passion ACADEMIC team.

YU-Medicine


**Sheet #16**

**Lec. Date :31\10\2019**

**Lec.Title: rest of Principle of antimicribial and begininng of cell wall inhibitors**

**Written by :Mustafa Tawaha & Ayah Obeidat**

# Principle of Antimicrobial
# Cell Wall inhibitors

General Pharmacology

M212

Dr. Laila M. Matalqah

Ph.D. Pharmacology

- **ملاحظة**: الكتابة باللون الازرق في السلايد هي التفريغ وايضا
  علامة # تعني سلايد كامل تفريغ

# Chemotherapeutic Spectra

A. **Narrow-spectrum antibiotics:** acting only on a single or a limited group of microorganisms e.g., Isoniazid is active only against mycobacteria tubercvulosis

**B. Extended-spectrum antibiotics:** antibiotics that are effective against gram-positive organisms and also against a significant number of gram-negative bacteria e.g. *Ampicillin*

**C. Broad-spectrum antibiotics:** affect a wide variety of microbial species and can alter the nature of the normal bacterial flora and precipitate a superinfection of an organism such as *Clostridium difficile ex., Tetracycline and fluoroquinolones*

#

- Chemotherapeutic agent = antimicrobial =antibiotic
- SPECTRUM mean what type of m.o can be killed by this drug (type mean genus of G+\-)
- احنا ما بنقسم الادوية وين بتأثر على specious معين بل على genus بشكل عام
- E.x:it is against staphylococcus means its against the entire staphylococcus (not only one specious,but hole genus ) يعني بتشمل

1-staphylococcus aureus (found in skin)

2-staphylococcus Endocarditis(found in endocardium in heart)

3-staphylococcus epidermins (found also in skin

#

- في بكتيريا بتكون موجودة على وفي جسمنا اسمها normal flora بتكون طبيعياً بجسمنا والها مكان معين ولازم تضل موجودة بهالمكان لانها احياناً بمجرد ما انها تغيير مكانها الاصلي ممكن تعمل infection and disease
- E.x:E.coli is located normally in GIT but if it is trnsported to the urine will make urinary tract infection
- Information about E.coli:

1-Very important in GIT digestion

2-Produce vit K and D

- So normal flora is already available in our body+its not harmful ,,,,can not cause any effect

# A.**narrow spectrum**:

- Effective against one type +sometimes one specious ,e.x:isoniazid can just only treat *mycobacteria tuberculosis*
- E.x:antipseudomonas aeruginosa is narrow
- B.**extended spectrum**:
- Effective against one genus
- Can be extended against a group of G+ or G-
- #معلومة ع جنب :G- all coccus are G+ except *Neisseria gonorrhoeae*
- C.**broad spectrum** :
- Effective against G+ + G- + our m.o(normal flora)
- يعني بتمسح وبتنظف كل البكتيريا بالمكان سواء كانت ضارة او نافعة
- هالاشي بكون ضار اكثر من نافع غالباً لانه انا قاعد بشيل ال normal flora فا بصير مكانهم فاضي ف رح ييجي بدالهم harmful m.o
- مثال: clostridium difficle بتيجي مكان normal flora بعد استخدام هيك ادوية وبتسبب diarrhea

#

- Broad spectrum مثل انو بقتل نملة ب صاروخ فا بعمل clear لكل اشي وبعتمد التحكم بهيك ادوية على duration of treatment
- That's why the duration of treatment not less than 5 days and not more than 14 days
- In sever infection like OSTEOMYELITIS (infection in bone marrow) maybe it will be 21 days (3 weeks)

*المعلومة الي فوق لفهم مبدأ broad spectrum

# Determinants of Rational frequency of Dosing

**3. Concentration-dependent killing:**

- antimicrobial show a significant increase in the rate of bacterial killing as the **concentration** of antibiotic increases from 4 to 64 fold the **MIC** of the drug for the infecting organism, e.g., aminoglycosides,
- Given by by a once-a-day bolus infusion (30 min) achieves high peak levels,

