

Antimicrobials Therapy

Pharmaceutical Microbiology

Dr. Rawan Abudalo

Department of Clinical Pharmacy and Pharmacy Practice

Faculty of Pharmaceutical Sciences

Hashemite University

Mechanisms of Action of Antibacterial Drugs

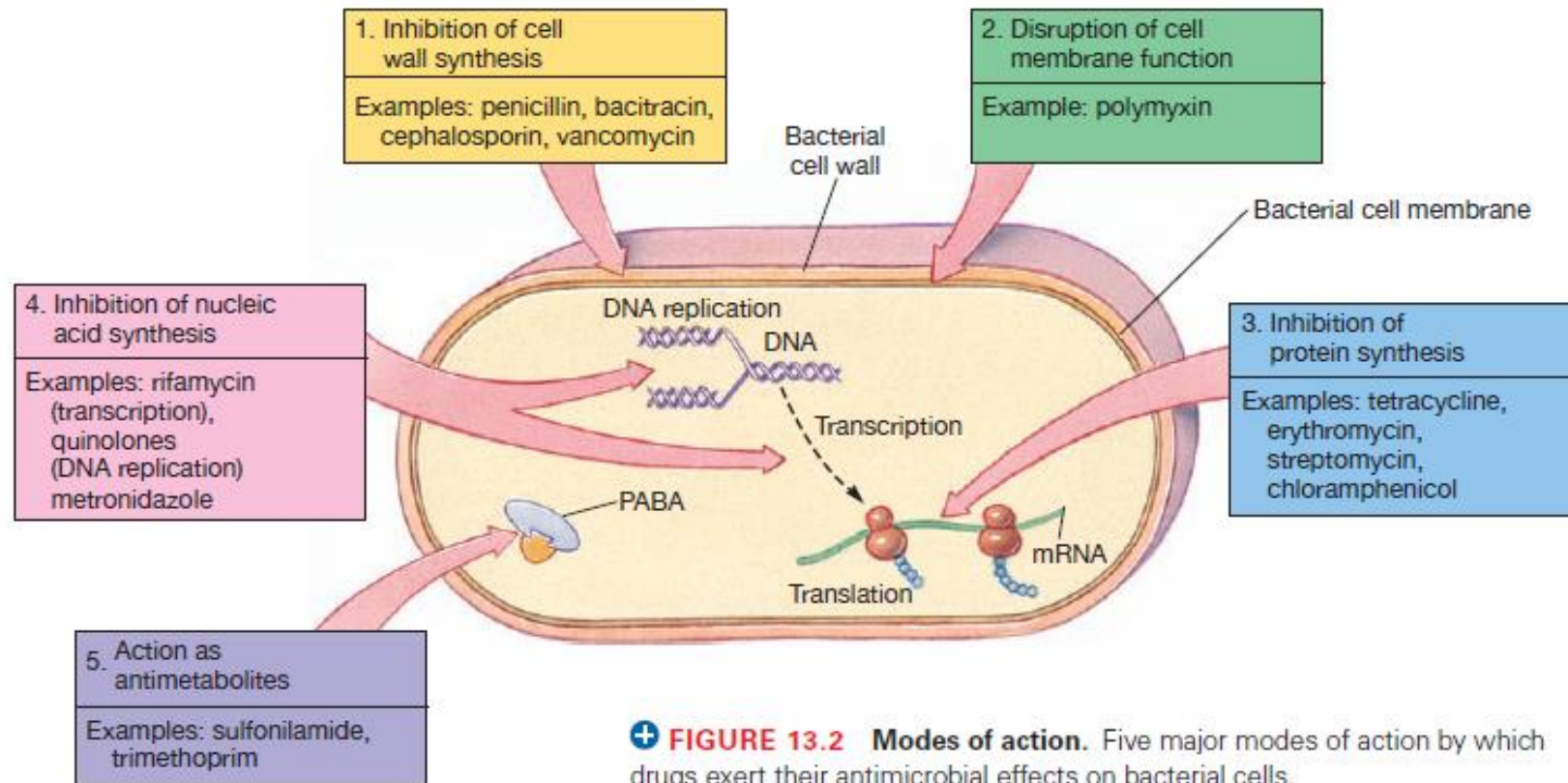
Antimicrobial drugs affect various bacterial cellular targets:

1. Inhibit cell wall synthesis
2. Inhibit protein synthesis
3. Inhibit nucleic acid synthesis
4. Injury to plasma membrane
5. Inhibit synthesis of essential metabolites

عشان يسهل علينا الحفظ
بنعمل رسم شجري لكل mechanism
وبندرج تحتها كل الادوية الخاصة فيها مع فروعهم^{٨٨}

Mechanisms of Action of Antibacterial Drugs

الاسماء الموجودة بالاسلايدات هي الحفظ



+ FIGURE 13.2 Modes of action. Five major modes of action by which drugs exert their antimicrobial effects on bacterial cells.

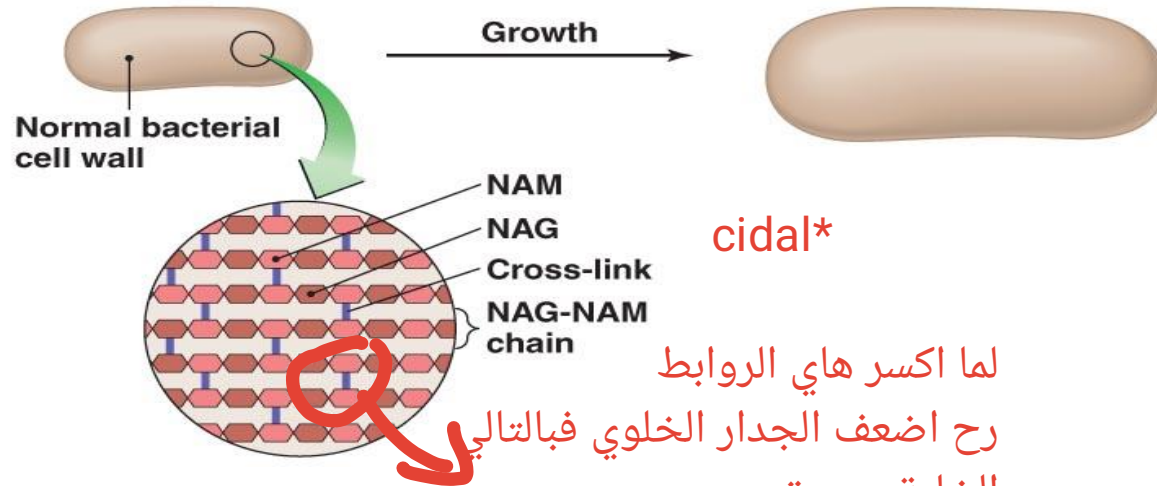
Inhibition of Cell Wall Synthesis

β -Lactam Drugs

- The main group of AB that act on bacterial cell wall is the '**beta lactams**'; so called due to presence of a β -lactam ring.
- Irreversibly inhibit enzymes involved in the final steps of cell wall synthesis
- These enzymes mediate formation of peptide bridges between adjacent stands of peptidoglycan (cross link, PBPs)
- Drug binds to enzyme, competitively inhibits enzymatic activity
- **β -lactam drugs include: Penicillins, Cephalosporins, Carbapenems and Monobactams**

A bacterial cell wall is composed of a macromolecule of peptidoglycan composed of NAG-NAM chains that are cross-linked by peptide bridges between the NAM subunits.

