Cephalosporins

subgroups	indication
First generation (Cefazolin, cephalexin)	surgical prophylaxis → to prevent postoperative infection
Second generation (Cefaclor, cefuroxime, and cefprozil)	active against H influenzae, sinusitis, otitis, and lower respiratory tract infections
Third generation (ceftriaxone, cefotaxime, cefpodoxime, cefdinir, cefixime) + ceftazidime	Meningitis, endocarditis, empirical therapy of sepsis in both the immunocompetent and the immunocompromised patient
Fourth generation (Cefepime)	Pneumonia, Empiric therapy in febrile neutropenic patients, UTI
Advanced generation-5th (Ceftaroline)	complicated skin and soft tissue infections and community-acquired pneumonia

gram ⊖ bacilli activity in 1st generation is limited

1st resistant MRSA

Cefaclor, cefuroxime: orally active

active against (+, −) → E.coli

ceftriaxone (given parenterally + not renally excreted + bile)

sexual transmitted disease like gonorrhea

ceftazidime: active against Pseudomonas aeruginosa

gram + activity mostly

Cefepime: IV, parenterally; respiratory inf

β case resist + wide spectrum; empiric therapy

4th and 5th are used in the emperic therapy → because of their wide spectrum of action

soft tissue staph, strep; respiratory tract inf.

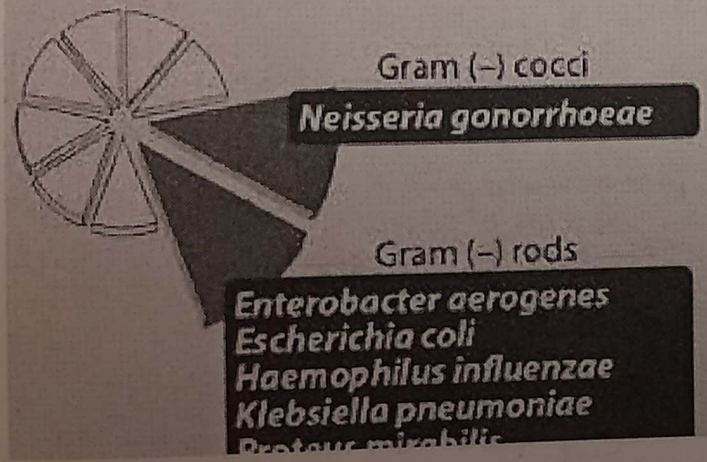
Advanced generation-5th (Ceftaroline)	complicated skin and soft tissue infections and community-acquired pneumonia

empiric therapy

4th and 5th are used in the emperic therapy → because of their wide spectrum of action

