



# Cell Wall Inhibitors

Pharmacology and Toxicology

General Pharmacology

Second Year Medical Students

Tareq Saleh, MD, PhD

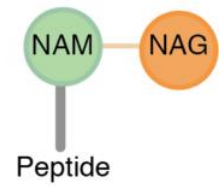
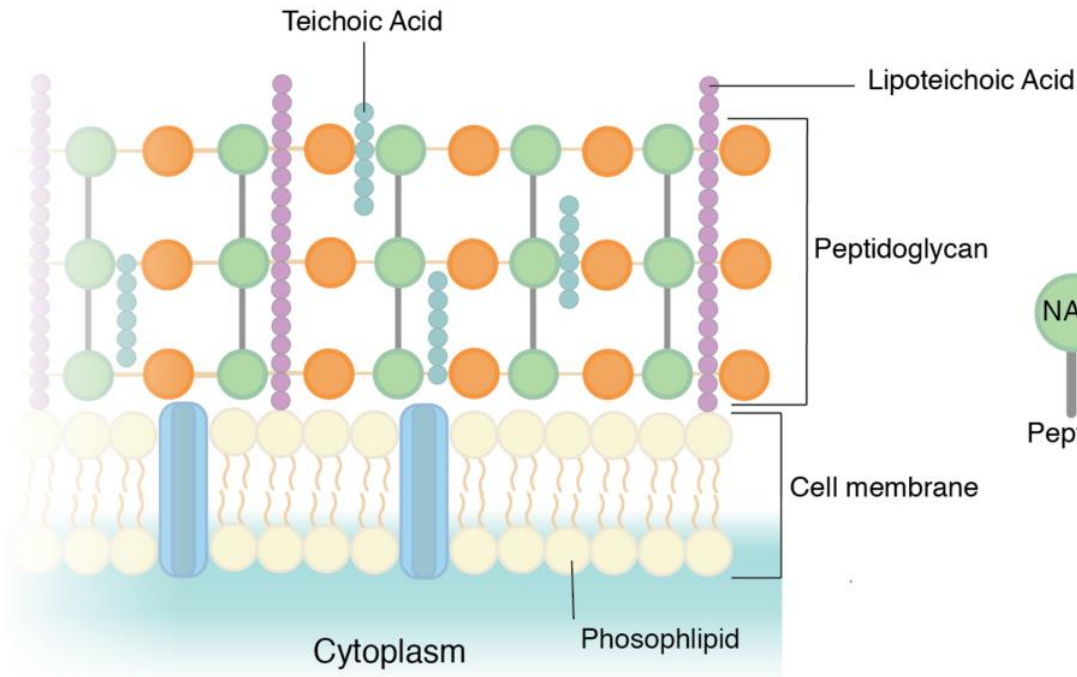
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The Hashemite University

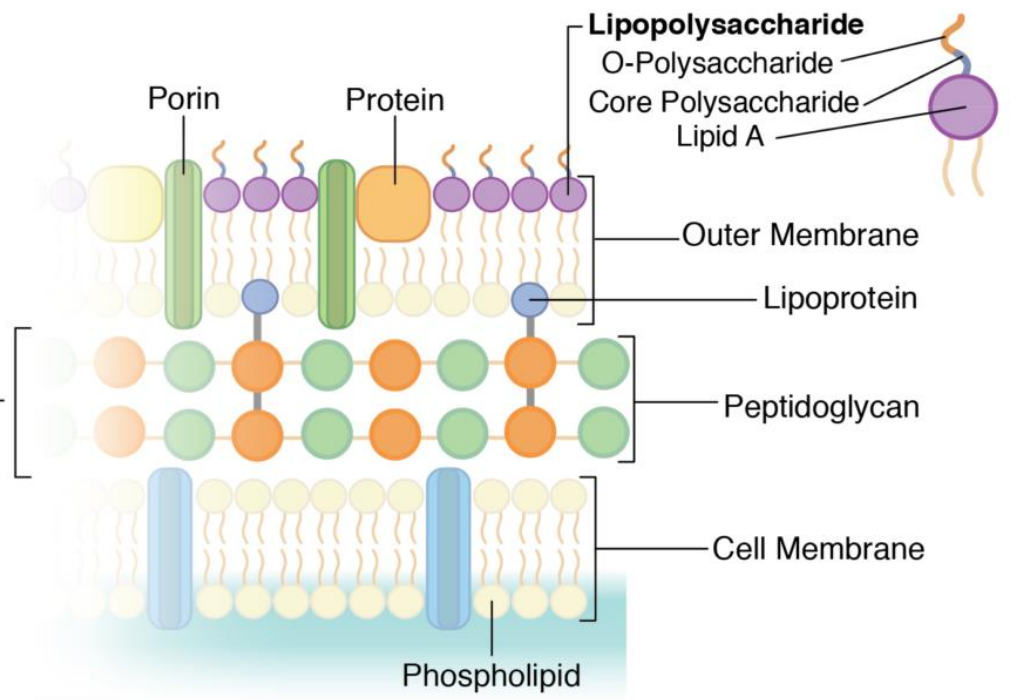
**Textbook:** Chapter 29 pp 369- 383



# Overview: Bacterial Cell Wall



Gram Positive Bacteria Cell Wall



Gram Negative Bacteria Cell Wall



# Overview: Synthesis of Bacterial Cell Wall

## 1. Cytoplasmic Stage:

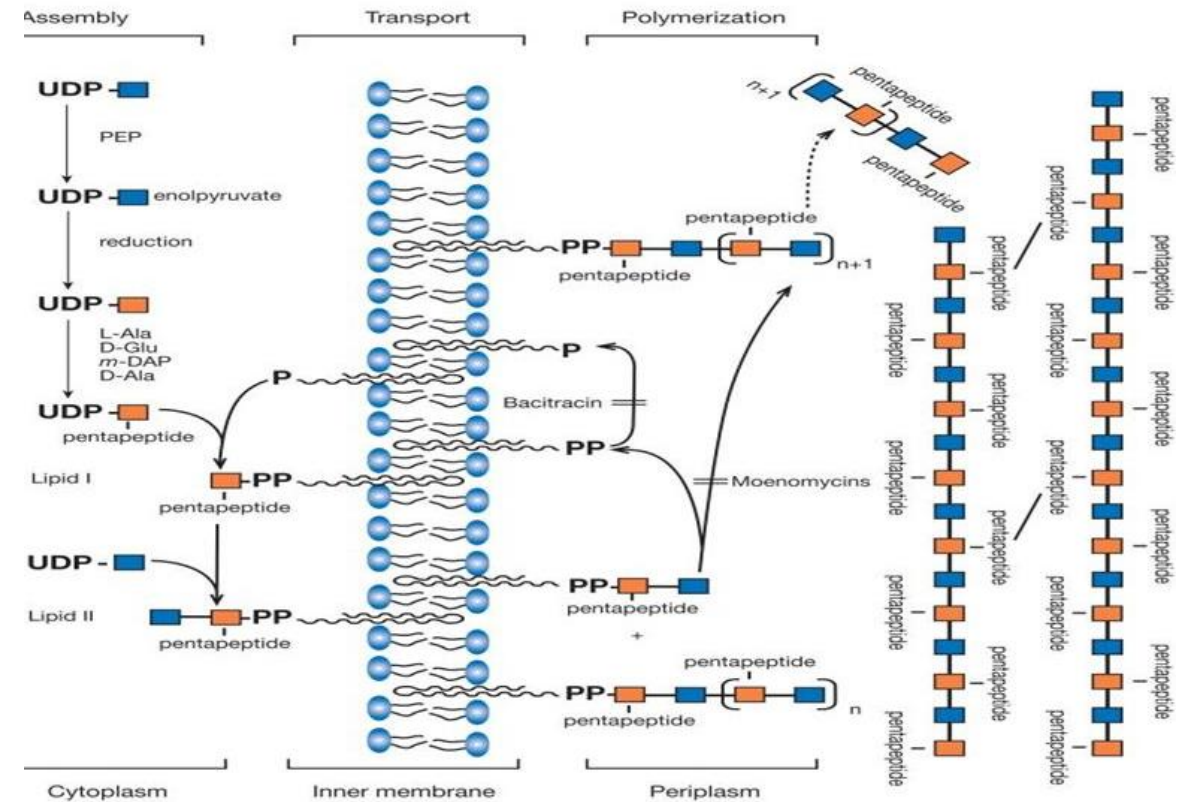
- Synthesis of glycan precursors:  
UDP-MurNAC-pentapeptide,  
UDP-GlcNAC

## 2. Cytoplasmic membrane Stage:

- Transfer to membrane receptors

## 3. Extracellular membrane stage:

- Transpeptidation via PBP





# Penicillins

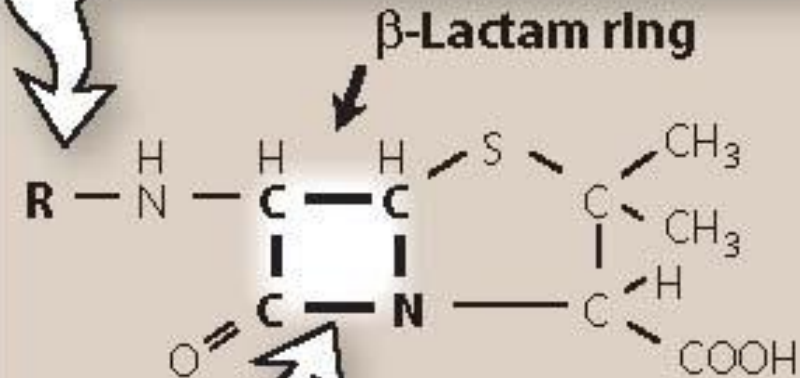


# Penicillins

## PENICILLINS

*Amoxicillin* AMOXIL  
*Ampicillin* PRINCIPEN  
*Dicloxacillin* DYNAPEN  
*Nafcillin*  
*Oxacillin*  
*Penicillin G* PFIZERPEN  
*Penicillin V*  
*Piperacillin*  
*Ticarcillin*

Nature of the R group determines the drug's stability to enzymatic or acidic hydrolysis and affects its antibacterial spectrum.



