



Pharmacology

Subject :

Lec no : 24

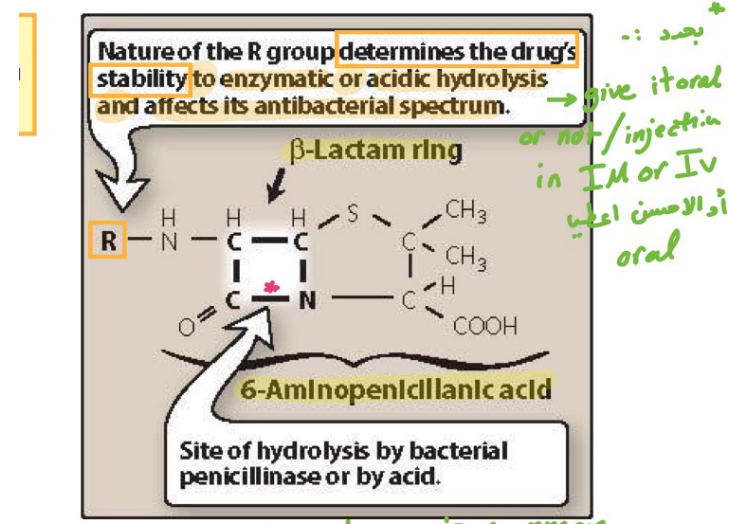
Done By : Raneem Azzam

وَقُلْ رَبِّ زِدْنِي عِلْمًا

الدكتور بالبداية عمل مراجعة ل 23

هسا شو الشي المشترك بين ال penicillins هو ال البيتا lactams ring... طب بهاي العيلة شو الايشي المختلفة بين كل drug والثاني هو ال R group لهيك بلاقي اختلاف بين الادوية الي من نفس عيلة ال penicillins

رجع ذكر حدود المعلومات
من المعاصرة الماضية



*The nature of this side chain affects the antimicrobial spectrum, stability to stomach acid, cross-hypersensitivity, and susceptibility to bacterial degradative enzymes (β-lactamases) → انزيم تفتتج الكبريتات لتكسر ال anti-biotic → β-lactam ring → عن طريق انزيم بتكسر ال β-lactam ring → C-N يربط بينه → Penicillinase → انه اسم انزيم



*Very few of penicillins taken oral like (اموكلان)
 +خلينا متذكرين انو هاد اسم تجاري بحيث هو عبارة عن
 Amoxicillin +clavulanic

Penicillins

Pharmacokinetics

• Routes of administration

- **IV, IM only:** ampicillin+sulbactam, piperacillin+tazobactam, nafcillin, oxacillin
- **Oral only:** Penicillin V, amoxicillin, amoxicillin+clavulanic acid, dicloxacillin
- **Depot forms:** Procaine penicillin G and benzathine penicillin G (IM)

(بعضهم على النوع البستلين)

مع بعض بكونو



its increased acid stability

مشاهدين منافس oral

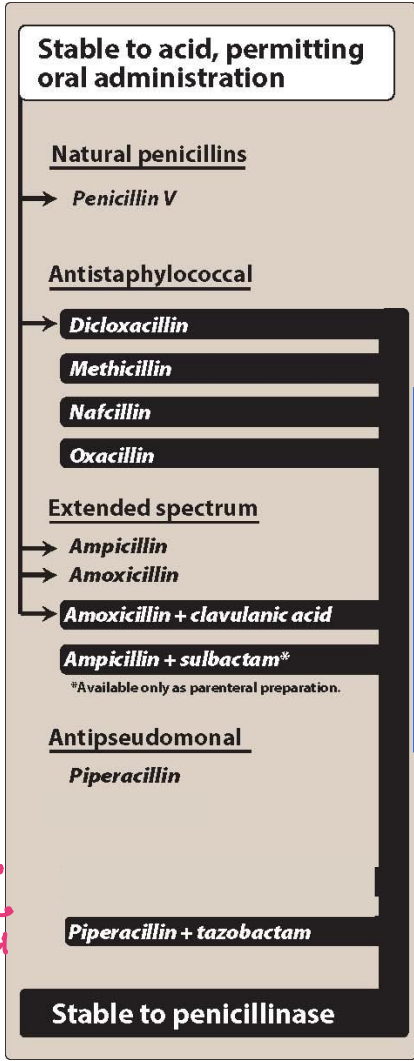
شاه

Penicillin G degrades more easily by stomach acid and has less than 30% bioavailability

سبب ماياضو؟ Prad

← ينغص بطريقتة slowly released ← [SR] مع د. شريف اخذناها

They are slowly absorbed into the circulation and persist at low levels over a long time period



الدكتور حكي عن penicillin v انو هو تمام stable بس بضل not completely absorption + طلعلني كثير resistant ومنو narrow spectrum



Penicillins

Pharmacokinetics

• Absorption

ال penicillins بحبوش ال gastric acid

- Most penicillins are **incompletely absorbed** after oral administration
- Empty stomach?