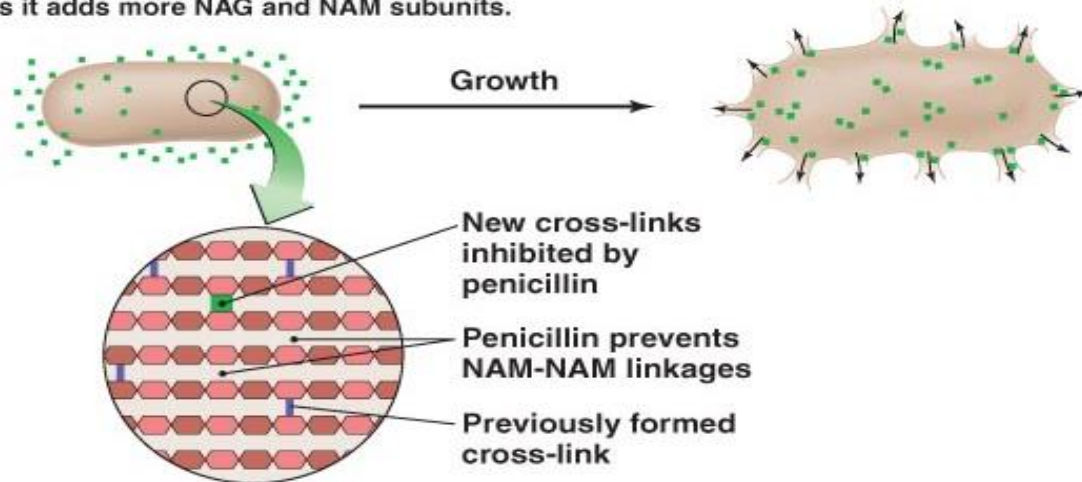
New NAG and NAM subunits are inserted into the wall by enzymes, allowing the cell to grow. Normally, other enzymes link new NAM subunits to old NAM subunits with peptide cross-links.



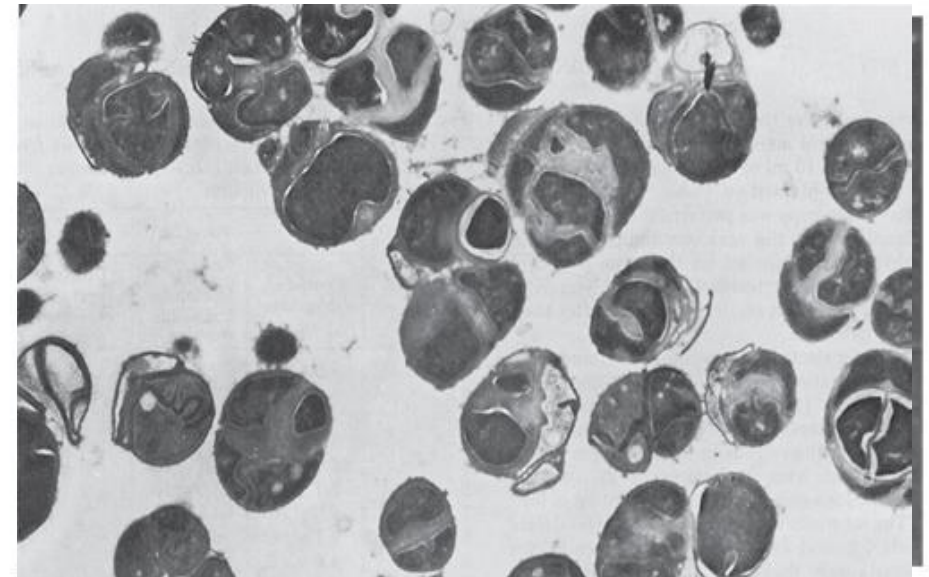
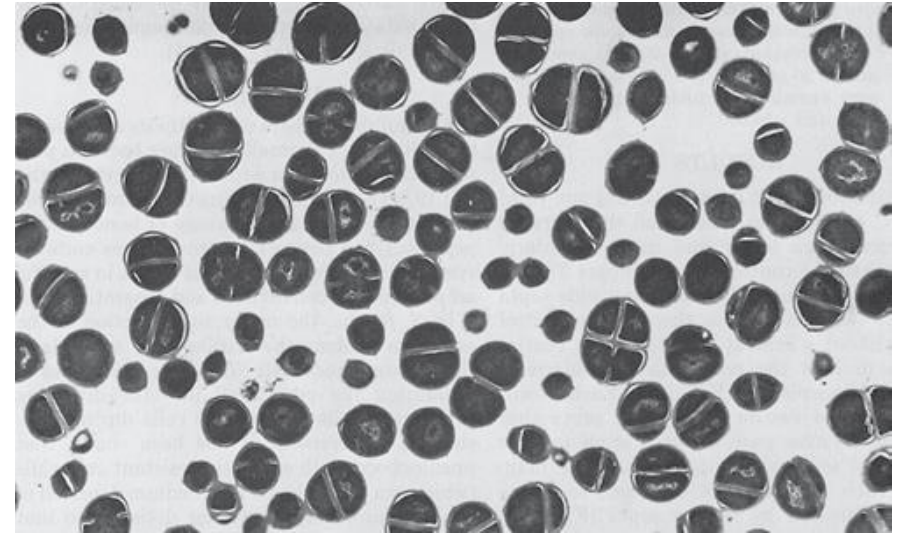
(a)

Penicillin interferes with the linking enzymes, and NAM subunits remain unattached to their neighbors. However, the cell continues to grow as it adds more NAG and NAM subunits.