6-Aminopenicillanic acid

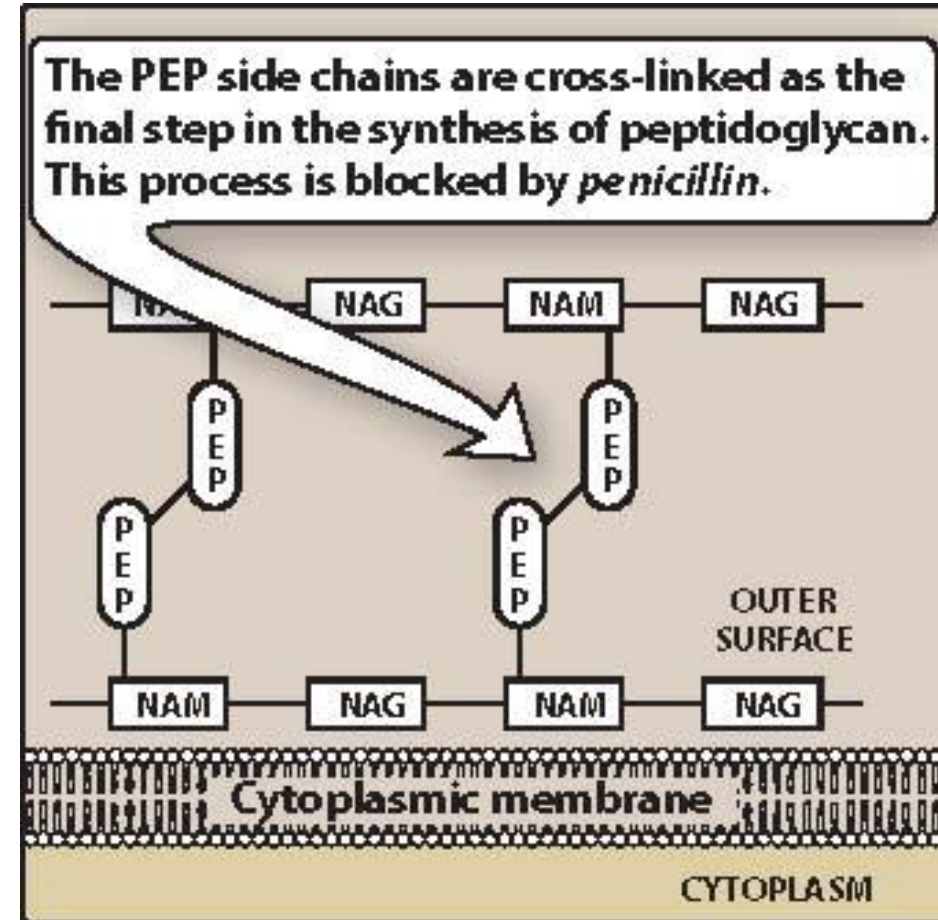
Site of hydrolysis by bacterial penicillinase or by acid.



# Quick Microbiology Reminder

## Penicillin-binding proteins:

- Penicillins bind and inactivate bacterial cell membrane proteins called: penicillin-binding proteins (PBPs).
- Bacterial enzymes involved in cell wall synthesis
- Variable among different species
- Involved in resistance

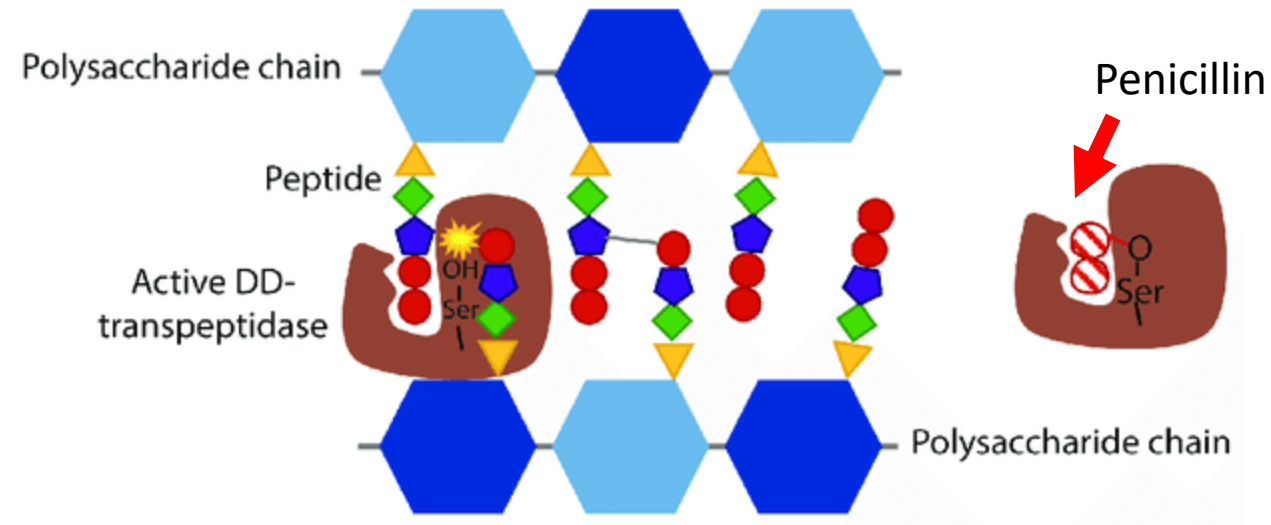




# Penicillins

## Mechanism of action

- Inhibit transpeptidation or cross-linkage (*last step* of bacterial wall synthesis)
- Prevent cross-linking catalyzed by the PBP transpeptidase



*What is the basis of selective toxicity?*



# Penicillins

**What are the *consequences of transpeptidation inhibition?***

- Bacterial cell lysis
- Bactericidal
- Time-dependent
- Effective against rapidly growing bacteria