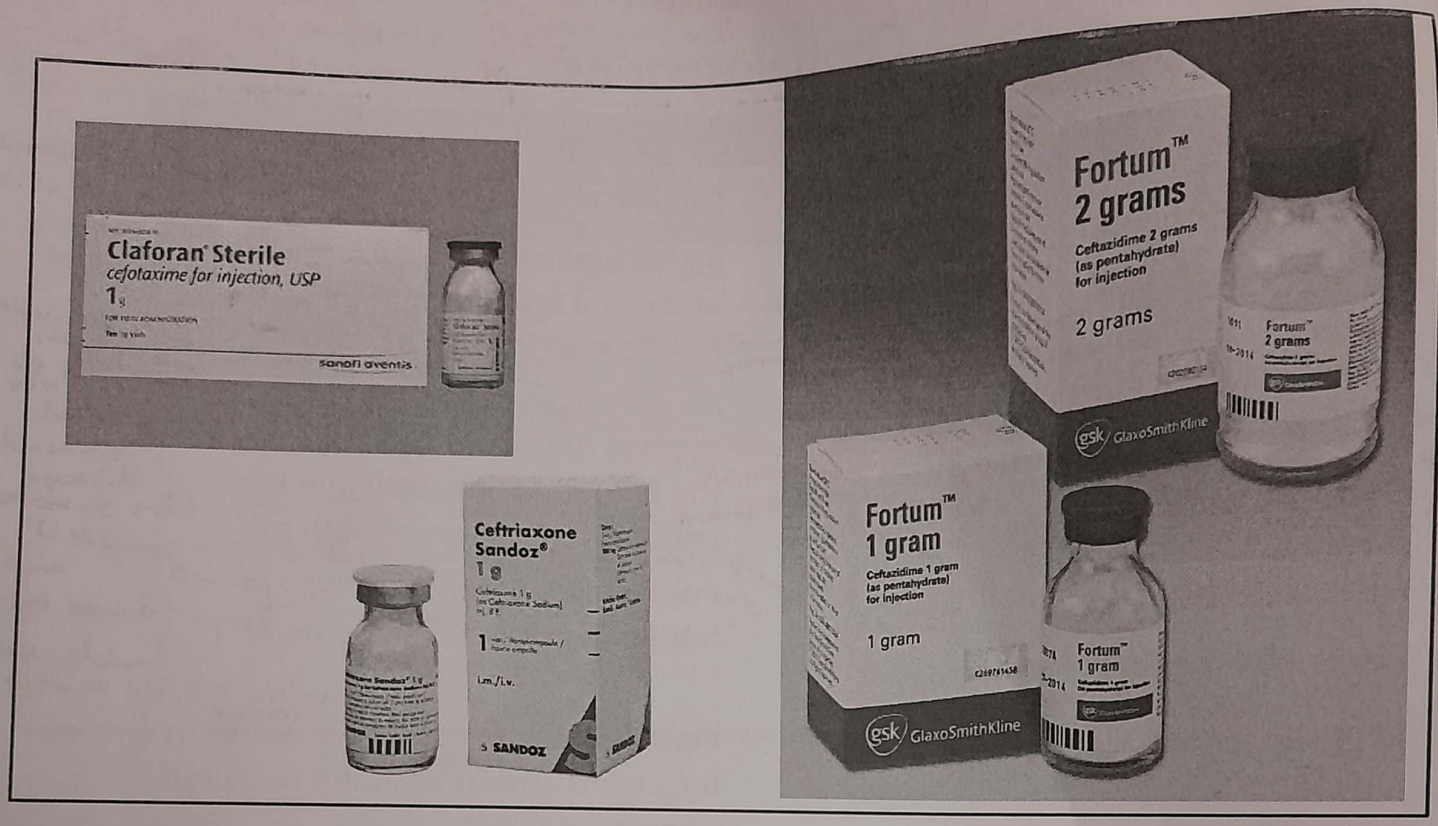
soft tissue ← staph
cause respiratory tract inf. ← strep

Third-generation cephalosporins



adequate therapeutic levels in the CSF, regardless of inflammation, are achieved only with the **third-generation cephalosporins.**

Are effective in the treatment of neonatal and childhood meningitis caused by H.influenzae. meningococcal meningitis.



Pharmacokinetics

1. Administration:
•Many of them must be administered IV or IM because of their poor oral absorption (however some can be given orally)

isn't preferable because it may cause pain but

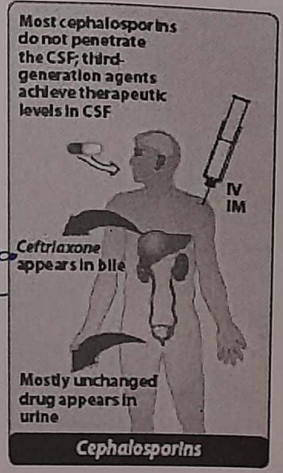
2. Distribution:
•CPNs distribute very well into body fluids but not to CSF.
•**Cefazolin** penetrates well into most tissues. It is a drug of choice for surgical prophylaxis including orthopedic surgery because of its ability to penetrate bone.
•Only **ceftriaxone** or **cefotaxime** achieve therapeutic levels in the CSF and have become agents of choice for meningitis.
•All CPNs cross the placenta.

only 3rd + 4th ceph can pass BBB to CSF

but they are safe in pregnancy + Lactation with some variability

3. Elimination:
•Tubular secretion and/or glomerular filtration
•Doses must be adjusted in cases of renal failure and can be used in renal failure
•Exception: **Ceftriaxone**, excreted through the bile.....Employed in patients with renal insufficiency

no other adjustment in renal failure



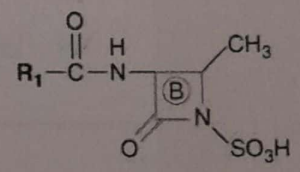
Adverse effects

- ✓pain after injection.
- ✓Diarrhea. → wide spectrum
- ✓Hypersensitivity reaction
  (10% cross- sensitivity, The highest rate with first-generation cephalosporins)

Some have anti-Vitamin K effect(bleeding).