The cell bursts from osmotic pressure because the integrity of peptidoglycan is not maintained.



(d)



(e)

SEM

0.5 μm

β -Lactams Antibiotics

زي ما بنشوف بالصور
البكتيريا في حالة binary fision
وال B lactam بتشتغل
بس لما تكون الخلايا بهاد ال phase
لانهما بتمنع تكون الجدار الخلوي
phase of growth & reproduction

β -Lactams

Cephalosporin

- Cefalexin
- Cefuroxime
- Cefotaxime
- Ceftriaxone

Monobactam

- Aztreonam

Carbapenem

- Meropenem
- Imipenem
- Doripenem
- Ertapenem

Penicillin

Narrow Spectrum

- Benzylpenicillin (Penicillin G)
- Phenoxymethylpenicillin (Pen V)
- Flucloxacillin

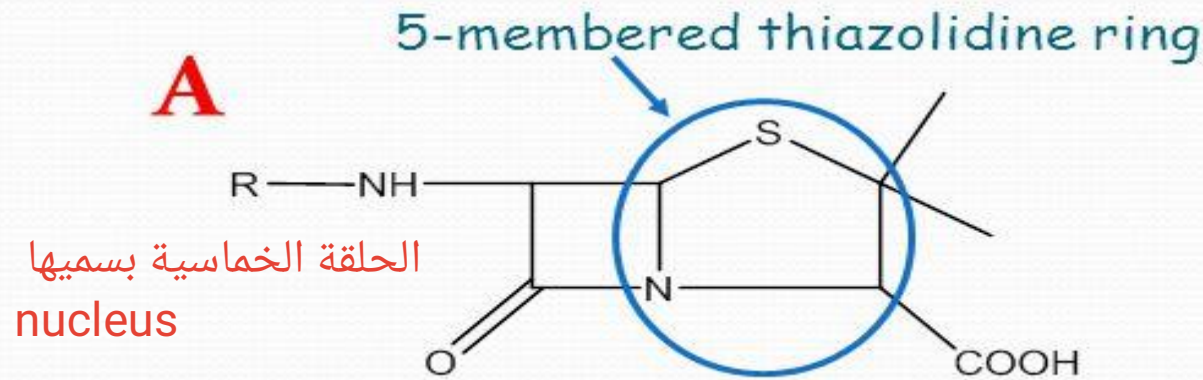
Broad Spectrum

- Amoxicillin/Co-amoxiclav
- Ampicillin

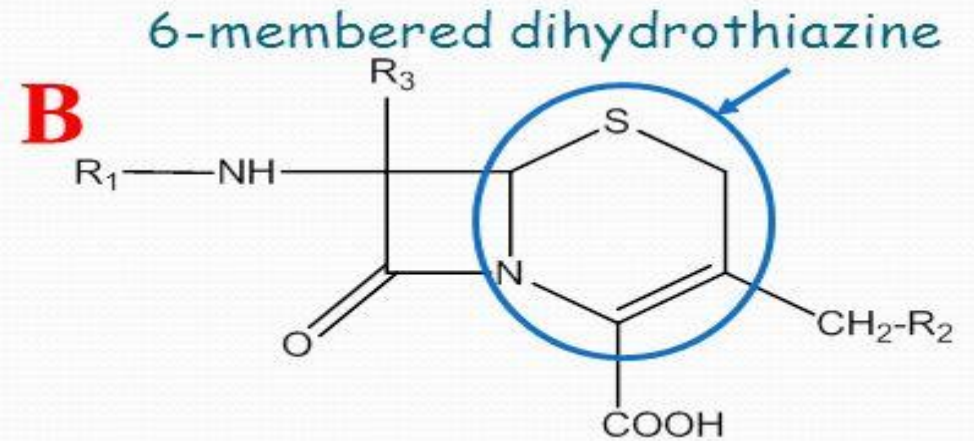
amoxicillin + tetracycline

ما بقدر اعطيهم مع بعض لاني هيك
بلغي دور البنسلين (الاموكسيسيلين)
لانه بيقتل البكتيريا ومن النوع اللي
بيمنع تكون الجدار الخلوي، بينما
التيتراسايكلين static بس ومن النوع
اللي بيمنع تكون البروتين