• Distribution

أهم

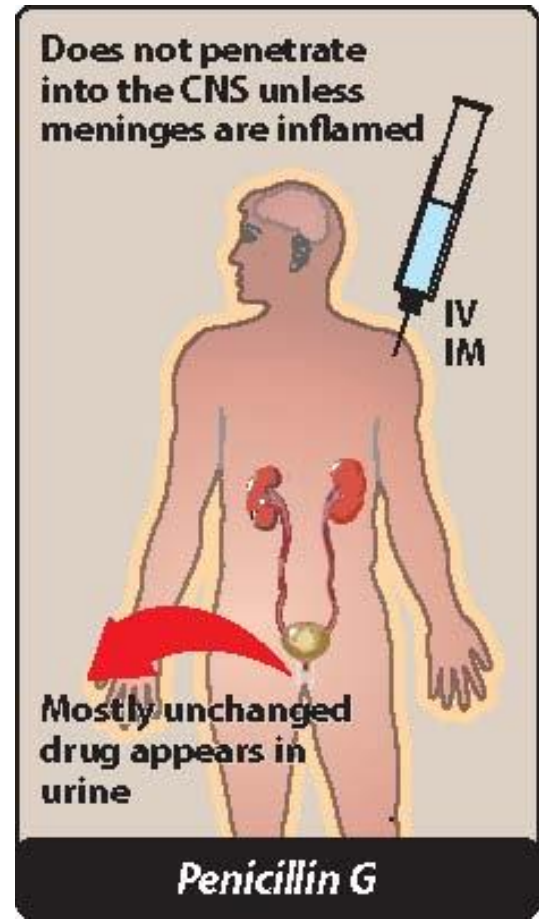
- Good distribution e.g., cross placenta (but no teratogenic effect)

أهم

- Insufficient penetration to bone or CSF (unless inflamed)

[Ampicillin + gentamicin] → بنجبت عليها نفس العكس

وتستخدم لعلاج ال Meningitis



البنسلين يدخل كل ال fluid
داخل جسمك ،، نيجي من
البداية :
البنسلين في الحالة العادية
يكون
non ionized
يعني يكون molecules
طيب وابن حلال قبل ما
يفوت دمك اول ما يفوت
دمك ويتعرض لل ph الدم
7.4 بتحول ل ionized
يعني شايل شحنة (شايل
شحنة يعني ما بعدي ال
bbb) والحالة الوحده الي
ممكن يعدي ال bbb هو
الشخص يكون مصاب ب
meningitis بسسسسس

- Empty stomach?

*they reach the intestine in sufficient amounts to affect the composition of the intestinal flora.

*Food decreases the absorption of all the penicillinaseresistant penicillins because as gastric emptying time increases, the drugs are destroyed by stomach acid.

*Therefore,

they should be taken on an empty stomach.

بعد الأكل ←

هل آمن اعطيه للحامل طيب؟

Yes,
هو ال drug choice لانو هو
بعدي المشيمة بس ما بسبب
تشوهات لدى الجنين شو
السبب؟ الجنين ما عندو
transpeptidas ال يرتبط
عليه البنسلين

