them now, and detail them throughout this sheet:

- 1) Ceftriaxon (tri=3) & Cefotaxime (تقسيم)  $\Rightarrow$  3rd generation/consider them one drug.
- 2) Cefdinir (دينار)  $\Rightarrow$  3rd generation, oral drug and has **one** common feature with the first one.
- 3) Ceftazidime & cefoperazone (mutual **z**)  $\Rightarrow$  3rd generation/ consider them one drug.
- 4) Cefepime (the only cephalosporin that has "fep")  $\Rightarrow$  4th generation.

## Third generation of Cephalosporines:

### ❖ SPECTRUM:

- **Generally** they are less active against gram +ve aerobes and have greater activity against gram -ve aerobes (**most** of them, including  $\beta$ -lactamase producing), See their names on slide #50.
- Exceptions for what I've just mentioned are [Ceftriaxone and Cefotaxime] and [Cefdinir -taken orally-] they have the best activity against gram +ve aerobes **INCLUDING penicillin-resistant pneumonia**, thus they have the widest spectrum in cephalosporins so far.

**NOTE:** {in all the drugs of third generation, the gram +ve activity is decreased except in Ceftriaxone, cefotaxime and cefdinir}.

➤ Why is that so important?

\* If we've treated otitis media (a type of upper respiratory tract infection caused mainly by *S.pneumoniae*) with **high dose** of Augmentin and there is no response, it means that *S.pneumoniae* is resistant to penicillins [In Jordan 30% of patients don't respond to high dose of Augmentin because of the resistance of *S.pneumoniae*, after 3-4 days we inject it with Ceftriaxone & Cefotaxime without culturing (which is wrong)].

- What about pseudomonas aeruginosa?

- Only two groups have activity against pseudomonas, which are: [Ceftazidime and Cefoperazone].
- Are they considered extended spectrum-as a result of being active on pseudomonas-?

\*No, because they have lost some activity against gram +ve bacteria. [They are NOT good enough to be in the next generation].

Again and again....

Most 3rd generation  $\Rightarrow$  gram -ve, less on gram +ve.

Ceftriaxone and Cefotaxime  $\Rightarrow$  Penicillin resistance *S.pneumoniae*.

Ceftazidime and Cefoporazon  $\Rightarrow$  pseudomonas.

## ❖ CLINICAL USES:

- Ceftriaxone and Cefotaxime: (they are very important to you as a doctor)
1. They have a good ability to penetrate to the CNS -they can cross the blood brain barrier-. Thus, they are used as an initial (empirical) treatment of meningitis in nonimmunocompromised (normal) patients. The second reason for their usage is their activity on all the bacteria causing meningitis {H.influenzae, N.meningitidis and strep (group B)}  
\*There are many drugs that cover these bacteria but they cannot penetrate the BBB.
  2. As we have mentioned before, they are active against penicillin resistant strains of pneumococci (pneumoniae) and are recommended for empirical therapy for serious infections caused by these strains, either 3 days injections of Ceftriaxone or 10 days orally of cefdinir.  
[Don't care about the doses].
  3. They are used against Neisseria gonorrhoeae (penicillin resistance) thus, treatment for all forms of gonorrhea. In addition, it is used to treat severe forms of Lyme disease in Africa.
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## **Finally, fourth generation of cephalosporins.**

{Only one drug: Cefepime (Trade name: Cefemax)}

- From its name (max) it covers everything (gram +ve, gram -ve and pseudomonas).
  - It is very close to pipercillin (have the widest spectrum in penicillins and is combined with tazobactam to form Tazocin, in order to cover H-influenzae) which also covers gram +ve, gram -ve and pseudomonas.
  - Example:
    - A patient who is allergic to penicillin is in the ICU, he has developed pneumonia (or any type of infection), the cause is unknown, what should you use.
      - \* We should cover every single cause, either by using pipercillin which we cannot use because of the patient's allergy. So we use Cefepime instead.
  - After all we have mentioned, what's its spectrum?
    - \* Simply everything:  
gram +ve {similar to ceftriaxone}
  - Gram -ve (including pseudomonas aeruginosa)  
{similar to Ceftazidime.}
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Now, are you feeling lost with all these names in the past three lectures?? Let's Summarize literally EVERYTHING we took:

❖ **Firstly, Penicillins:**

➤ Penicillin G & V :

- 1) Strep throat & Rheumatic fever
- 2) Definite therapy if tests assured the susceptibility of bacteria to them.