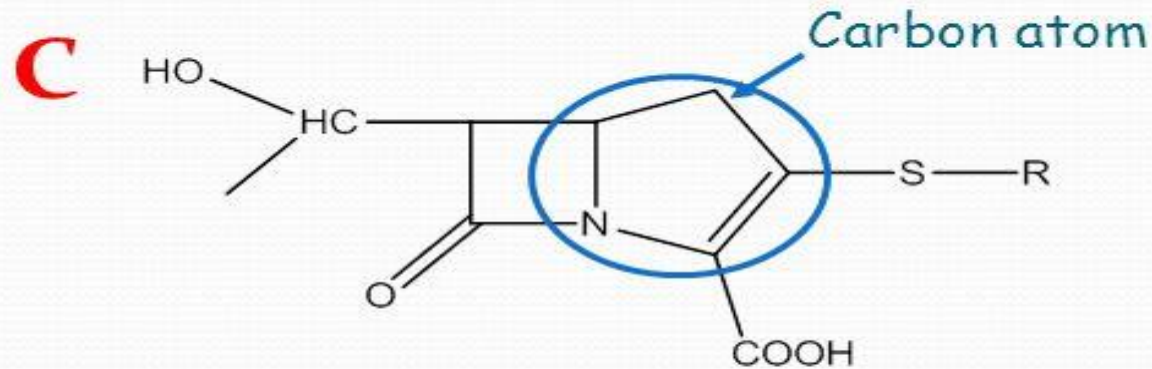
β -lactam antibiotics



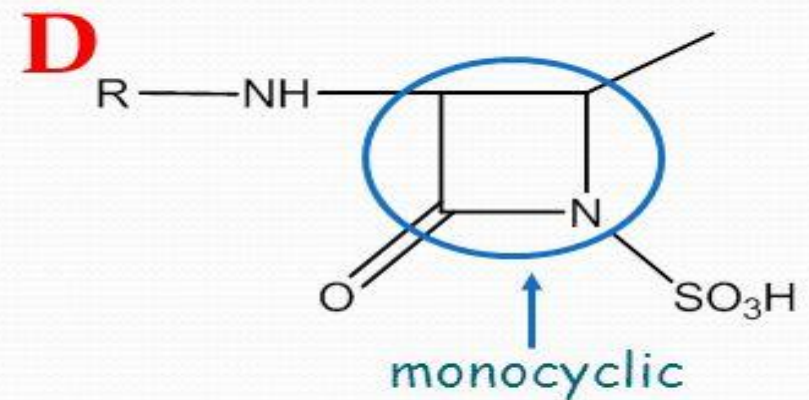
Penicillin nucleus
انواع البنسلين مختلفة ب side chain