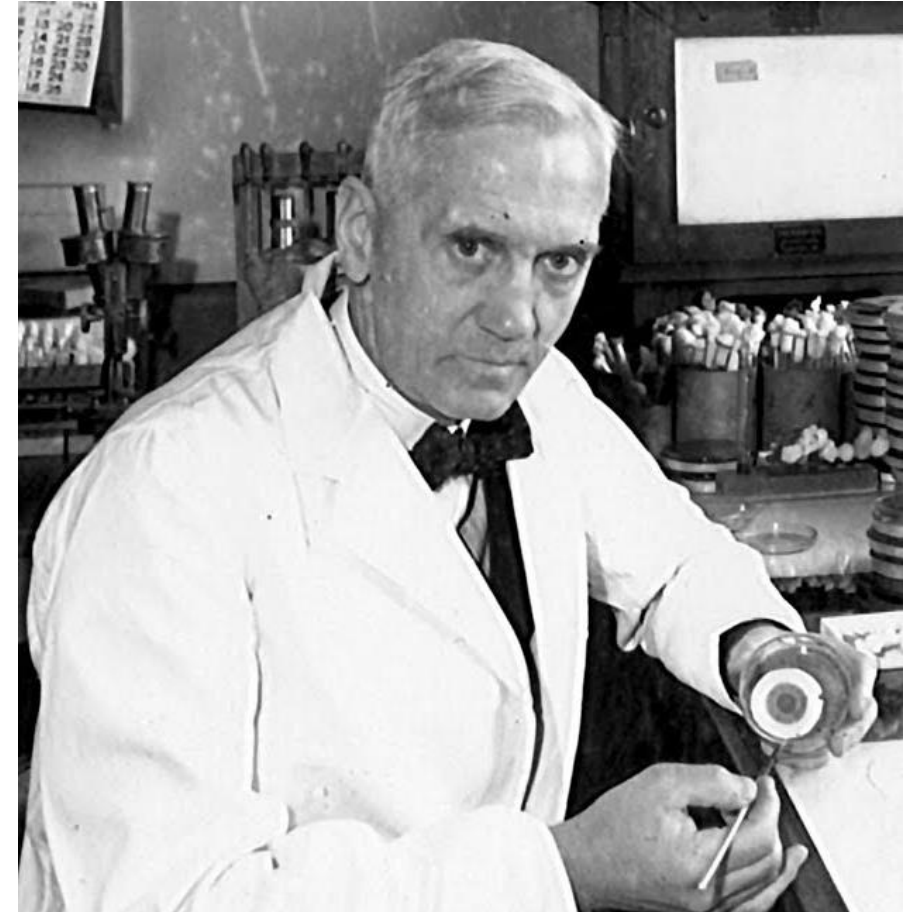


# Penicillins

## Antibacterial spectrum

### 1. Natural penicillins:

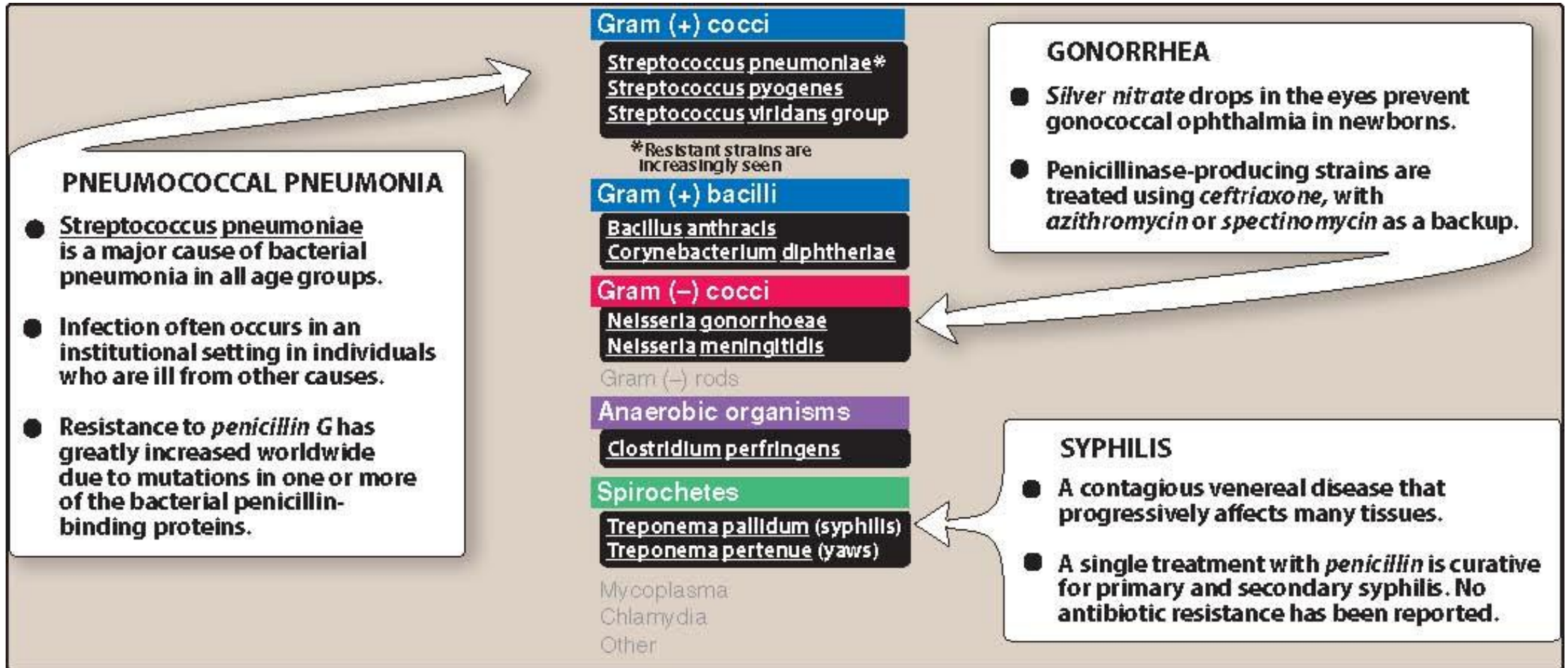
- Penicillin G, Penicillin V: *Penicillium chrysogenum*
- Drugs of choice for the treatment of **gas gangrene** (*Clostridium perfringens*) and **syphilis** (*Treponema pallidum*).
- Penicillin V is the oral form of penicillin





# Penicillins

## Antibacterial spectrum





# Penicillins

## Antibacterial spectrum:

### 2. Extended-spectrum penicillins:

- Semisynthetic: ampicillin, amoxicillin
- Spectrum: extended to include gram-negative bacilli

❑ Ampicillin: **drug of choice** for gram-positive bacillus *L. monocytogenes*

**\*\*Also for enterococci, resp infections**

❑ Amoxicillin: Ear, nose, and throat infections, dental prophylaxis

### A. Antimicrobial spectrum of ampicillin

Gram (+) cocci

Enterococci

Gram (+) bacilli

*Listeria monocytogenes*

Gram (-) cocci

Gram (-) rods

*Escherichia coli*

*Haemophilus influenzae*

*Proteus mirabilis*

*Salmonella typhi*

Anaerobic organisms

Spirochetes

Mycoplasma

Chlamydia

Other



# Penicillins

## Antibacterial spectrum:

### 2. Extended-spectrum penicillins:

- Combined with  $\beta$ -lactamase inhibitors

*e.g., MSSA is resistant to ampicillin and amoxicillin IF given without a  $\beta$ -lactamase inhibitors*

#### A. Antimicrobial spectrum of ampicillin

Gram (+) cocci

Enterococci

Gram (+) bacilli

Listeria monocytogenes

Gram (-) cocci

Gram (-) rods

Escherichia coli

Haemophilus influenzae

Proteus mirabilis

Salmonella typhi

Anaerobic organisms

Spirochetes

Mycoplasma

Chlamydia

Other



# Penicillins

## Antibacterial spectrum

### 3. Antistaphylococcal penicillins:

- Methicillin, nafcillin, oxacillin, dicloxacillin
- Effective against penicillinase-producing staphylococci (MSSA)
- Minimal activity against gram-negative
- Methicillin not used clinically (toxic)





# Penicillins

## Antibacterial spectrum:

### 4. Antipseudomonal penicillins:

- Piperacillin
- Effective against gram-negative bacilli (but not against *Klebsiella*)
- Common combinations:

**Piperacillin + tazobactam**

## B. Antimicrobial spectrum of ticarcillin and piperacillin

Gram (+) cocci  
Gram (+) bacilli  
Gram (-) cocci

### Gram (-) rods

**Enterobacter species**  
**Escherichia coli**  
**Proteus mirabilis**  
**Proteus (indole positive)**  
**Haemophilus influenzae**  
**Pseudomonas aeruginosa**

Gram (-) rods  
Anaerobic organisms  
Spirochetes  
Mycoplasma  
Chlamydia  
Other

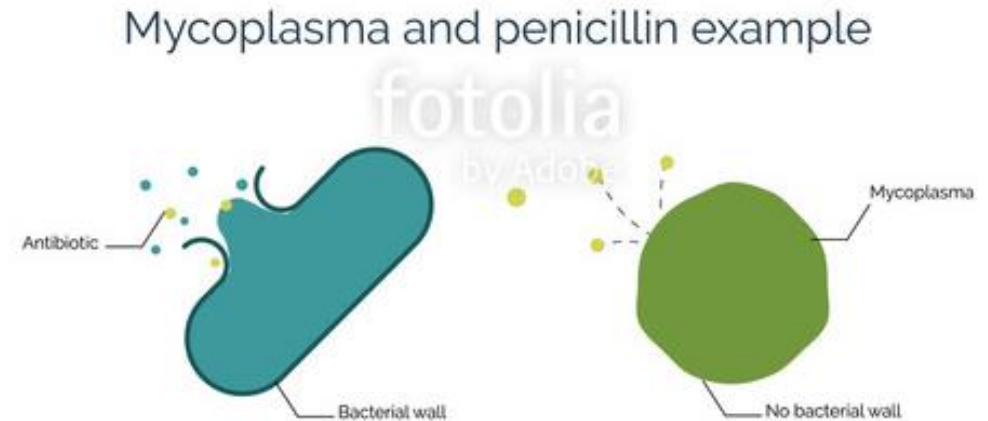


# Penicillins

## Mechanisms of resistance

- **Intrinsic Resistance:**

- Microorganisms that lack peptidoglycans cell walls e.g., *M. pneumoniae*
- Microorganisms that have impermeable cell walls