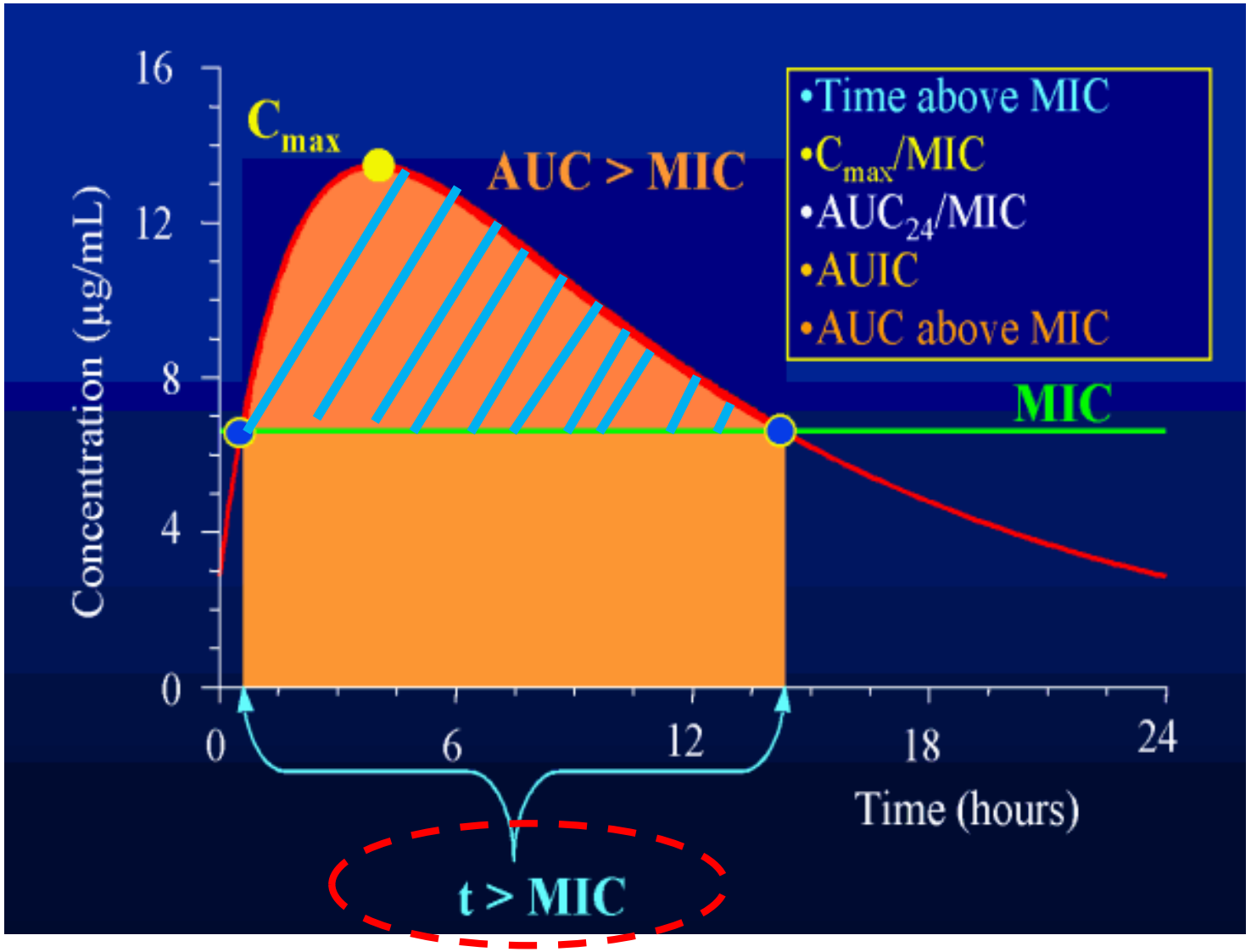
**2. Time-dependent killing:**

- The effect is directly proportional to the percentage of **TIME** the concentration of the antibiotic at the site of infection is ABOVE the MIC. , e.g., β-lactams AND macrolides, clindamycin
- Therefore, continuous (24 hours) infusions can be utilized to achieve prolonged time above the MIC and kill more bacteria

#

- احنا اخذنا قبل عن steady stateالي هي تعتبر حالة اكيدة والمفروض الدوا يوصل الها دايما لهيك تعتبر constant conecentration
- (If the concen less than it it will be subtherapeutic and if more will be toxic,so it should be constant )
- هسا الوضع ب antibiotics بختلف شوي في عندنا هون الادوية بتنقسم حسب طريقة شغلها وقتلها للبكتيريا لثلاث اقسام:
- 1- **conecntration dependent killing** :
- increase in concen ⟶ increase in killing rate
- لكن شرط لتطبق هالقاعدة انو يكون التركيز فوق MIC , اذا قل اصلا ما راح يكون في قتل للبكتيريا وبتتخوث عليك وع الفارما بتاعتك هه
- كيف بحسبها ؟ بالمساحة تحت المنحنى بس ما فوق ال MIC المظللة باللون الازرق(السلايد الي بعد هاظ)
- E.x:aminoglycoside ,when u give it ,must monitor to ensure that concen is more than MIC

# “Time Dependant vs. Conc dependent”



#

- تكملة لشرح السلايد الي قبل

- Aminoglycoside is given once daily with highly dose in bolus infusion ( يعني ضخ شوي شوي) to ensure achieving high concen
- Aminoglycoside is only given IV(no orally)
- فلهيك انا ما بكون بهمني الوقت بقدر انو بهمني اعطي high cocen و هالاشي كثير بيحمي ال kidney لهيك هالدواء يعطى مرة باليوم
- One dose regimen can protect the kidney
- هون بهمني dose اكثر من ال frequency
- 2- **Time dependent killing :**
- هون يعتمد على الوقت وانا كم الوقت الي لازم اخلي تركيز الدوا فوق MIC
- هون بعطي الدوا بجرعات قليلة بس اكثر من مرة خلال اليوم لنحافظ ع اطول وقت فوق MIC
- هون بهمني frequency اكثر من ال dose

# Determinants of Rational frequency of Dosing

**3. Postantibiotic effect (PAE)**

- is a persistent suppression of microbial growth that occurs after levels of antibiotic have fallen below the MIC
- Antimicrobial drugs exhibiting a long PAE (for example, aminoglycosides and fluoroquinolones) often require only **one dose per day**, particularly against gram-negative bacteria.