غالبية ال antibiotic بتتأثر ب موضوع الاكل مش بس
الpenicillins الي

To improve absorption

على فعدة فاصية ←

← من شرح دكتور فودة



Penicillins

Pharmacokinetics

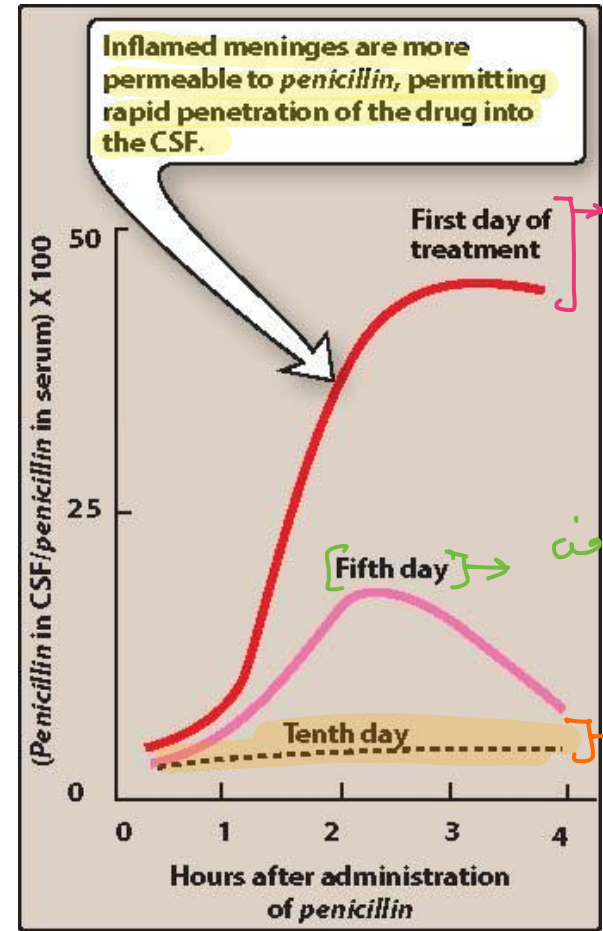
• Absorption

- Most penicillins are well absorbed after oral administration
- Empty stomach

• Distribution

- Good distribution to all body tissues (but no teratogenic effect)
- Insufficient penetration to bone or CSF (unless inflamed)

Inflamed meninges are more permeable to the penicillins, resulting in an increased ratio of the drug in the CSF compared to the serum



هون واضح
بداية المرض
كثرت الاضغاث

صبار اقل
المنه

دليل
ان
المريض
جانب



Penicillins

This is due to the fact that penicillin molecules are relatively small and polar, allowing them to be filtered by the kidneys and excreted in the urine.

لها بالسبب
يستخدم لعلاج ال
تreat urinary tract infections.

Most penicillins aren't metabolite + most of penicillins are extracted unchanged in urine

Pharmacokinetics

• Metabolism

- Insignificant metabolism

- Exceptions? **Anti staphylococcal**

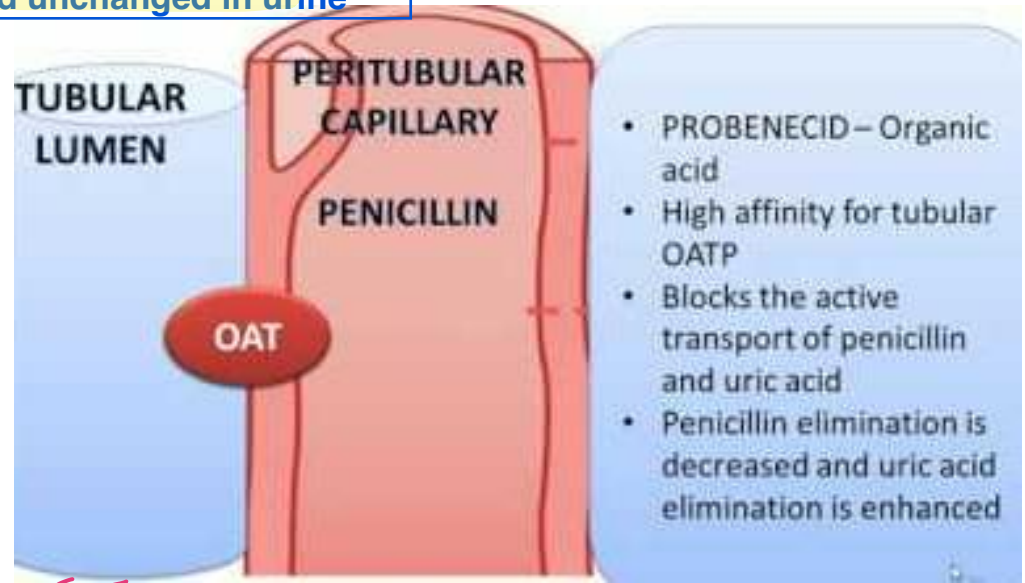
• Excretion:

- Renal: tubular secretory system

- (Probenecid) is an inhibitor of renal tubular excretion of penicillin

عن طريق
ال
kidney

يستخدم
لعلاج
القرص



الدم تنزح حياه

قال ناخذ مثال في penicilline كيف بيصير ال elimination

glomerular filtration and active tubular transport

بستخدمه لو بدي أخلي البنسلين يطول أكثر بال Blood Stream لأزيد ال effect
 + حاس خليكم فتذكروني
 Half life ≠ duration of drug of action
 uricosuric agents

يعني زيدي
بمن ال duration
يا يعرف
Half life

يعني زيدي ال excretion ل uric acid حتى ال urine
لعلاج ال Gout؛ لهيك مرات بطنو أقل من جرعة البنسلين.