Cephalosporin nucleus



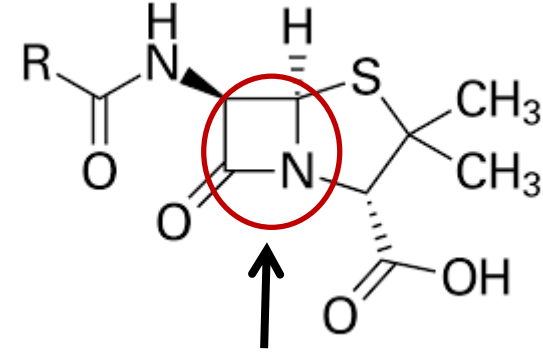
Carbapenem nucleus



Monobactam nucleus

Penicillins

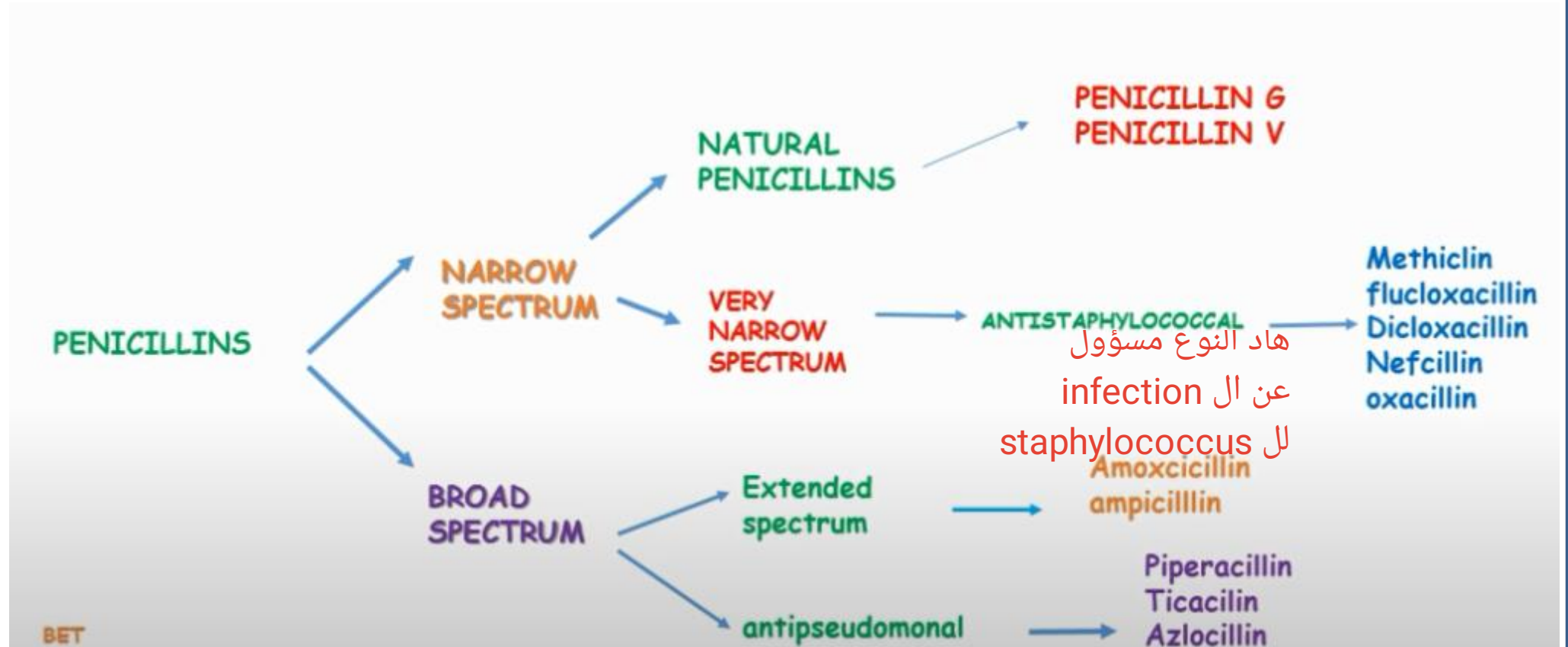
- Have β -lactam ring + نواة + سايد تشين
- Bacteriocidal



هي المسؤولة عن
antibacterial action **β -lactam ring**

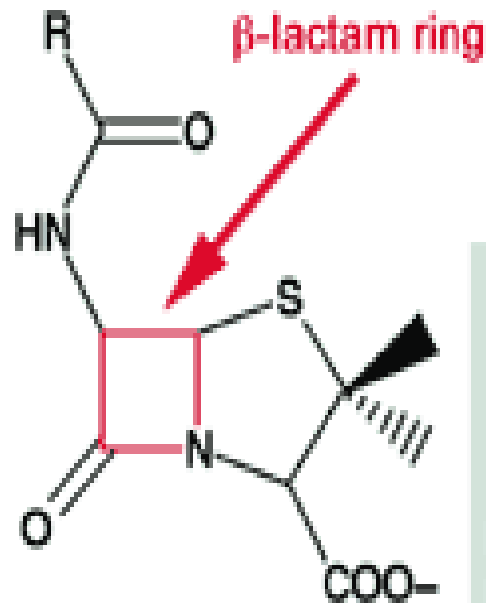
- Their official names usually include or end in “**cillin**”