#107592263



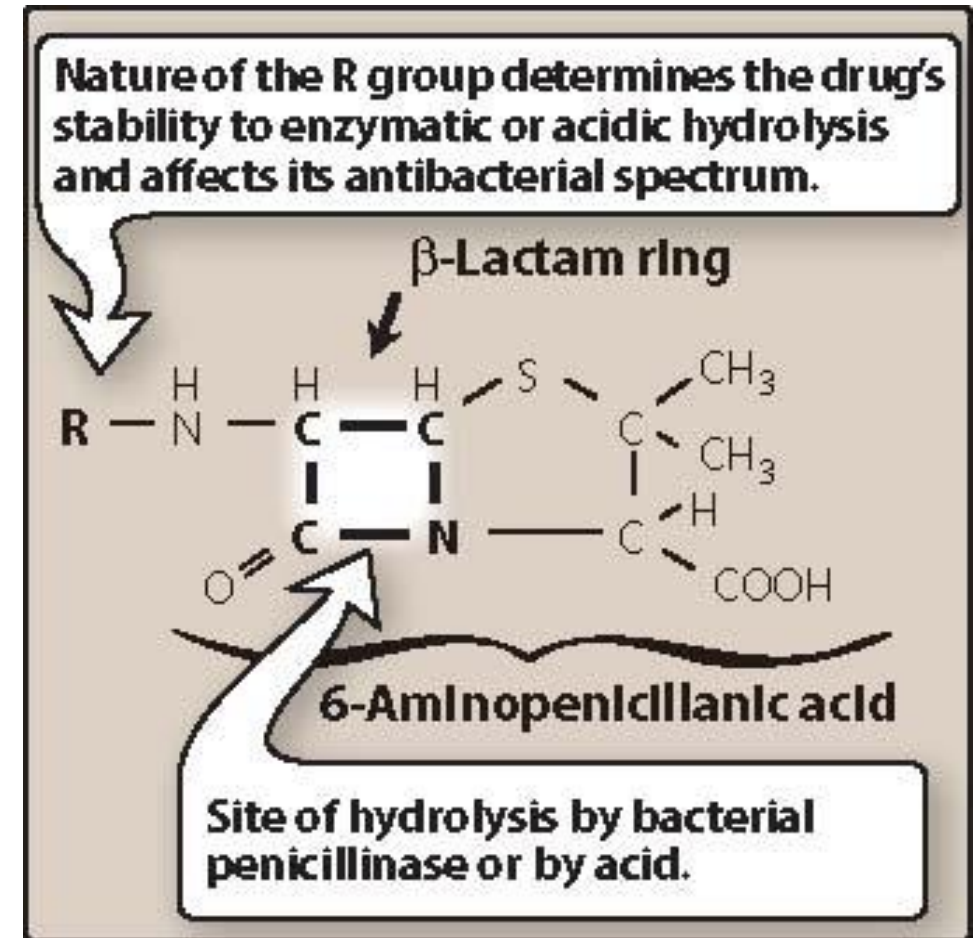
# Penicillins

## Mechanisms of resistance

### • Acquired Resistance:

#### 1. $\beta$ -Lactamase activity:

- Enzymes that hydrolyze the cyclic amide bond of the  $\beta$ -lactam ring
- Mostly acquired (plasmids)
- **Gram-positive**: secrete  $\beta$ -lactamases extracellularly
- **Gram-negative**: periplasmic  $\beta$ -lactamases



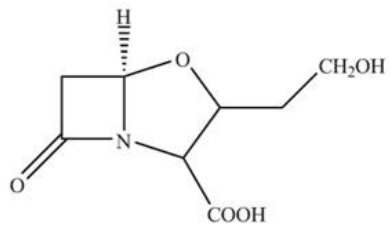




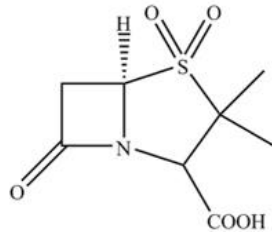
Production of  $\beta$ -Lactamases is the main resistance mechanism against  $\beta$ -Lactams.

How is this problem solved?

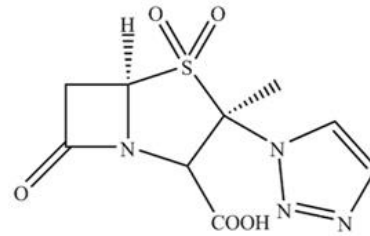
# $\beta$ -Lactamase Inhibitors



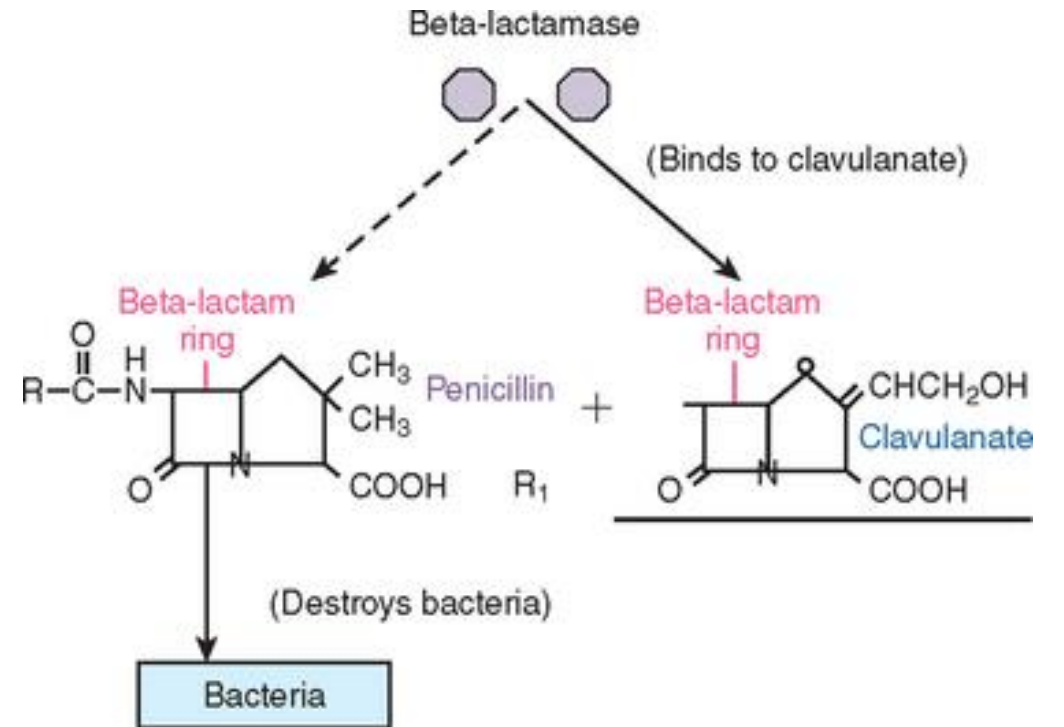
Clavulanic acid



Sulbactam



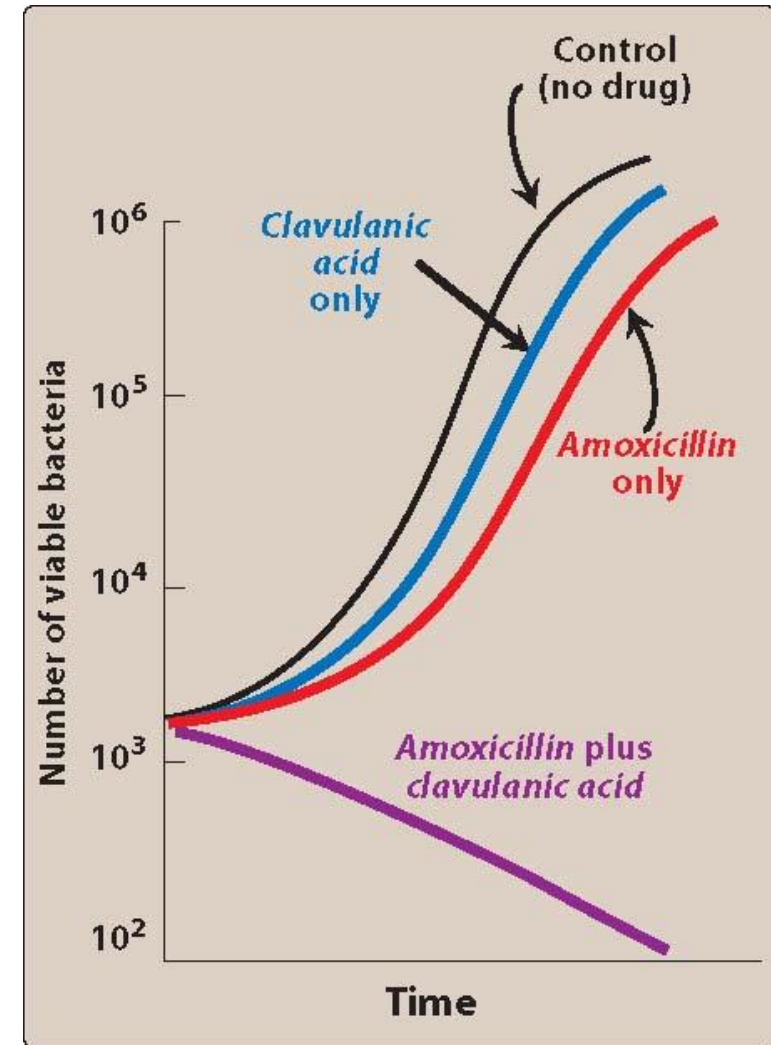
Tazobactam





# $\beta$ -Lactamase Inhibitors

- Contain  $\beta$ -Lactam rings
- BY THEMSELVES, no antibacterial activity
- Protect antibiotics that are normally substrates for  $\beta$ -Lactamases
- Example.....?