ADE بس هاد مش فعالتو انو جالو

Penicillin

شو السبب انو البنسلين يعتبر in general safe
They target specific components of bacterial cell walls
(احنا ماعنا cell wall)
فهو (selective of bacteria),
disrupting their structure and preventing bacterial growth....

Adverse effects

قال الدكتور خذها قاعدة انو الدوا ال جاي من natural substance بكون مربوط مع hypersensitivity, allergies احتمال ظهور

1. Hypersensitivity:

وفي صنف درجات ارجعولها بالاعراضه الي قبل

- 5-10% percent of patients (simple rash to angioedema to anaphylaxis)

- Cross-allergy → other drugs with similar structure (تامين لنفس المبيه)

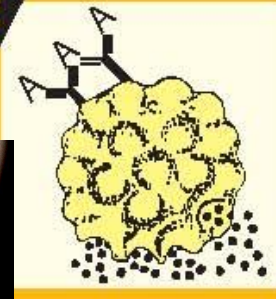
- Always inquire about penicillin allergy

2. Diarrhea:

killing normal flora

- Caused by intestinal flora imbalance

- More with extended-spectrum agents



Hypersensitivity



Diarrhea

*Cross-allergic reactions occur among the β -lactam antibiotics.

*To determine whether treatment with a β -lactam is safe when an allergy is noted patient history regarding severity of previous reaction is essential.



Penicillins

Adverse effects

3. Nephritis:

in 23 lec

حتى نفوف MRSA / MSSA

- Methicillin: no longer used because of this

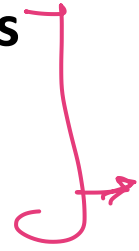
4. Neurotoxicity:

injection in spinal cord

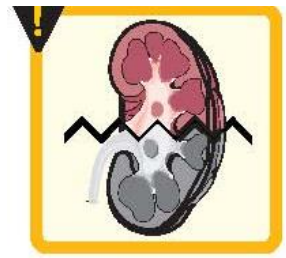
- If injected intrathecally

5. Hematological toxicities

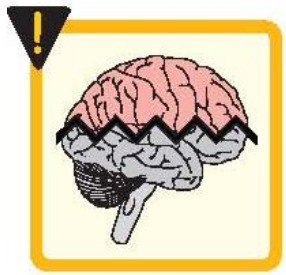
- Decreased coagulation
- Cytopenias



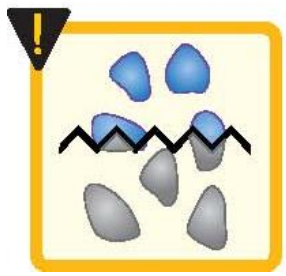
بعرقتش شو
وضعمهم بس
ما ذكرهم



Nephritis



Neurotoxicity



Hematologic toxicities



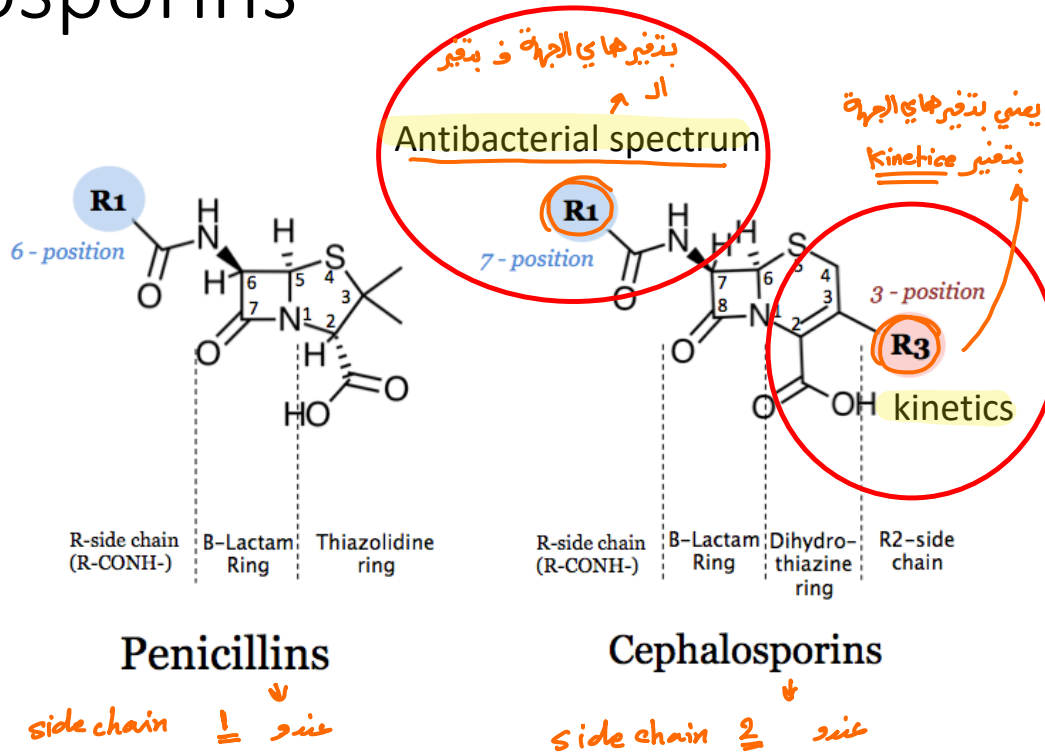
Quick Revision

- Name a penicillin that is effective against penicillinase-producing *S. aureus* (MSSA)? 1. Nafcillin / Oxacillin / dicloxacillin
2. ampicillin + Sulbactam.
- Name a penicillin that is effective against penicillinase-producing *S. aureus* (MRSA)? ولا احد من اي عرفناهم



Cephalosporins

- β -lactams \rightarrow تحت عيابة
- Structurally/functionally related to penicillins
- Semisynthetic
- More resistant to certain β -lactamases than penicilline





Cephalosporins

- **Classified into generations:**

-first

-second

-third

-fourth

-advanced

CEPHALOSPORINS

Cefaclor CECLOR

Cefadroxil DURACEF

Cefazolin KEFZOL

Cefdinir OMNICEF

Cefepime MAXIPIME

Cefixime SUPRAX

Cefotaxime CLAFORAN

Cefotetan CEFOTAN

Cefoxitin MEFOXIN

Cefprozil CEFZIL

Ceftaroline TEFLARO

Ceftazidime FORTAZ

Ceftibuten CEDAX

Ceftizoxime CEFIZOX

Ceftriaxone ROCEPHIN

Cefuroxime CEFTIN

Cephalexin KEFLEX



Cephalosporins

* Antibacterial spectrum *غالباً* very similar to penicilline

• First-generation cephalosporins:

- penicillin G substitutes *بديل*
- They cover MSSA (resistant to penicillinase) but not MRSA

* Cefazolin

* Cephalexin

* cefadroxil

هل بزيط يكونو substitute في حالة ال
 ؟penicillin allergy
 Yes ,
 بس ممكن يكون في عنا حساسية للاثنين بس
 بنسبة قليلة جدا بين 3%-5% حكينا اسمها
 Cross allergy

First-generation cephalosporins

Gram (+) cocci

Staphylococcus aureus*
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus pyogenes
 Anaerobic streptococci

Gram (-) rods

Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis

*Methicillin-resistant staphylococci are resistant

*Not MRSA

for ENT infection



Cephalosporins

لايزن كيونوا احسن من
first generation

↑ Antibacterial spectrum

- **Second-generation cephalosporins:**
 - Wider gram-negative spectrum: *H. influenzae*, *Klebsiella*, *Proteus*, *Moraxella catarrhalis*, and some *Neisseria* species

- * Cefotetan
- * Cefuroxime
- * Cefoxitin
- * Cefprozil

Non are first line

Second-generation cephalosporins

Gram (+) cocci

Staphylococcus aureus
Streptococcus pneumoniae
Streptococcus pyogenes
 Anaerobic streptococci

Gram (-) cocci

Neisseria gonorrhoeae

Gram (-) rods

Enterobacter aerogenes
Escherichia coli
Haemophilus influenzae
Klebsiella pneumoniae
Proteus mirabilis

Anaerobic organisms**

***Cefoxitin* and *cefotetan* have anaerobic coverage



لا هون لسا فاحلينا مشكلتة
MRSA



Cephalosporins

They have increased risk of super infection

use in
empirical treatment

Antibacterial spectrum

- **Third-generation cephalosporins:**
- Greater activity against gram-negative bacilli
(broad-spectrum) يجب استخدامه بحذر بسبب "الأضرار الجانبية"
- Drugs of choice for the treatment of meningitis
- Must be used with caution "collateral damage"

Third-generation cephalosporins

- Gram (+) cocci**
 - Streptococcus pneumoniae
 - Streptococcus pyogenes
 - Anaerobic streptococci
- Gram (-) cocci**
 - Neisseria gonorrhoeae
- Gram (-) rods**
 - Enterobacter aerogenes
 - Escherichia coli
 - Haemophilus influenzae
 - Klebsiella pneumoniae
 - Proteus mirabilis
 - Pseudomonas aeruginosa*
 - Serratia marcescens

*only ceftazidime

كثير
مريض

- Ceftriaxone → for ⊕
⊖
- Cefotaxime
- Ceftazidime activity against pseudomonas aeruginosa
- Cefdinir ↑ الفرق بينه

Ceftriaxone and cefotaxime → the drugs of choice for treatment of pneumonia and meningitis.