Other B-Lactam Antibiotics- Monobactams

- They are drugs with a monocyclic β-lactam ring.
- Their spectrum of activity is limited to aerobic Gram-negative organisms (including *P aeruginosa*).
- Aztreonam is resistant to the action of B-lactamases.
- It is administered either IV or IM. Every 8 hrs
- this drug **may offer a safe** alternative for treating patients who are allergic to penic &/or cephalosporins.



★ هاد من الي دوليج الا خلق ولي الاشهر (بالمستشفيات مستخدم (under supervision)
بالمستشفيات في مجموعة دكاترة ← (steward ship) ← control prescribing antibiotics → in order to prevent any resistant in hospital

Other B-Lactam Antibiotics- Carbapenems

- broad-spectrum B-lactam antibiotics. against -ve
- Examples: Doripenem, Imipenem, Meropenem, Etrapenem.
- They resist hydrolysis by most B-lactamases.
- Carbapenems are active against P aeruginosa and Acinetobacter species (except ertapenem).
- These agents have a very broad spectrum of action and are usually restricted to use in hospitals for treatment of serious infections.

Other B-Lactam Antibiotics- Carbapenems

- All are cleared renally, and the dose must be reduced in patients with renal insufficiency.
- Excessive levels of imipenem in patients with renal failure may lead to seizures.
- Imipenem is formulated with cilastatin, which prevents hydrolysis of imipenem by renal dihydropeptidase.

by kidney

so we can extend the duration of action by blocking this enzyme

Glycopeptide Antibiotics -

- **Vancomycin**

Administered Oral , IV

Narrow spectrum(G+ ve)

Bactericidal /not B-lactam.

mechanism of action → inhibit cell wall synthesize in the bacteria however it doesn't bind to penicillin binding protein where the site B-Lactam bind

- **Orally:- every 6 hrs** for refractory pseudomembranous colitis due to C. difficile.

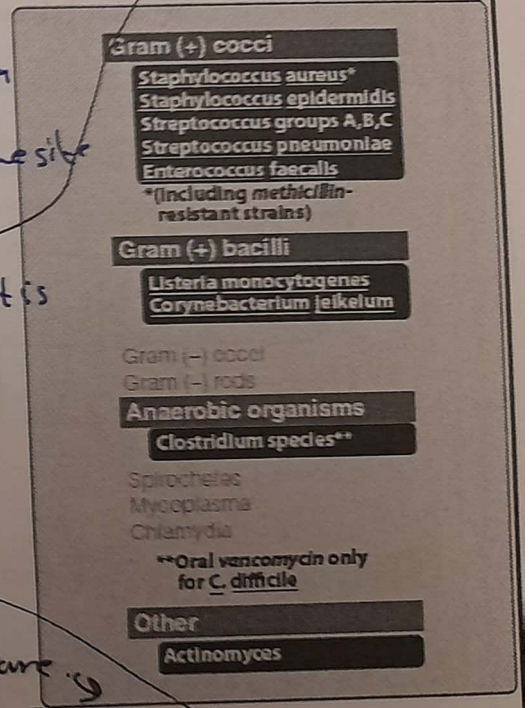
it is poorly absorbed orally however it is givin orally to treab local GIT infc

- **Slow IV infusion (1-2 hrs)** for treatment of systemic infections or prophylaxis.

- is effective against MRSA.(DOC) The drug of choice
- Vancomycin in combination with A.G alternative regimen to treatment of enterococcal endocarditis.

however the close adjusment is needed in renal failure because both are complicated with nephrotoxicity

- **Teicoplanin** is a glycopeptide antibiotic that is very similar to vancomycin in mechanism of action and antibacterial spectrum.