The in vitro growth of Escherichia coli in the presence of amoxicillin, with and without clavulanic acid.



# Penicillins

## Mechanisms of resistance

- **Acquired Resistance:**

- 2. Decreased permeability to the drug:**

- Reduced permeability e.g., *Pseudomonas aeruginosa*
- Efflux pump e.g., *Klebsiella pneumoniae*.

- 3. Altered PBPs:**

- Modified PBPs with lower affinity for  $\beta$ -lactams e.g., MRSA resistance to most  $\beta$ -lactams.

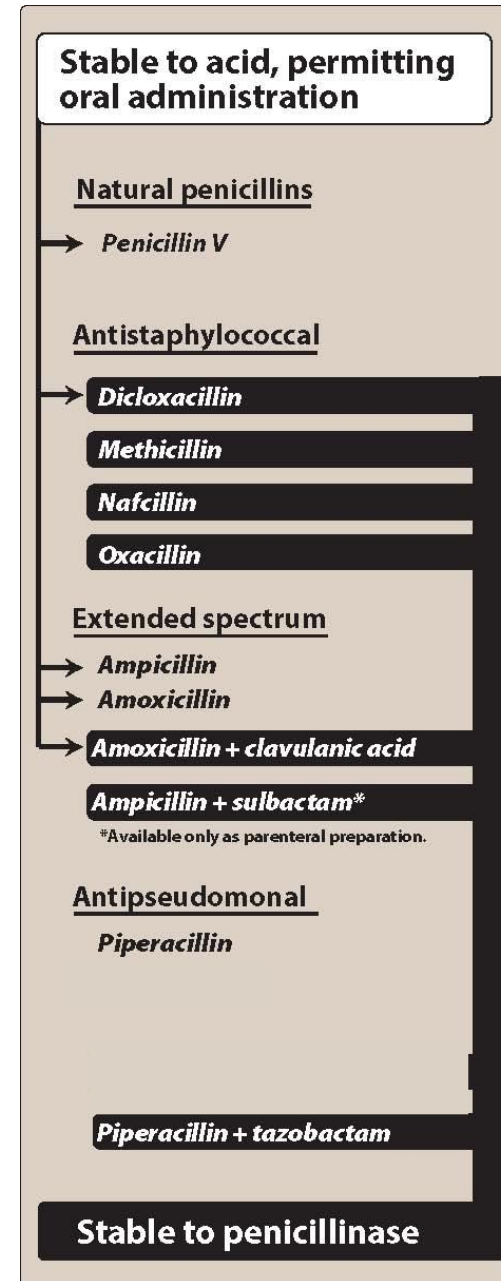


# Penicillins

## 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)





# Penicillins

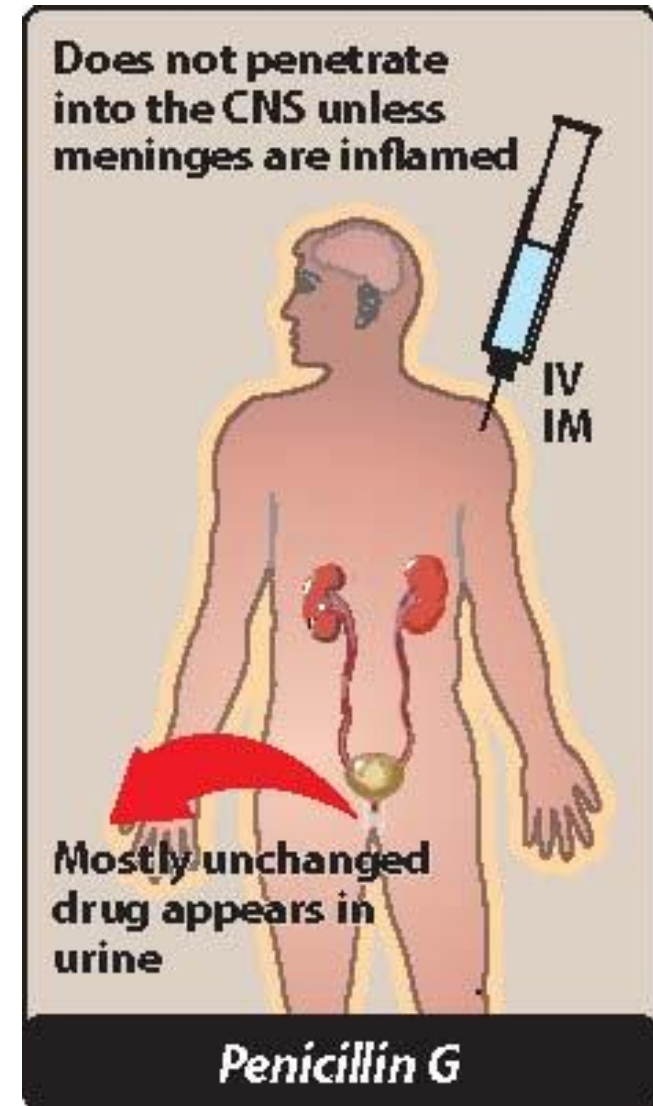
## Pharmacokinetics

- **Absorption**

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

- **Distribution**

- Good distribution e.g., cross placenta (but no teratogenic effect)
- Insufficient penetration to bone or CSF (unless inflamed)





# Penicillins

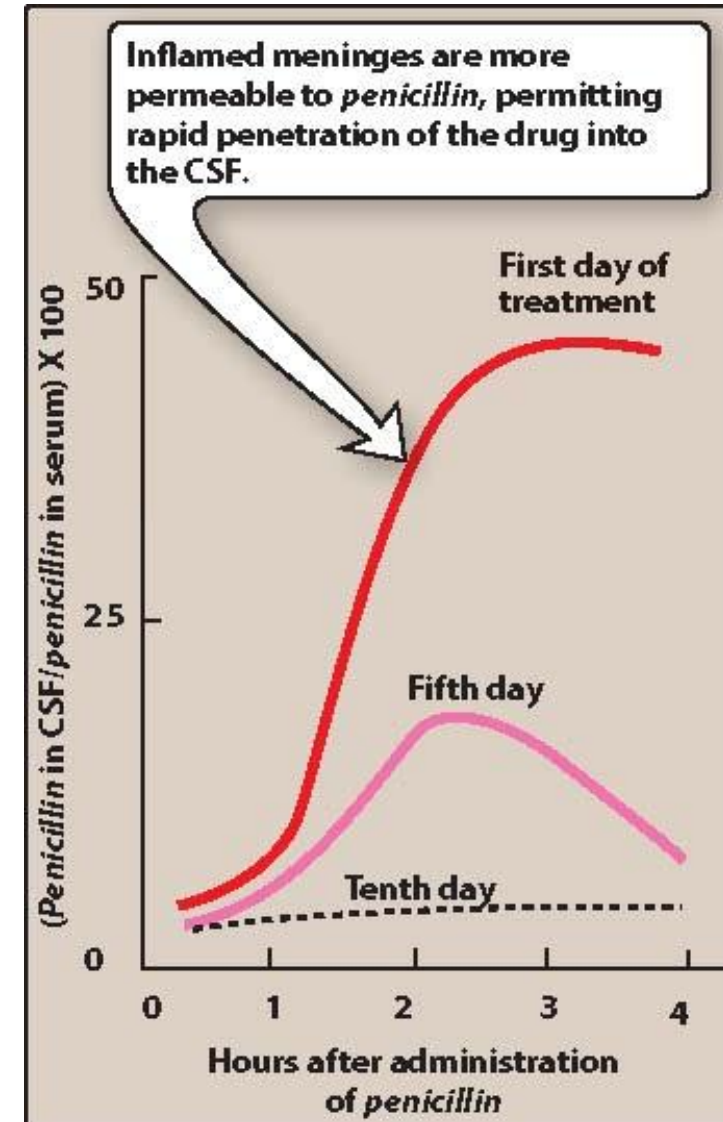
## Pharmacokinetics

### • Absorption

- Most penicillins are incompletely absorbed after oral administration
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# Penicillins