- Must be used with caution "collateral damage"

They have increased risk of super infection

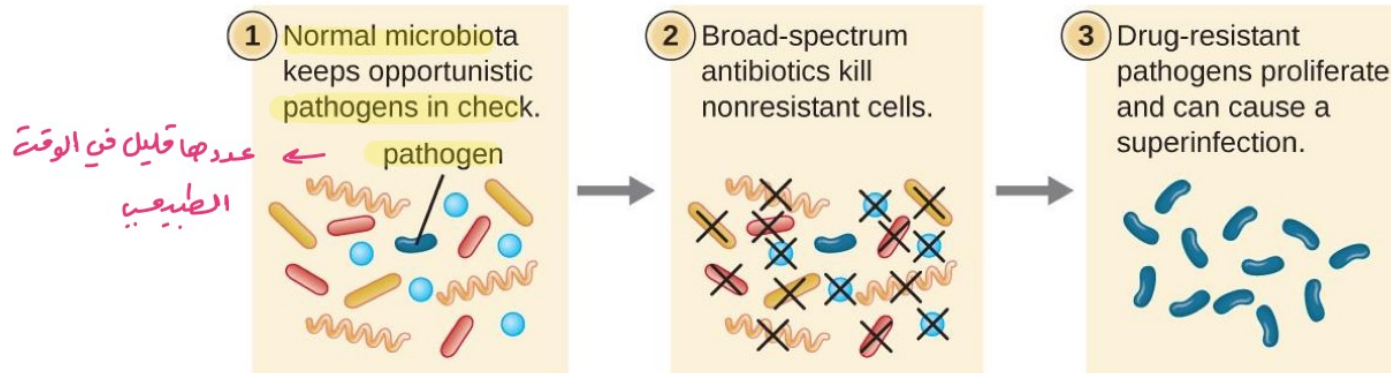
طبيب نتذكر شو هو ال super infection:

Superinfection refers to a secondary infection that occurs on top of an existing infection or during the course of treatment for another infection. It happens when the normal balance of microorganisms in the body is disrupted, allowing opportunistic pathogens to thrive and cause additional infections. Superinfections can result from antibiotic use, weakened immune system, or invasive medical procedures.

C. Superinfections:

- mainly with broad-spectrum agents
- Overgrowth of opportunistic organisms

يعني انت عم بتعالج مريض باستخدام ال antibiotic بس بالغلط عم بتضيف infection ، كيف يعني ؟
 نرجع لل broad spectrum و بتعالج واحد عندو pneumonia باستخدام broad هو good
 بس احنا حكينا انو ال borad (doesn't only infect the pathogenic bacteria ال normal flora ممكن كمان يخرّب ال
 ال beneficial bacteria و خلت منها ال harmful والي هي بتعمل resistant
 فهون انت بتكون قتلت ال



الكلام هاد للتذكير لانو صلوة حكاها الدكتور و موجودة بالكتاب

from the book → cephalosporins must be used with caution, as they are associated with significant "collateral damage," including the induction of antimicrobial resistance and development of **Clostridium difficile** infection.

diarrhea and colitis (an inflammation of the colon).

(Pseudomembranous colitis)

التوزيع بس

يسبب الغشاء الزائف) تغيرات في طبقة القولون، حيث يترافق ذلك مع الإفرازات المخاطية والتقرحات التي تتكون على سطح الأمعاء. تعتبر البكتيريا المعروفة باسم Clostridium difficile العامل الأكثر شيوعاً المسبب للتهاب القولون الزائف.