#

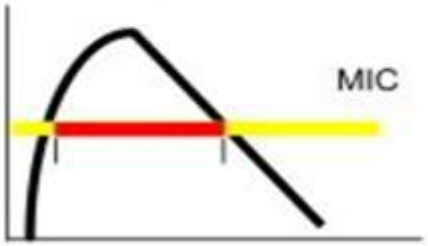
- **3. Postantibiotic effect (PAE)**
  - المبدأ هون انو هيك نوع ادوية بتضلها تقتل البكتيريا حتى لو قل التركيز لاقل من MIC وهالنوع من الادوية نادر وقليل جداً
  - *تشبيه الدكتورة:كأنك بتعرض البكتيريا لاشعة لتحرقها ولما تشيل الاشعة بستمر الحرق ,يعني انت بتعرضوا لل dose وبضل القتل مكمل حتى لو قل تركيز الدوا لاقل من MIC
  - واكبر مثال عليه هو aminoglycoside بقدر اعطية مرة باليوم

Because of both its concen dependent and postantibiotic effect

يعني مفعوله ونتيجته حتضل وتطووول لانو بشتغل فوق الMIC وتحته

## Pharmacokinetic/Pharmacodynamic Profiles of Antimicrobials

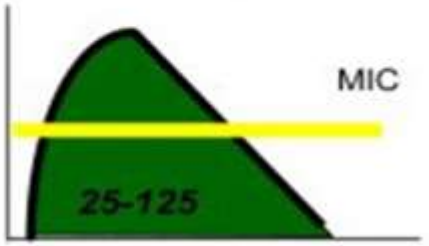
### Time>MIC
time-dependent activity




- Penicillins
- Cephalosporins
- Macrolides
- Clindamycin

**Optimal profile:**
**Free serum antibiotic level exceeds MIC for at least 40-50% of dosing interval**

### AUC/MIC
concentration-dependent activity




- Quinolones
- Aminoglycosides
- Azithromycin
- Ketolides

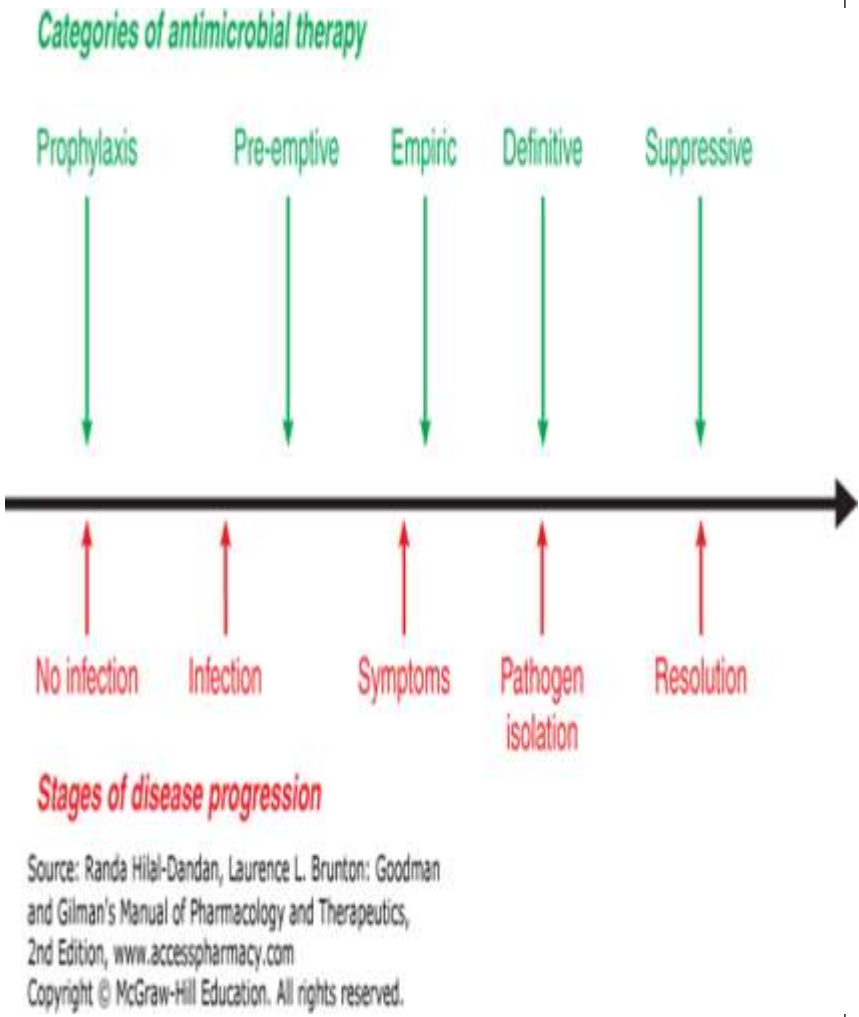
**Optimal profile:**
**Free serum AUC/MIC ratio at least: 25-30 for Strep. or other gram-positive bacteria, and 125 for aerobic gram-negative bacilli**