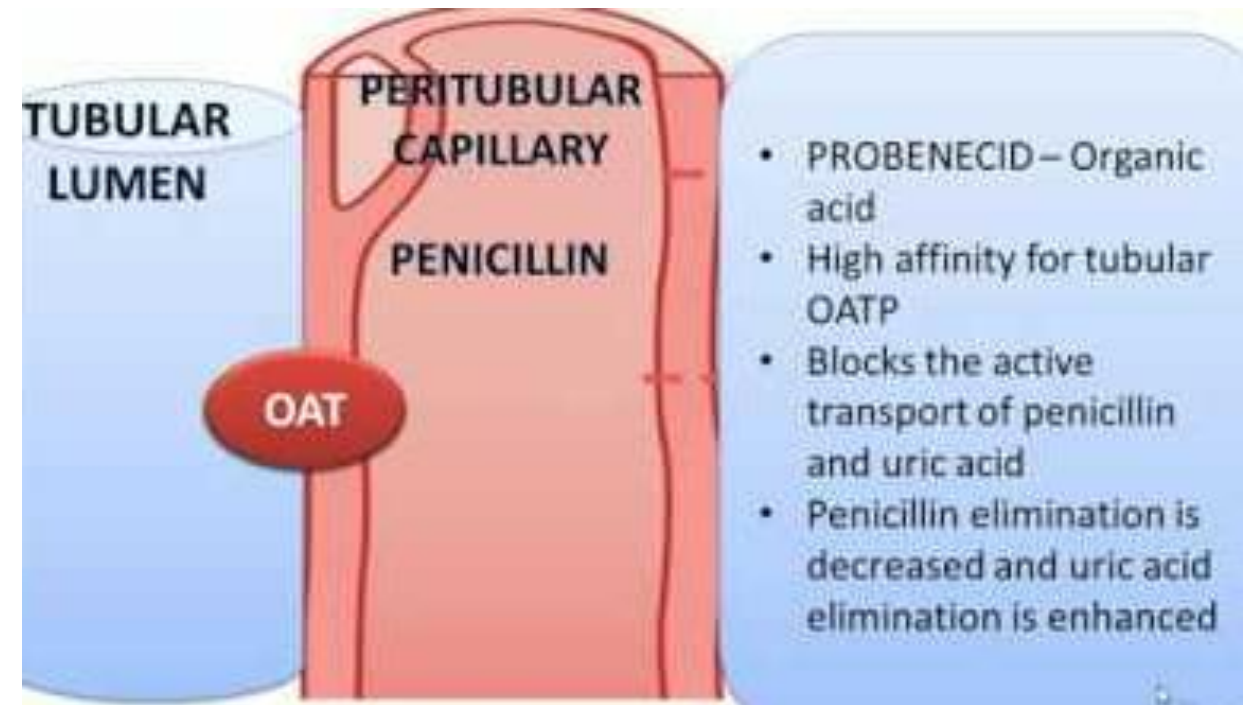
## Pharmacokinetics

- **Metabolism**

- Insignificant metabolism
- Exceptions?

- **Excretion:**

- Renal: tubular secretory system
- *Probenecid* is an inhibitor of renal tubular excretion of penicillin







# Penicillins

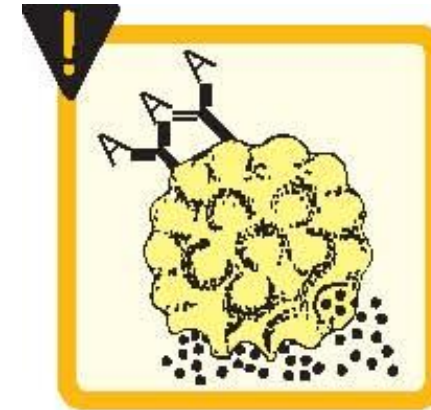
## Adverse effects

### 1. Hypersensitivity:

- 5-10% percent of patients (simple rash to angioedema to anaphylaxis)
- Cross-allergy
- Always inquire about penicillin allergy

### 2. Diarrhea:

- Caused by intestinal flora imbalance
- More with extended-spectrum agents



Hypersensitivity



Diarrhea



# Penicillins

## Adverse effects

### 3. Nephritis:

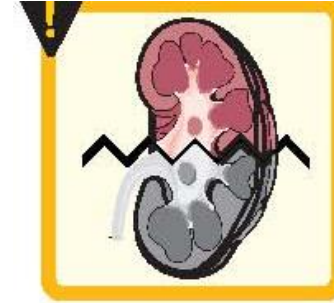
- Methicillin: no longer used because of this

### 4. Neurotoxicity:

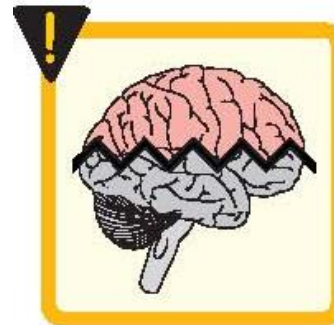
- If injected intrathecally

### 5. Hematological toxicities

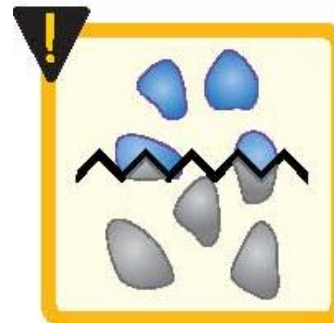
- Decreased coagulation
- Cytopenias



Nephritis



Neurotoxicity



Hematologic toxicities



# Quick Revision

- Name a penicillin that is effective against penicillinase-producing *S. aureus* (MSSA)? \_\_\_\_\_
  
- Name a penicillin that is effective against penicillinase-producing *S. aureus* (MRSA)? \_\_\_\_\_

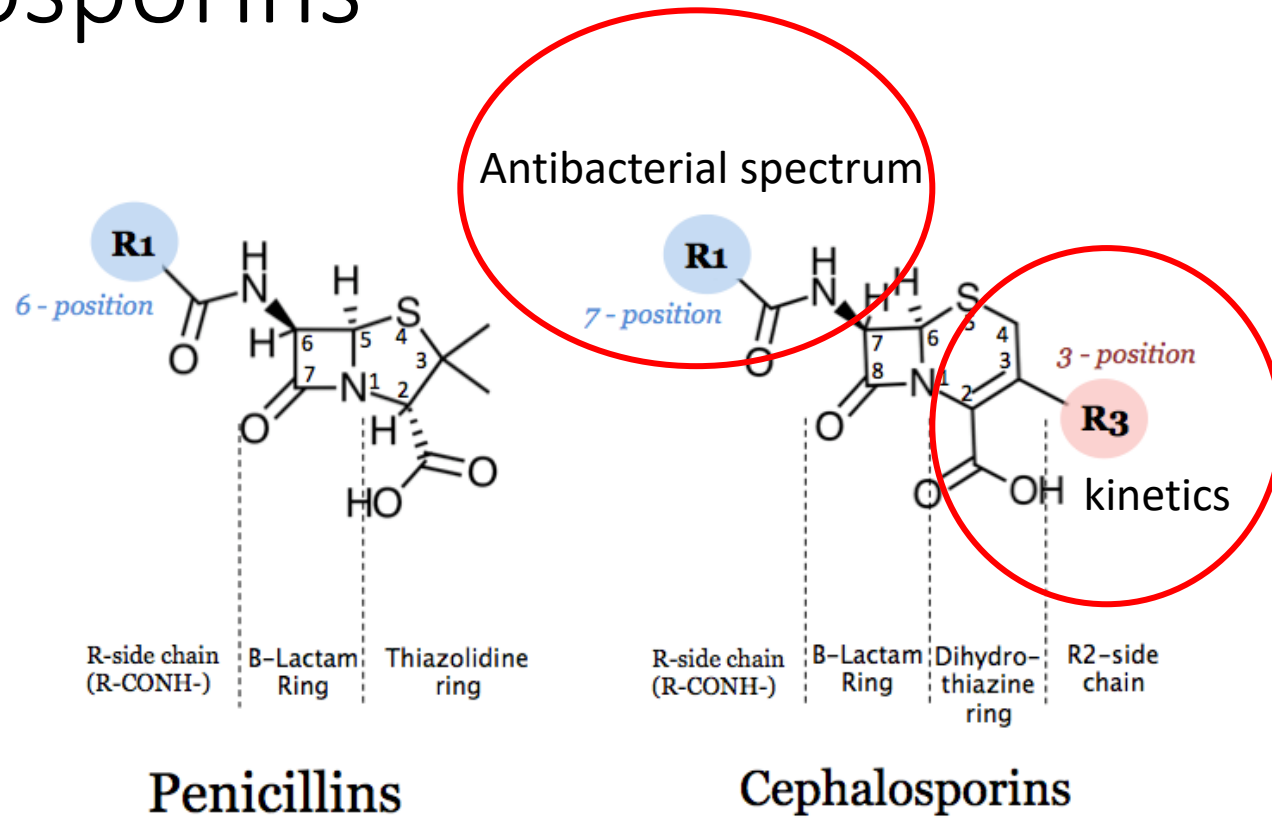


# Cephalosporins



# Cephalosporins

- $\beta$ -lactams
- Structurally/functionally related to penicillins
- Semisynthetic
- More resistant to certain  $\beta$ -lactamases