restricted for serious inf

both aerobic anaerobic

drug of choice

metronidazole

resistance

price

Vancomycin

MRSA resistant

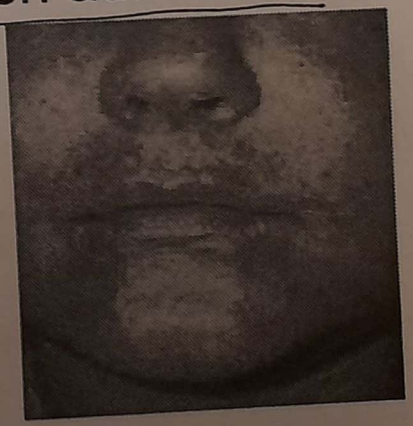
binding site

cephalo + penicillin

site
cephalo + penicillin

Vancomycin

- S.E:-
- 1-Flushing (**red man syndrome**) with a **rapid** infusion.(**More common**)
- Prevented by prolonging the infusion period OR pretreatment with an antihistamine such as diphenhydramine.
- 2- phlebitis(inflammation of vein) at site of injection.
- 3- ototoxicity & nephrotoxicity (rare) but increased risk when administered with A.G.



Other Cell wall synthesis inhibitors

+ daptomycin + Linazolide

Fosfomycin :

- **Therapeutic use :** It is indicated for urinary tract infections caused by E. coli or E. faecalis.
- Rapidly absorbed after oral administration & distributes well to the kidneys, bladder, and prostate

لعلاج prostatitis

Bacitracin → for topical use

- It is highly nephrotoxic when administered systemically and is only used topically

→ used in hospitals (resistance تقل)

Other Cell wall synthesis inhibitors

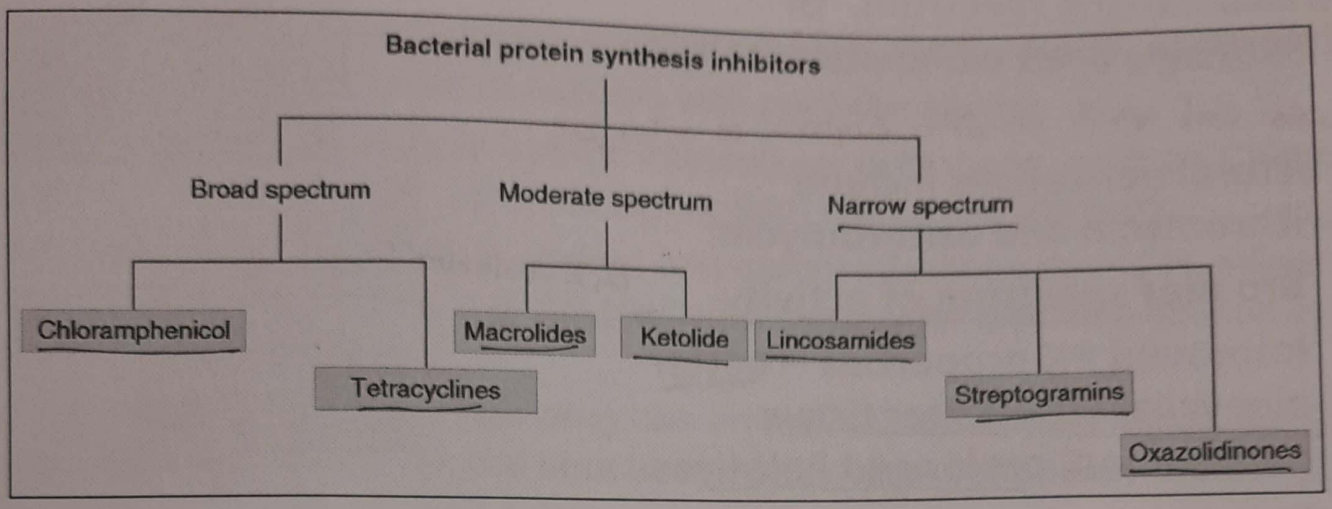
Daptomycin – is a new lipopeptide antibacterial drug.

- **Therapeutic use:**
- for treating infections caused by resistant gram-positive organisms, including MRSA and *vancomycin* resistant enterococci (VRE)
- is indicated for the treatment of complicated skin and skin structure infections and bacteremia caused by S. aureus,

- **Adverse effect :**

Myopathy and creatine phosphokinase levels elevation.