# Principles of antibiotic use

## Antibiotic use by purpose

| | |
|---|---|
| Prophylactic | • Prevent infection |
| Preemptive | • Abort infection |
| Empiric | • Initial control of infection |
| Definitive | • Cure infection of know etiology |

5




Source: Randa Hilal-Dandan, Laurence L. Brunton: Goodman and Gilman's Manual of Pharmacology and Therapeutics, 2nd Edition, www.accesspharmacy.com

# Prophylactic Use Of Antibiotics

- Certain clinical situations, such as dental procedures and surgeries, require the use of antibiotics for the prevention rather than for the treatment of infections

**1**

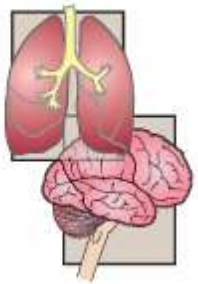
Pretreatment may prevent streptococcal infections in patients with a history of rheumatic heart disease. Patients may require years of treatment.

**2**

Pretreating of patients undergoing dental extractions who have implanted prosthetic devices, such as artificial heart valves, prevents seeding of the prosthesis.

**3**

Pretreatment may prevent tuberculosis or meningitis among individuals who are in close contact with infected patients.



**4**

Treatment prior to most surgical procedures can decrease the incidence of infection afterwards. Effective prophylaxis is directed against the most likely organism, not eradication of every potential pathogen.

#

- الان انت ك طبيب ليش بدك تعطي antibiotic؟ ومتى بدك تعطيه ؟
- احنا عندنا معايير للاختيار( criteria for selection)
- عنا 4 اهداف او معايير لحتى اختار antibiotic:

- 1)**Prophylactic (وقائي)**
- E.x:an elderly person have a heart problem and have a mitral valve (replacement valve زارع صمام صناعي) and want to do tooth extraction

هاذ لما بدي اعمله tooth extraction لازم اعطيه antibiotic مثل penicillin for whole day in order to protect from staphylococcus

لانو بحكيلك staphylcoocusممكن تنتقل من الاسنان للقلب وتعمل عندي endocarditisالي هو التهاب بالطبقة الداخليه للقلب لهيك معرضين للخطر ولازم نعطيهم كورس البنسلين لنحميهم

#

- مثال اخر اذا شخص عندو Tb وعايش مع اهله (الي يعتبروا ال contactors) بنعطيهم كورس قصير من الa.b برضو لنحميهم
- برضو نفس الاشي بنعمل بالنسبة لمرضى pneumonia
- بالجراحة كمان بعد العملية post operativeبنصرف مباشرة a.b لنحمي المريض واحتياط من اي عدوى

Because there is no sign or symptoms,this is to prevent the infection in the area of surgery

- Then prophylactic happen before the symptoms and there is no sign .But there is indicators that based on we give the antibiotics

#

- **2)AND 3) Preemptive and Empric**
  - هون بكون عندك المرض بس ما بكون في اعراض
  - لما انت يصير عندك +infection detected by blood
  - But we don't have any clinical symptoms
  - مثال شخص عمل فحص لل Tb وطلعت ال Tb ← postive

لكن ما عنده اي اعراض ظاهرة عليه معناها انا بعطيه preemptive

To prevent symptoms

واساساً postive Tb is inactive Tb وما بتحول لنشط الا لما يصير خلل بالمناعة

والدواء الي بنعطى بهالحالة بختلف عن الدوا الي بنعطى لمرضى الTb وعندهم اعراض

#

- اما ال empiric فا واحد بكون عندو المرض postive+ عندو symptoms
- مثال:واحد مريض اجاك بالطوارئ وانت عملت culture للبكتيريا الي عندو وبعثتها للمختبر طيب وبعدين شو بتعمل ؟ اكيد مش راح تستنا 3 ايام لتطلع نتيجة ال culture والمريض يموت
- راح تعطيه empirical depending on your knowledge
- يعني هو عبارة عن تحكم مبدئي بالعدوي لحتى نعرف نوع البكتيريا ونتأكد فا انت مثلا بناء ع خبرتك لما ييجيك مريض عندو areal pneumonia فا انت بتعرف انو empirically can contain streptococcus pneumonia ف بنعطي دواء بناء ع هالاشي لحد ما تطلع نتائج الفحص ونعرف البكتيريا الصح ونحدد الدوا الصح
- ممكن احيانا اختيارك للدواء empirically يطلع نفس الدوا المطلوب
- **4)Definitive**
- Very accurate
- هاي بتيجي بعد ما تعرف نتيجة الفحص ونوع البكتيريا فا بتختار الدواء الصح لعلاجها