# 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

- **First-generation cephalosporins:**
  - penicillin G substitutes
  - They cover MSSA (resistant to penicillinase) but not MRSA

Cefazolin

Cephalexin

cefadroxil

### 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



# Cephalosporins

## 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





# Cephalosporins

## Antibacterial spectrum

- **Third-generation cephalosporins:**
  - Greater activity against gram-negative bacilli (broad-spectrum)
  - Drugs of choice for the treatment of meningitis
  - Must be used with caution “collateral damage”

Ceftriaxone

Cefotaxime

Ceftazidime

Cefdinir

## 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



# Cephalosporins

## Antibacterial spectrum

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

**Cefepime**

Tareq Saleh ©

## Antibacterial spectrum

- **Advanced-generation cephalosporins:**
  - Broad-spectrum
  - Only  $\beta$ -lactam that is active against MRSA
  - Indicated for complicated skin MRSA infections and pneumonia
  - How about pseudomonas? ESBL?
  - *What are the limitations for using ceftaroline?*

**Ceftaroline**

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# Quick Exercise

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

- amoxicillin
- ampicillin
- amoxicillin/clavulanate
- cefazolin
- cephalexin
- ceftriaxone
- cefepime
- ceftaroline



# Cephalosporins

## Mechanisms of resistance

- Similar to penicillins

Susceptible to

Penicillinases (*staph*)

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

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*



# Cephalosporins

## Pharmacokinetics

- **Administration:**

- Poor oral absorption, mostly given IV, IM

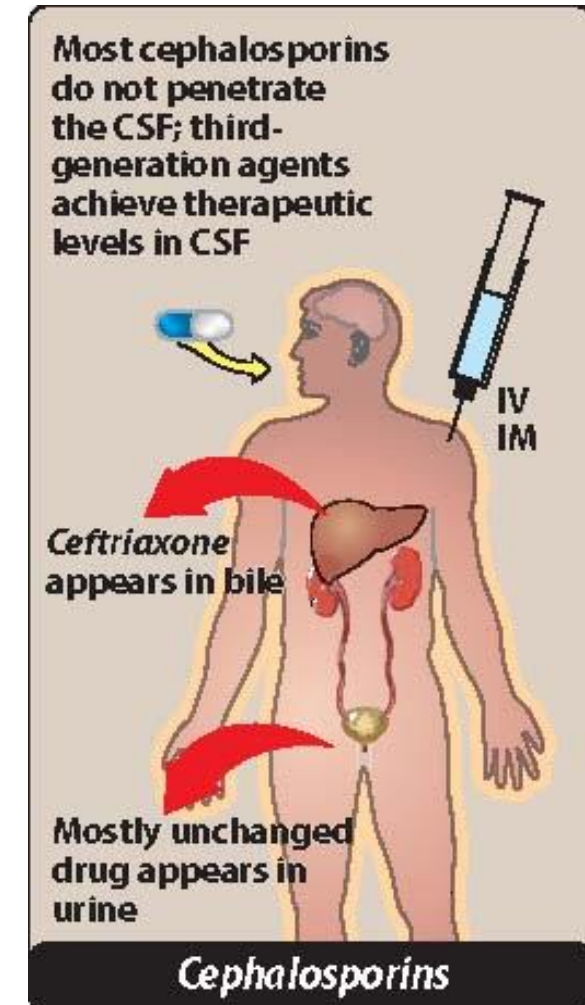
- **Distribution:**

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

- cefazolin can penetrate bone

- **Elimination:**

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





# Cephalosporins

## Adverse effects

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





## 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  $\beta$ -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*.



# Other $\beta$ -Lactams





# Carbapenems

## CARBAPENEMS

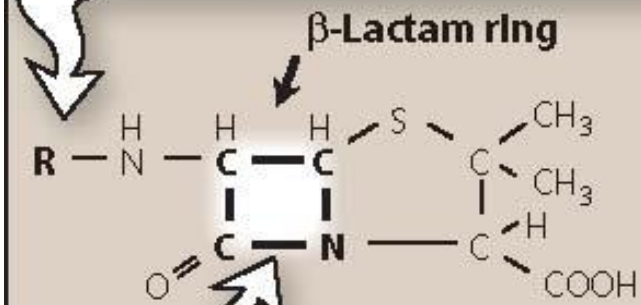
*Doripenem* DORIBAX

*Ertapenem* INVANZ

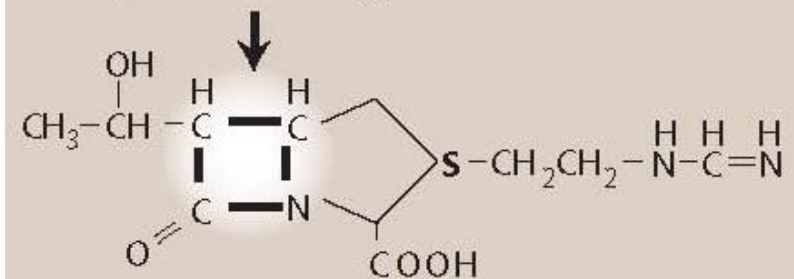
*Imipenem/cilastatin* PRIMAXIN

*Meropenem* MERREM

Nature of the R group determines the drug's stability to enzymatic or acidic hydrolysis and affects its antibacterial spectrum.



$\beta$ -Lactam ring



*Imipenem*  
(a carbapenem)



# Carbapenems

## Antibacterial spectrum

- Broad-spectrum (used for empiric therapy)
- Resist  $\beta$ -lactamases
- Effective against  $\beta$ -lactamase-producing gram-positive and gram-negative organisms, anaerobes, and *P. aeruginosa*

<b>Gram (+) cocci</b>
<u>Staphylococcus aureus*</u> <u>Staphylococcus epidermidis</u> <u>Enterococcus faecalis</u> <u>Streptococcus groups A, B, C</u> <u>Streptococcus pneumoniae</u>
<small>*Methicillin-resistant staphylococci are resistant</small>
<b>Gram (+) bacilli</b>
<u>Listeria monocytogenes</u>
<small>Spirochetes Mycoplasma Chlamydia</small>
<b>Other</b>
<u>Actinomyces</u> <u>Nocardia species</u>

<b>Gram (-) cocci</b>
<u>Neisseria gonorrhoeae**</u> <u>Neisseria meningitidis</u>
<small>**including penicillinase-producing strains</small>
<b>Gram (-) rods</b>
<u>Acinetobacter species</u> <u>Citrobacter species</u> <u>Enterobacter species</u> <u>Escherichia coli</u> <u>Gardnerella vaginalis</u> <u>Haemophilus influenzae</u> <u>Klebsiella species</u> <u>Proteus species</u> <u>Providencia species</u> <u>Pseudomonas aeruginosa</u> <u>Salmonella species</u> <u>Serratia species</u>

\*Not MRSA

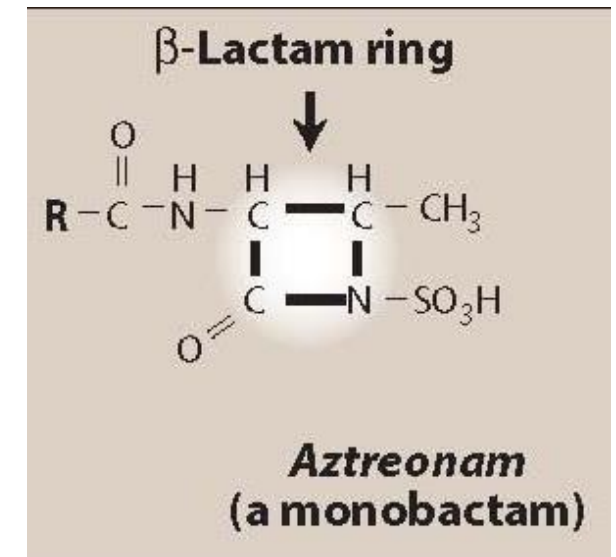
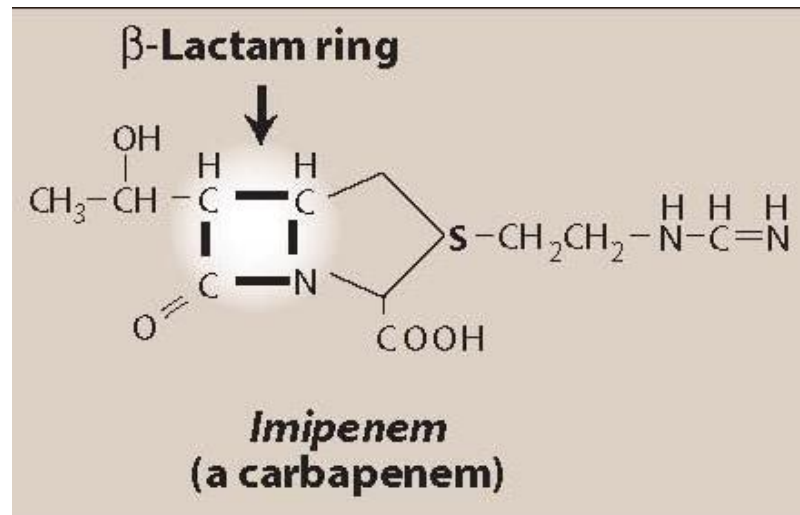