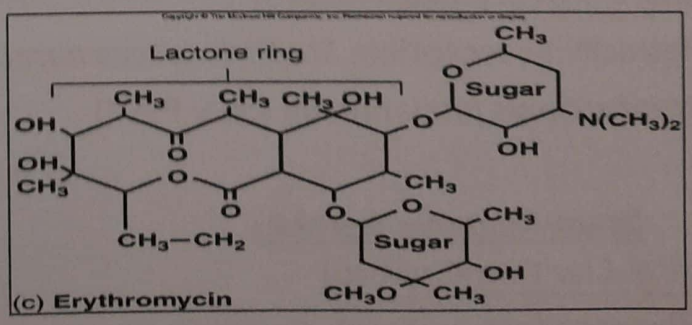
Protein Synthesis Inhibitors



Large lacton ring ← (macro) lo ide ring

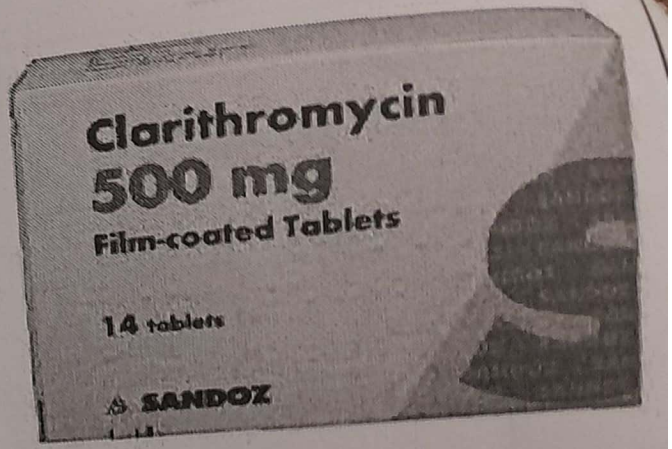
I. Macrolides

- Generally bacteriostatic
- Their names end in "romycin" and mostly in "thromycin"

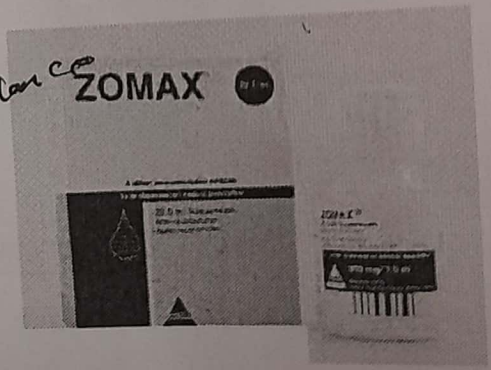


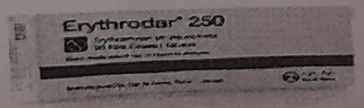
Macrolides

- **Erythromycin**– problems with acid liability, narrow spectrum, GI intolerance, short elimination half-life



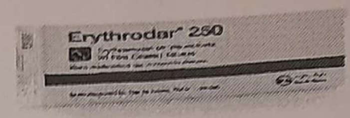
- Structural derivatives include **clarithromycin** and **azithromycin:**
  - **Broader spectrum of activity**
  - **Improved PK properties** – better bioavailability, better tissue penetration, prolonged half-lives
  - **Improved tolerability**





penetration, prolonged half-lives

- Improved tolerability



*هدول بغطو gram (+ , −) مع انه ما في اختلاف بال spectrum بس في

Macrolides Spectrum of Activity

عادة ال macrolid بغطو ال aerobic
+ anaerobic لكن عادة ال macrolide بغطو
ال aerobic اكثر

Anaerobes – activity against upper airway anaerobes

Atypical Bacteria – all macrolides have **excellent** activity against atypical bacteria including:

- *Legionella pneumophila*
- *Chlamydia sp.*
- *Mycoplasma sp.*

اكثر اشي بميز ال macrolide

* عادة اكثر اشي استخداما لل upper respi ← azithromycin
caused by mycobacteria
استخدموه بكورونا لانه حسوا انه ال anti-inflam.
* بيفيد لل atypicals ← بنستخدم ال erythromycin

Gram-Positive Aerobes – erythromycin and clarithromycin display the best activity

(Clarithro>Erythro>Azithro)

Methicillin-susceptible *Staphylococcus aureus*

Streptococcus pneumoniae (only PSSP)

Gram-Negative Aerobes

(Azithro>Clarithro>Erythro)

H. influenzae (not erythro), *Neisseria sp.*