# Mechanisms of Resistance

- **1)Enzymatic inactivation:** Generating enzymes that inactivate the antibiotic (beta lactamase) **:**
  1) β-lactamases ("penicillinases") that hydrolytically inactivate the β-lactam ring of penicillins, cephalosporins, and related drugs;
  2) acetyltransferases: inactivating chloramphenicol or aminoglycosides;
  3) esterases that hydrolyze macrolides
- **2)Changing structure of target site** (beta lactams – change in penicillin-binding protein)
- **3)Preventing cellular accumulation of antibiotics** by altering outer membrane proteins or using efflux pumps
  - Gram negatives possess an outer membrane and cytoplasmic membrane preventing passage of abx through porins
- **4)Changing the metabolic pathway** that is being blocked

#

- 1)**Enzymatic inactivation** +2)**Changing structure of target site :**
- Sulfonamide act on tetrahyrofolices enzyme >>bacteria make different enzyme structure + maybe change pathway
- **3)Preventing cellular accumulation of antibiotics:**
- في ادوية معينه مثل clindomycin من الادوية الي اذا بتعطيها للبكتيريا اذا كانت عاملة resistance بتصير تضخ الدوا لبرا ( do efflux pumping) وتمنعه يدخل لجوا ويصير تجمع بالتالي ليقتلها

# Drug toxicity

**A. Hypersensitivity**

- Hypersensitivity or immune reactions to antimicrobial drugs or their metabolic products frequently occur. For example, the penicillins, can cause serious hypersensitivity problems, ranging from urticaria (hives) to anaphylactic

**B. Direct toxicity**

- High serum levels of certain antibiotics may cause toxicity by directly ffecting cellular processes in the host. For example, aminoglycosides can cause ototoxicity

**C. Superinfections**

- broad-spectrum antimicrobials can lead to alterations of the normal microbial flora of the upper respiratory, oral, intestinal, and genitourinary tracts, permitting the overgrowth of opportunistic organisms, especially fungi

#

- هسا معظم ال antibiotics safe ولكن بضل عنا عوامل معينه :
- **A. Hypersensitivity**
- كثير ناس بكون عندها allergic to certain drugs or family of drugs
- Cross allergic:occurs when u r for example allergic for penicillin ,so u will be allergic any B lactam drug because they r same structure
- **C. Superinfections**
- It is general character for all broad spectrum drugs
- Most important symptom is **<u>sever diarrhea</u>**
- هسا رقم 1 و 3 يعتبروا general اما رقم 2 direct toxicity ف...

- هاي بتكون مختصه بادوية معينه مثل :

- Vancomycin + aminoglycoside can cause ototoxicity and nephrotoxicity that's why we have certain condition to use them,,,for example in pneumonia patient that is resistance for everthing except aminoglycoside and he have sever infection so u need to give him this drugs but u need to keep monitoring him

# Cell Wall inhibitors

## General Pharmacology
## M212

Dr. Laila M. Matalqah

Assistant professor in Therapeutic and clinical pharmacology

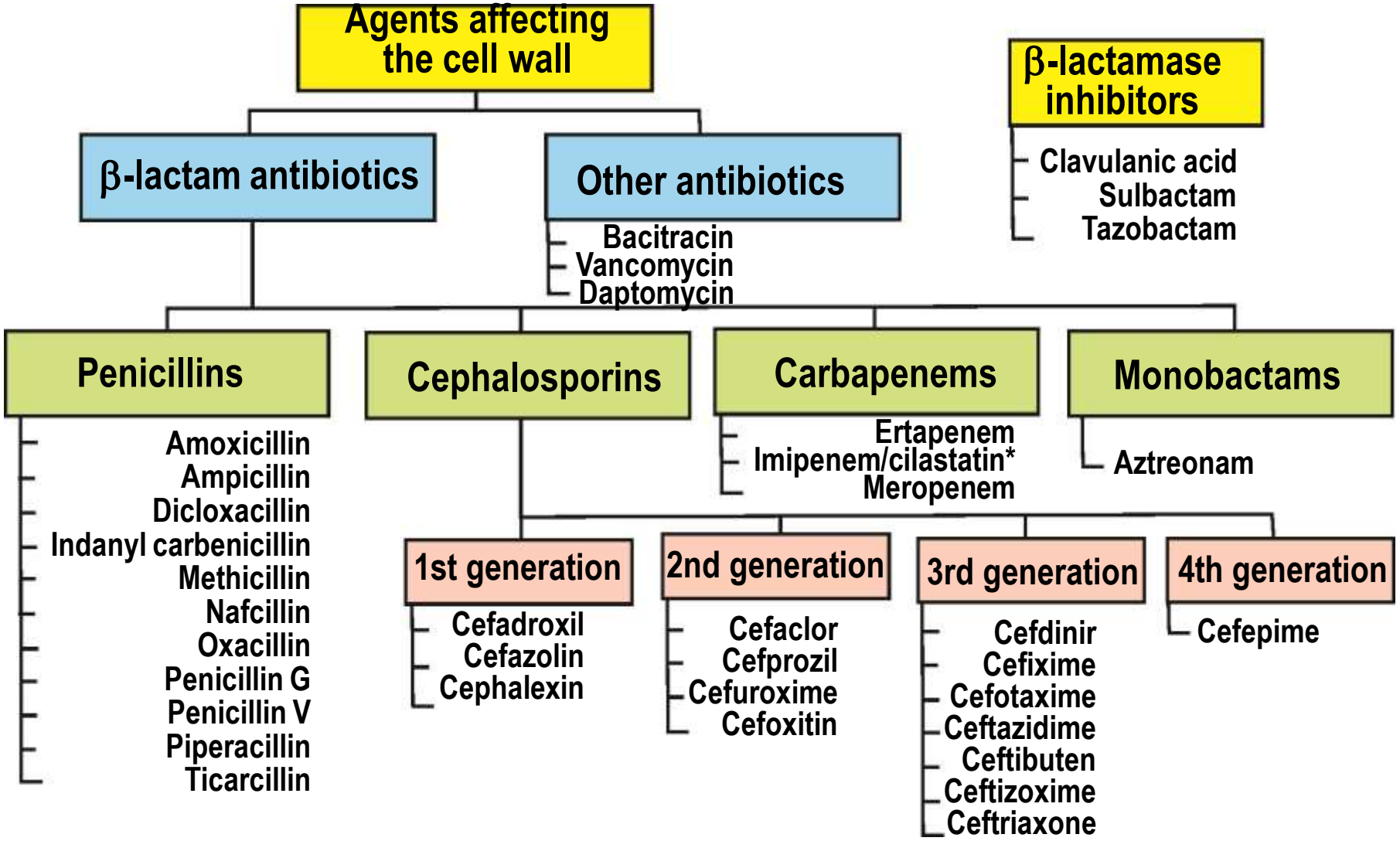
- **ملاحظة**: الكتابة باللون الازرق في السلايد هي التفريغ وايضا علامة # تعني سلايد كامل تفريغ