Classification of Penicillins



Some bacteria produce β -lactamase enzyme that breaks the critical β -lactam ring

Penicillin Resistance



Penicillin

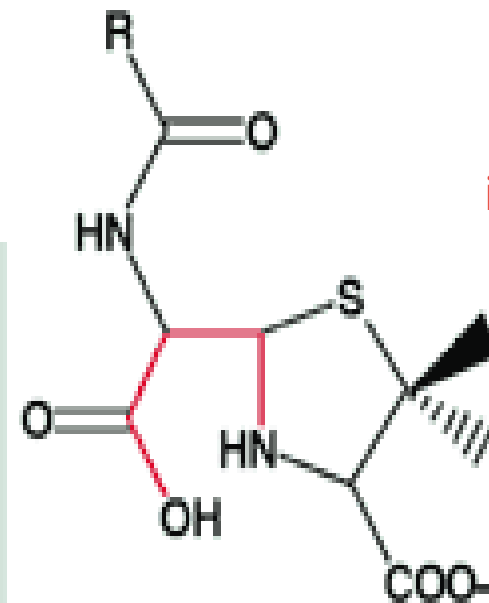
البكتيريا رح تفرز هاد الانزيم
عشان تقاوم بس مش دايما



بفيد

β -lactamase

β -lactamase breaks a bond in the β -lactam ring of penicillin to disable the molecule. Bacteria with this enzyme can resist the effects of penicillin and other β -lactam antibiotics.



inactive

Penicilloic acid

B-lactamase inhibitors

او بالاحرى very minimum

Substance **don't** have antibacterial activity but they have the ability to **inhibit** the B-lactamase enzyme....

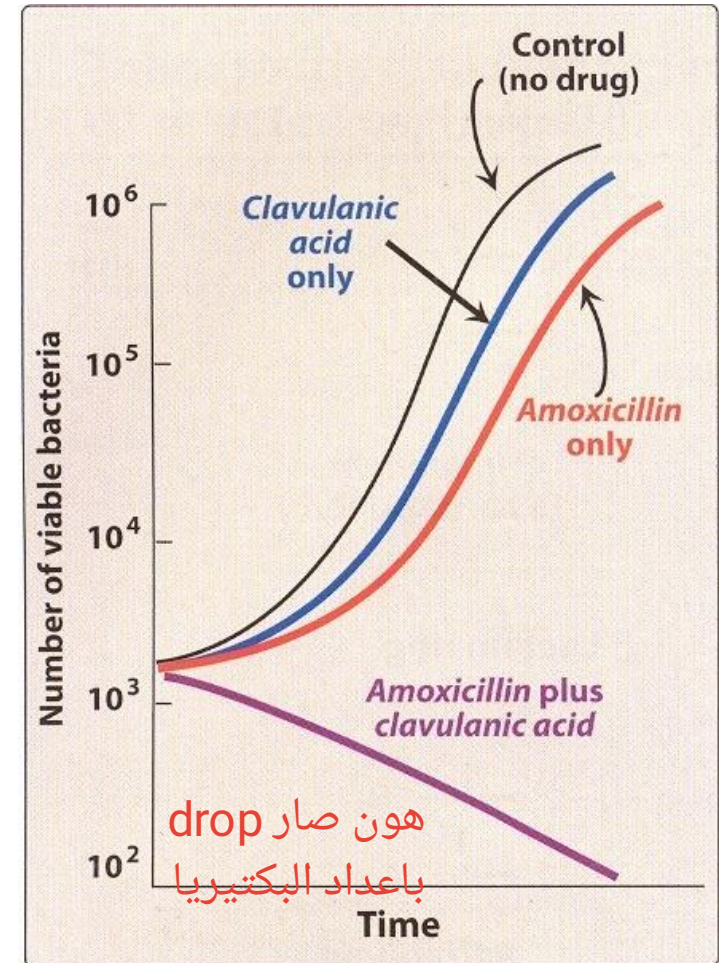
Ex. Clavulanic acid

هاد الاسيد بستخدمه عشان احمي
المضاد من تكسير ال ring تبعه

For exemplar clavulanic acid Binds to beta-lactamase and competitively protects amoxicillin

*They potentiating amoxicillin against beta-lactamase producing bacteria.