Cephalosporins

وهاء مفروضه
يكون احسن من

Antibacterial spectrum

- **Fourth-generation cephalosporins:**
- Broad-spectrum **empirical treatment**
- Active against strep and staph species (not MRSA)
- Active against aerobic gram-negative species including (P. aeruginosa) =

for it : 1) Cefepime
2) Ceftazidime
3) piperacilline
مسما ذكرونا قبل انه
(piperacilline + tazobactam) الدكتور حان في اصل

Cefepime

Tareq Saleh ©

Antibacterial spectrum

- **Advanced-generation cephalosporins:**
- Broad-spectrum
- Only β -lactam that is active against MRSA \leftrightarrow
- Indicated for complicated skin MRSA infections and pneumonia
- How about pseudomonas? ESBL? *Not active against them*
- What are the limitations for using ceftaroline? *The twice-daily dosing regimen also limits use outside of an institutional setting.*

ما يزال gap
مفتوحا

Ceftaroline

Ceftaroline is primarily administered through intravenous (IV) infusion, limiting its use to hospital or healthcare settings. There is currently no oral form available.



← إلى ذكر والدكتور عرضا وقال فزودهن عارفينها عن Micro / قواعد سرية للفهم

When treating infections caused by *Pseudomonas* bacteria or cases of Extended Spectrum Beta-Lactamase (ESBL), a variety of appropriate antibacterial drugs are used. These include antibiotics effective against Gram-negative bacteria such as quinolones (e.g. ciprofloxacin), aminoglycosides (e.g. amikacin), cephalosporins (e.g. ceftriaxone), and carbapenems (e.g. imipenem). However, the selection of the appropriate drug should be based on the bacteria's sensitivity to antibiotics and the treating physician's recommendation. It is important to consult a doctor for specific medical advice for each case.

عند معالجة العدوى ببكتيريا البسيودوموناس (*Pseudomonas*) أو حالات الإنزيم الخاص بالبيتالكتاماز الموسع (ESBL)، يتم استخدام مجموعة من الأدوية ضد البكتيرية المناسبة. تشمل هذه الأدوية المضادة للبكتيريا الجرام السلبية، مثل الكوينولونات (مثل سيبروفلوكساسين) والأمينوجليكوزيدات (مثل أميكاسين) والسيفالوسبورينات (مثل سيفترياكسون) والكاربابينيمات (مثل إيميبينيم). ومع ذلك، يجب أن يتم اختيار الدواء المناسب وفقاً لحساسية البكتيريا للمضاد الحيوي وتوصية الطبيب المعالج. يجب استشارة الطبيب للحصول على نصيحة طبية محددة لكل حالة.

10:29 PM



Quick Exercise

Which of the following cell wall synthesis inhibitors is effective **against MRSA?**

- amoxicillin
- ampicillin
- amoxicillin/clavulanate
- cefazolin
- cephalexin
- ceftriaxone
- cefepime
- ceftaroline** → advanced generation



Cephalosporins

شو ال target حقهم؟ نفس البنسلين
Penicillin binding proteins

Mechanisms of resistance

- Similar to penicillins →

same target
same mechanism of action
نفس ال
البنسلين

Susceptible to

Penicillinases (*staph*)

Extended spectrum beta-lactamase ESBL (*E.coli*, *Klebsiella*)

Extended Spectrum Beta-Lactamases (ESBLs) are enzymes produced by certain bacteria, particularly *Escherichia coli* (*E.coli*) and *Klebsiella* species. These enzymes have the ability to break down and deactivate a broad range of beta-lactam antibiotics, which includes penicillins, cephalosporins, and monobactams.

للتوضيح

ESBL
a group of plasmid-mediated, diverse, complex and rapidly evolving enzymes which share the ability to hydrolyze third-generation cephalosporins and aztreonam

Rawat et al, 2010



* الاسباء الي بتخص
الاسم حنين وصفنا

Cephalosporins

Cefixime is the exception in the third generation cephalosporin class that can be given orally. It is available as an oral tablet or suspension

* سؤال عنو الدكتور بالجامعة *

Pharmacokinetics

جيل 1/2 جيل 4/3

• Administration:

- Poor oral absorption, mostly given IV, IM

• Distribution:

in 3rd gen

- To CSF: ceftriaxone and cefotaxime are effective in the treatment of neonatal meningitis caused by *H. Influenzae*

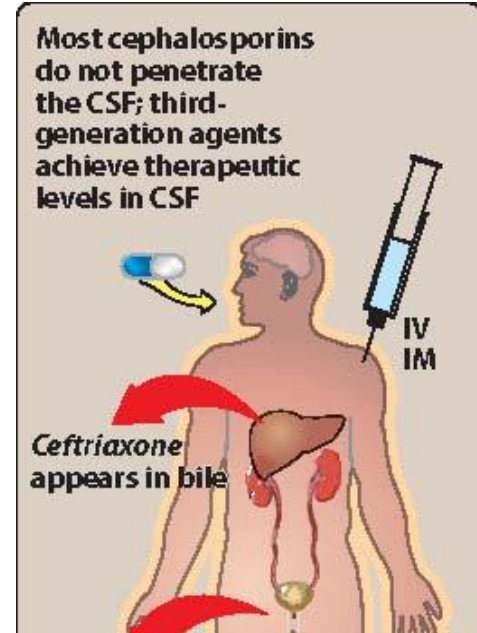
نبي
عنه

- cefazolin can penetrate bone used for infections in bone

• Elimination:

- Renal tubular secretion (except ceftriaxone, eliminated in bile)

عنه



Most of cephalosporins do not undergo hepatic metabolism so they excreted unchanged in the urine. (very good to patients of hepatic failure)

.ceftriaxone, which is excreted through the bile into the feces and, therefore, is frequently employed in patients with renal insufficiency

choice of drug

التامة
الامة
زي

المعلومة من الكتاب ما ذكرها الدكتور بس اغلب اسئلة الدكتور كيسز ف ممكن ننسال عنها عادي .. لو عندي المريض عندو مشاكل بالكلى يفضل ما اعطيه ادوية يتم التخلص منها عن طريق الكلى ف يستخدم السيتريفاكسون، النوا الجسم بتخلص منو بطريقة لاتعتمد على الكلى .



Cephalosporins

Adverse effects

- Hypersensitivity (cross-reactivity with penicillin)
- Highest rate of allergic cross-sensitivity with penicillin → 1st generation
- Remember: broad-spectrum antibiotics are associated with superinfections

يعني واحد عندو penicillin, allergy ما في داعي تعطيه first generation لانو في chance يكون عندو حساسية منو

لا تقسوها كل ما قلنا في super
5/4/3 اع. نزيد ال chance لا. super



As we said even if the drug is safe the side effects may occur.

Cephalosporins and penicillin are related to each other in structure and function so if the patient has an allergy from penicillin, he might have allergy from cephalosporins.
-superinfections → mainly with 3rd, 4th and advanced cephalosporins → because of their broad spectrum activity → they may kill the normal flora allowing the growth of pathogenic bacteria, example (Clostridium difficile) → cause pseudomembranous Colitis.



First Generation

Cefazolin ←

This first-generation parenteral cephalosporin has a longer duration of action and a similar spectrum of action, compared to other first-generation drugs. It penetrates well into bone.

Cefadroxil

Cephalexin ←

This is the prototype of first-generation, oral cephalosporins. Oral administration twice daily is effective against pharyngitis.

Second Generation

Cefuroxime sodium ←

This prototype second-generation, parenteral cephalosporin has a longer half-life than similar agents. It crosses the blood-brain barrier, and it can be used for community-acquired bronchitis or pneumonia in the elderly and for patients who are immunocompromised.

Cefuroxime axetil ←

Administered twice daily, this drug is well absorbed and is active against β -lactamase-producing organisms.

Third Generation

Cefdinir
Cefixime ←

These are administered orally once daily.

Cefotaxime ←

This penetrates well into the CSF.

Ceftazidime ←

This is active against Pseudomonas aeruginosa.

Ceftibuten

This drug has the longest half-life of any cephalosporin (6 to 8 hours), which permits once-a-day dosing. High levels of the drug can be achieved in blood and CSF. It is effective against genital, anal, and pharyngeal penicillin-resistant Neisseria gonorrhoeae. The drug is excreted in bile and may be used in patients with renal insufficiency. It has good penetration into bone.

Ceftriaxone ←

Fourth Generation

Cefepime ←

This is active against Pseudomonas aeruginosa.

Only β -lactam that is active against MRSA \rightarrow **Ceftaroline**

Handwritten notes:
 - oral (next to Cefuroxime axetil)
 - 5th gen (next to Ceftaroline)
 - no MRSA (with a red underline)
 - crisis (with a red underline)



من نوزيع دفعة ايه
قبلنا

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WOLTERS KLUWER



Very important

اقرأه كلو واعرفوه لانو جدا مهم وهون بعض الاضافات الي ضافها الدكتور .

Cefuroxime axetil → given orally / can be used in family medicine clinics

We said the penicillin G can be used for treatment of Neisseria gonorrhoea but the resistance increased to penicillin G so → the drug of choice now to Neisseria gonorrhoea is ceftriaxone.

In cephalosporins we have 2 drugs active against pseudomonas aeruginosa →

1-cefepime

2-cefotaxime (3rd generation)

In penicillin we have piperacillin active against pseudomonas aeruginosa.