**نصيحة** : تأكد من دراستك لمحاضرة principles كويس ,هاي بتعتمد بشكل كبير عليها

#

- CELL WALL INHIBITORS is the most important antibiotic because :
- 1)the safest
- 2)cover huge range of m.o(G+,G-,..)
- 3)bactericidial
- 4)time-dependent killing

# Summary of antimicrobial agents affecting cell wall synthesis




(according to Lippincott´s Pharmacology, 2009)

#

- نظرة عامة للأدوية كاملة ,هون المجموعات الاربعة بالاخضر بتنتمي ل B-lactam بالتالي بتشاركوا بأنه عندهم:
- 1)Have B-lactam ring 2)same MOA 3)almost same structure <<<<But they differ in spectrum
- اما ال other antibiotic عندهم نفس الوظيفة( cell wall inhibitor) لكن ما عندهم B-lactam ring

#

-هسا بالنسبة لمجموعة B-lactamase inhibitors بالاصفر هي enzyme
inhibitors يعني شغلها بكون ع الانزيمات الي بتفرزها الخلية البكتيرية حتى تدافع عن نفسها ضد ال a.b فا هالادوية بتوقف عملها لتخلي ال a.b يكمل شغله (يعني هي بتعادل صفر في معادلة 1+0=2 potentiating effect ) *ما الها اي مفعول antibacterial

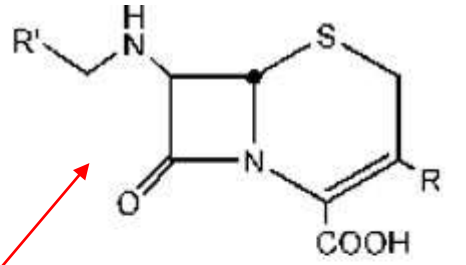
- -بناءاً على هالكلام بنقدر نخلطها مع اي penicillins مثلا لتعطينا مفعول اقوى واحسن وبتخلي الدواء يطلع درجة ويتطور :
- دواء narrow spectrum بصير extended spectrum
- دواء extended spectrum بصير broad spectrum
- e.x:amoxicillin which is extended spectrum when combined with clavulanic acid become amoclan which is broad spectrum
- Amoclan=amoxicillin+clavulanic acid
- وهالاشي كثير مهم للبكتيريا الي بتطور وبتصير R for pencillin لانها بتصير تفرز penicillinase بالتالي حلها الوحيد نعمل هيك
- ***وظيفة lactamase أنها تكسر B-lactam ring بالتالي بخرب الدوا
-

# Cell Wall Inhibitors

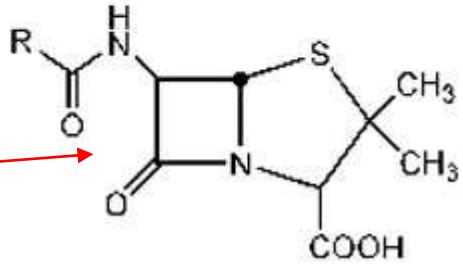
- β-Lactam Antibiotics
  - Penicillins
  - Cephalosporins
  - Carbapenems
  - Monobactams
- Other Antibiotics
  - Vancomycin
  - Daptomycin
- β-Lactamase Inhibitors

  Clavulanic acid, Sulbactam, Tazobactam

# β-Lactam Antibiotics : Contain a beta-lactam ring




Cephalosporin




Penicillin

β-lactam ring


قصة فلامينغ المعروفة لما وقعت قطعة من العفن داخل صحن فيها بكتيريا ولاحظ انها قتلتها كان بداية اكتشاف ال penicillin

# β-Lactam Antibiotics: **Penicillins**

- **Mechanism of action (for all of them,not only penicillin)**
  - Inhibit the last step of bacterial cell wall synthesis (transpeptidation or cross-linkage), THEN Cell lysis
  - Many mechanism and pathways??