* It is called "suicide inhibitor"



Penicillins adverse effects

- Allergy to penicillin is rare among children but occurs in 1 to 10% of adults.

- Mild: rash

- Severe: anaphylaxis & death

لو المريض عنده حساسية بنسلين او

مش متأكد انه ما عنده حساسية

وقتها لازم ابعد عن كل ال B lactam

ما عدا ال Aztreonam بقدر اعطيه

- ✓ There is cross-reactivity among all Penicillins

- ✓ Penicillins and cephalosporins ~5%

وممكن المريض ما يكون

عنده حساسية بس يصير

فجأة عنده حساسية

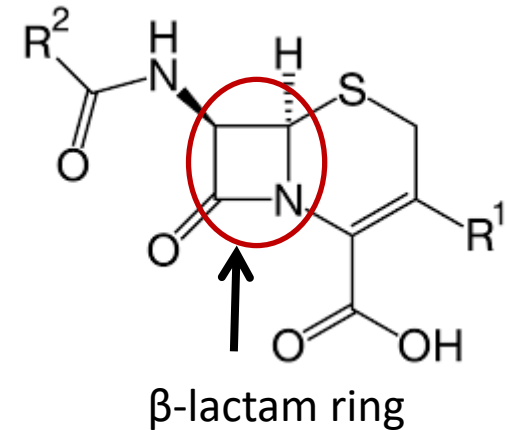
wide therapeutic window

- Penicillins are **generally nontoxic**, but large doses can have toxic effects on the kidneys, liver, and central nervous system

Cephalosporins

- Different generations (1st, 2nd, third and fourth.)
- Bactericidal medications
- Safe in general
- 1st and 2nd generation drugs are not used for CNS Infections

لأنها ما بتركب عال B.B.B



- They are recognised by the inclusion of “cef” or “ceph”
- they tend to be more resistant than Penicillins to β -lactamases

ما بتحتاج اضيف اي مادة تحميها

Cephalosporins

- Since cephalosporins are structurally similar to penicillins, 4-15% of patients who are allergic to penicillins are also allergic to cephalosporins
- Penicillins & cephalosporins exert their activity against growing bacteria

WHY???

Penicillins and cephalosporins have the same four-member “core” beta-lactam ring, but cephalosporins have an additional atom in the side ring.

Other β -lactam antibiotics:

- **Monobactam/Aztreonam**

بهاد السلايد كل شي حفظ

- Against Gram-negative bacteria,

- poor against gram positive

- **Carbapenem (Imipenem, Meropenem)**

reserve for severe infections

عشان المقازمة تبعها

يعني حتى لو عندي نيمونيا ما باخدها

- A group of β -lactams that are highly resistant to β -lactamases

- Active against G+ve & G-ve bacteria including *Pseudomonas aerogenosa* & *Enterococcus*

مش B lactam بس برضه بتمنع تكون الجدار الخلوي

Vancomycin

- *is a large, complex molecule produced by the soil actinomycete *Streptomyces orientalis*.*
- It can be used to treat infections caused by methicillin-resistant staphylococci and enterococci. It is also the drug of choice against antibiotic-induced **pseudomembranous colitis** الالتهاب اللي بالامعاء
- Vancomycin is fairly toxic, causing **hearing loss** and **kidney damage**
- **Red man syndrome** (red rash)

MRSA :

بتقاوم كل عائلة ال

methicillin

اللي حكينا انها عائلة بتحارب

كل امراض بكتيريا

staphylococcus

المضادات اللي لها broad spectrum

normal flora بتعمل اسهال لانها بتقتل ال

وبهاي الحالة الصيدلاني ما بيتدخل

وبحول المريض عالدكتور

عشان لازم يعالج الالتهاب اللي صار بالامعاء

بسبب المضاد بمضاد ثاني اسمه vancomycin



sarah khader



Artery Academy