➤ Oxacillin, flucloxacillin and cloxacillin:

- 1) Staph producing  $\beta$ -lactamase.
- 2) The usage of them has decreased.
- 3) They produced MRSA.

➤ Augmentin

- 1) Amoxicillin with clavulanic acid **or** Ampicillin with tazobactam.
- 2) Upper respiratory tract infection (they cover all the causes of it).

➤ Extended piperacillin:

- 1) we put with it tazobactam to include H-influenzae Producing  $\beta$ -lactamase & staph producing  $\beta$ -lactamase.
- 2) In hospital to cover everything (except MRSA).

## ❖ **Secondly, Cephalosporins:**

### ➤ **First generation**

- 1) For strep and staph
- 2) Soft tissues and skin

### ➤ **Second generation:**

- 1) Alternative for Augmentin (Cefuroxime)
- 2) Active against anaerobes "Bacteroids" (cefoxitin, cefotetan).

### ➤ **Third generation:**

- 1) Ceftriaxone & Ceftaxime : all gram -ve excluding pseudomonas/ resistant *S.pneumoniae*/ meningitis.
- 2) Ceftazidime & cefoperazone: include pseudomonas/ less gram +ve.

### ➤ **Fourth generation: Cefepime**

- 1) Everything.
- 2) When allergic to penicillins.



Let's continue with Cephalosporins

- What are **the Side effects of all cephalosporins?**

**1. Hypersensitivity**

\*Read this sentence carefully:

"Patients who have an anaphylactic response to penicillin should avoid cephalosporins"

Is it correct?? **No, it's not** (10 % of the population are allergic to penicillin, from these 10% there is another 10% (**1% of the total**) allergic to cephalosporins).

**2. Certain cephalosporins with a certain chemical structure [it is enough to know : Cefotetan "2nd generation/against bacteroid fragilis " and Cefoperazone "3rd generation/ against pseudomonas] Have certain effect:**

**A)** Bleeding, remember when we said that some penicillins (carbenicillin & ticarcillin) reduces agglutination & cause bleedings [slide #39, these cephalosporins do the same thing and cause (hypoprothrombinemia).

**B)** Reacts with aldehyde dehydrogenase and inhibits it (used in the metabolism of alcohol)

{ Alcohol -----> aldehyde -----> degraded by aldehyde dehydrogenase into final metabolites. }

Thus, the inhibition causes building up of aldehyde. This effect is called "Disulfiram-like effect".

Disulfiram is used in treating social (psychological) addiction [different from physiological addiction].

How?

The accumulation of aldehyde causes the patient to be agitated (always nervous with tremor) which is very annoying, thus it's helpful in getting rid of alcohol addiction.

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## **Cephalosporins interactions:**

- Did you ask yourself why do we always say ceftriaxone and ceftaxime together? Why not to choose only one?

\*Because ceftriaxone have two problems in which we decide to use ceftaxime, and these problems are:

**1-** In 2011, FDA warning said that if we had injections of ceftriaxone & in the same time there are calcium products entering the patient's body (infusion of supplements), there would be an interaction and calcification of ceftriaxone in Liver & kidney which may cause death.

**2-** ceftraixone is linked to jaundice which is caused by high level of bilirubin (hyperbilirubinemia) ceftraixone interacts with bilirubin & calcifies it.

Where is the interaction with bilirubin mostly important?

\* In infants because they usually have high bilirubin levels in the first 28 days if he was born normally {if he was born on the 7th month it's in the first 2 months+ 28 days}, in this period we cannot give ceftriaxone, we give cefotaxime instead.

{ Note that meningitis is mostly common in infants, }  
{ That's why we are talking about them. }

The last **important thing** that you need to know about cephalosporins is:

- Cefoperazone and Ceftriaxone can be given even to a patient with renal failure. Why? Because they are excreted in the bile and not in the kidney.

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**That's it!**

**I am Sorry for any mistake I may have done 😊**