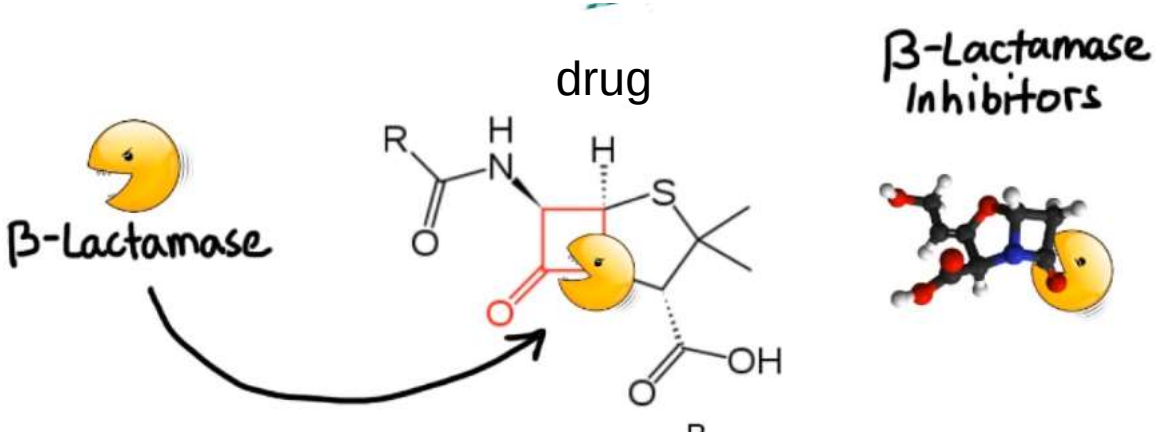
1. **Inactivate penicillin-binding proteins (PBPs)** Some PBPs catalyze transpeptidase and interfere the cross-linkages between peptidoglycan chains
2. **Inhibition of transpeptidase:**
3. **Production of autolysins:** degradative enzymes

- Most effective when bacterial cells are dividing
- Note: they are **inactive** against organisms lack cell wall structure, such **as mycobacteria, protozoa, fungi, and viruses,mycoplasma**.

#

- طريقة عمله MOA: باخر مرحلة في صنع cell wall لما يجي يرتبط نهاية اثنين peptidoglycan في انزيم اسمو PBP بخليهم يرتبطوا فا الدواء عنا بيجي ع binding sites برتبط فيها بالتالي بمنع ارتباطهم وتكوين cell wall لل PBP

- PBP:enzyme catalyse peptidase (making cross linkage between peptidoglycan chains in order to make cell wall)and its member of transpeptidase group
- penicillin is similar to the ending of peptidoglycan chains so, it binds with PBP → no cross linkage → defected cell wall have spores and holes →cell lysis(killing)
- 90% of the  of cell wall inhibitors do this MOA



#

- **3.Autolysin** is enzyme that hydrolyze itself so,bacteria starts killing itself
- Just 10% of cell wall inhibitors do this MOA
- Alterations in some of these PBPs provide the organism with resistance to the penicillins. [Note: Methicillin resistant Staphylococcus aureus (MRSA) are because of such an alteration.

# Penicillins

- Range from very narrow spectrum to very broad spectrum depend on their ability to cross the bacterial peptidoglycan cell wall to reach the PBPs
  - Factors : **the size, charge, and hydrophobicity** of the particular β-lactam antibiotic.
  - Gram-negative micro organisms have an outer lipopolysaccharide membrane (envelope) acts s barrier to the water-soluble penicillins but some have porins to permit transmembrane entry?
- The β-lactams are BACTERICIDAL
- The β-lactams are "time-dependent" killers

# Penicillins Classification

1. **Natural penicillins**
   - Penicillin G (I.V) , Penicillin V (oral)

2. **Extended-spectrum penicillins (Aminopenicillins)**
   - Ampicillin, Amoxicillin
   - ضفنا عليه amino group ف صار اسمه Aminopenicillins و هي semisynthetic

3. **Antistaphylococcal penicillins**
   - Oxacillin, Dicloxacillin, Nafcillin

4. **Antipseudomonal penicillins:**
   - Ticarcillin, Piperacillin,

# 1. Natural penicillins

- obtained from fermentations of the mold *Penicillium chrysogenum.*
- Spectrum: gram-positive and gram-negative cocci and gram-positive bacilli
- Penicillins are susceptible to inactivation by β-lactamases (penicillinases).
- **Penicillin G:** Available IM, IV
- Long-acting forms (IM) :
  - 1-Procaine PenG (12 hrs)
  - 2-Benzathine PenG (4 weeks)
- **Penicillin V:** Orally is more acid-stable