# Monobactams

## MONOBACTAMS

*Aztreonam* AZACTAM

- Effective against gram-negative (including *P. aeruginosa*)
- Lacks activity against gram-positive
- Susceptible to ESBLs
- Relatively non-toxic
- little cross-reactivity with other  $\beta$ -lactams





# Can Cephalosporins and Carbapenems Be Combined with $\beta$ -lactamase inhibitors?

- Ceftolozane + tazobactam: used for multidrug resistant *P. aeruginosa* and some ESBLs-producing bacteria
- Ceftazidime + avibactam: used against ESBL-producing bacteria  
\*\*\*both indicated for the management of complicated intra-abdominal and urinary tract infections caused by multidrug resistant bacteria
- Meropenem + vaborbactam: used against ESBL-producing bacteria  
\*\*\*indicated for the management of complicated urinary tract infections



# Vancomycin

- tricyclic glycopeptide
- **What is the mechanism of action of vanco?**
- Effective against gram-positive bacteria INCLUDING MRSA and MRSE
- Oral and IV
- IV vanco used in patients with MRSA skin infections, infective endocarditis, ....
- Oral vanco used for severe antibiotic associated pseudomembranous colitis
- Vanco is not absorbed after oral administration

## Gram (+) cocci

**Staphylococcus aureus\***  
**Staphylococcus epidermidis**  
**Streptococcus groups A,B,C**  
**Streptococcus pneumoniae**  
**Enterococcus faecalis**

\*(including *methicillin*-resistant strains)

## Gram (+) bacilli

**Listeria monocytogenes**  
**Corynebacterium jeikeium**

Gram (-) cocci

Gram (-) rods

## Anaerobic organisms

**Clostridium species\*\***

Spirochetes

Mycoplasma

Chlamydia

\*\*Oral *vancomycin* only for C. difficile

## Other

**Actinomyces**



# Vancomycin

- Bactericidal
- Time- and concentration-dependent

**Homework:** What is the best predictor of vancomycin's antistaph activity?

## **Adverse effects**

- Nephrotoxicity
- Red man syndrome
- Ototoxicity

## **Mechanisms of resistance:**

- Alteration in binding affinity to peptidoglycan precursors



# Daptomycin

- cyclic lipopeptide
- bactericidal
- concentration-dependent
- Effective against gram-positive INCLUDING MRSA vancomycin-resistant enterococci (VRE)
- Not used for pneumonia. **WHY?**

Gram (+) cocci
<u>Enterococcus faecalis</u> <u>Enterococcus faecium</u> <u>Staphylococcus aureus</u> (MRSA and MSSA) <u>Streptococcus pneumoniae</u> (penicillin resistant) <u>Streptococcus pyogenes</u>
Gram (+) bacilli
<u>Corynebacterium jeikeium</u>
Gram (-) cocci
Gram (-) rods
Anaerobic organisms
Spirochetes
Mycoplasma
Chlamydia
Other



	<b>VANCOMYCIN</b>	<b>DAPTOMYCIN</b>
<b>Mechanism of Action</b>	Inhibits bacterial cell wall synthesis	Causes rapid depolarization of the cell membrane, inhibits intracellular synthesis of DNA, RNA, and protein
<b>Pharmacodynamics</b>	Combination of time and concentration-dependent Bactericidal	Concentration dependent Bactericidal
<b>Common Antibacterial Spectrum</b>	Activity limited to gram-positive organisms: <u>Staphylococcus aureus</u> (including MRSA), <u>S. agalactiae</u> , penicillin-resistant <u>S. pneumoniae</u> , <u>Corynebacterium jeikeium</u> , <u>vancomycin-resistant E. faecalis</u> , and <u>E. faecium</u>	
<b>Unique Antibacterial Spectrum</b>	<u>Clostridium difficile</u> (oral only)	<u>Vancomycin-resistant E. faecalis</u> and <u>E. faecium</u> (VRE)
<b>Route</b>	IV/PO	IV





	VANCOMYCIN	DAPTOMYCIN
<b>Typical Administration Time</b>	60- to 90-minute IV infusion	2-minute IV push 30-minute IV infusion
<b>Pharmacokinetics</b>	Renal elimination Normal half-life: 6–10 hours Dose is adjusted based on renal function and serum trough levels	Renal elimination Normal half-life: 7–8 hours Dose is adjusted based on renal function
<b>Unique Adverse Effects</b>	Infusion related reactions due to histamine release: Fever, chills, phlebitis, flushing (red man syndrome); dose-related ototoxicity and nephrotoxicity	Myalgias, elevated hepatic transaminases and creatine phosphokinases (check weekly), and rhabdomyolysis (consider holding HMG-CoA reductase inhibitors [statins] while on therapy)
<b>Key Learning Points</b>	Drug of choice for severe MRSA infections; oral form only used for <i>C. difficile</i> infection; resistance can be caused by plasmid-mediated changes in permeability to the drug or by decreased binding of <i>vancomycin</i> to receptor molecules; monitor serum trough concentrations for safety and efficacy	<i>Daptomycin</i> is inactivated by pulmonary surfactants and should never be used in the treatment of pneumonia



# Lipoglycopeptides

## Telavancin

- Bactericidal
- Concentration-dependent
- Similar antibacterial spectrum as vancomycin (but better)
- Alternative to vancomycin for the treatment of ABSSSIs and nosocomial pneumonia caused by MRSA
- More toxic: nephrotoxicity and cardiotoxicity



# Fosfomycin

- Derivative of phosphoric acid
- Bactericidal
- **MOA:** blocks cell wall synthesis by inhibiting the enzyme UDP-N-acetylglucosamine *enolpyruvyl transferase* (*first step* in peptidoglycan synthesis)
- First line therapy for acute cystitis
- Cross-resistance is unlikely



# Polymyxin B (Colistin)

- Cation polypeptides
- **MOA:** bind phospholipids on the bacterial cell membrane of gram-negative bacteria (disrupt cell membrane not cell wall)
- Active against most gram-negative bacteria including *P. aeruginosa*
- Bactericidal
- Concentration-dependent
- Limited use because of nephrotoxicity/neurotoxicity
- **Spared for multi-drug resistant infections**



# In Jordan

- We are starting to see bacterial infections (mainly gram-negative) that are resistant to almost all antibiotics except for colistin.
- 76.8% of *Acetivobacter baumannii* isolates were MDR and 99.2% were carbapenem-resistant.
- Resistance patterns indicated
  - **high resistance** for most cephalosporins, carbapenems, and fluoroquinolones
  - **moderate resistance** for trimethoprim/sulfamethoxazole and ampicillin/sulbactam,
  - **low resistance** for aminoglycosides and tetracyclines, while colistin and tigecycline, have the lowest resistance rates

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1-Phosphate-*N*-acetylglucosamine



UDP *N*-acetyl-glucosamine



UDP *N*-acetylglucosamine pyruvate



UDP *N*-acetylmuramic acid



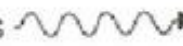
*N*-acetylglucosamine-*N*-acetyl-  
muramic acid-acceptor

|  
L-Ala-D-Glu-Lys-D-Ala-D-Ala

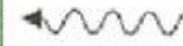
Peptidoglycan  
(bacterial cell wall)



Cephalosporins



Penicillins



Fosfomycin



Cycloserine  
Bacitracin  
Vancomycin  
Teicoplanin





# Quick Exercise

**Name five cell wall synthesis inhibitors that have antipseudomonal activity.**

1. \_\_\_\_\_
2. \_\_\_\_\_
3. \_\_\_\_\_
4. \_\_\_\_\_
5. \_\_\_\_\_



A 55-year-old male patient has been hospitalized for the last 3 days after suffering from severe upper gastrointestinal bleeding. While in the hospital, and possibly due to aspiration, the patient started developing fever, dyspnea, and productive cough, with pleuritic chest pain. On examination, the patient had purulent sputum and auscultatory signs of pulmonary consolidation. Radiography showed widespread pulmonary infiltrates suggestive of MRSA infection. Your initial evaluation highly favors the possibility of nosocomial aspiration pneumonia. Which of the following antibiotics must be included in your empiric therapy regimen?



- Linezolid
- Daptomycin
- Ceftriaxone
- Cefepime
- Nafcillin