* Penicillin G → given IV

Penicillin V → given GI (Oral)

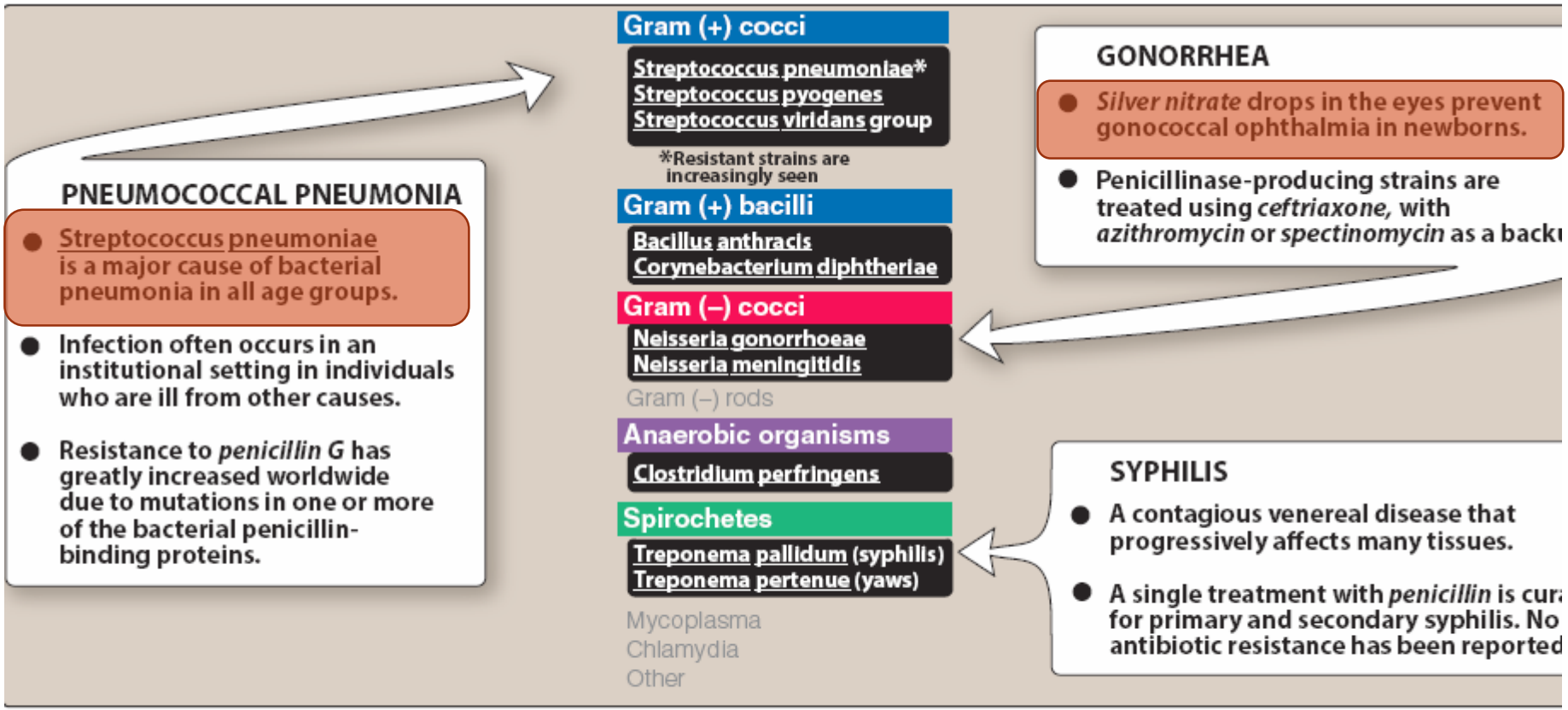



**Figure 38.4**
Typical therapeutic applications of *penicillin G*.

#

- لما نحكي G+ يعني ← Staphylococcus,streptococcus,neisseri gonorrhea

- **Neisseria gonorrhea** is G- coccus and diplococcus
- **GONORRHEA** and **SYPHILIS** are sexual transmitted diseases
- when the mother has **GORORRHEA** (it is vaginal infection) ,it can cause eye infection(gonoccoal opthalmia) for her baby while delivery so,we give Silver nitrate as eye drops for newborns in postdelivery to prevent it

# 2. Extended-spectrum penicillins (Aminopenicillins)

- **Ampicillin and Amoxicillin: I.V and Orally**
- **Spectrum:** same like Penicillin G but more against gram-negative bacilli.
  - Listeria monocytogenes
  - Enterococcus
  - Dental Prophylaxis .
  - Integral in H. pylori
- Amoxicillin is better tolerated orally
- These extended-spectrum agents are also widely used in the treatment of respiratory infections, and amoxicillin is employed prophylactically by dentists in high-risk patients for the prevention of bacterial endocarditis.

#

- **Endocarditis** can be treated with penicillin,but amoxicillin is better

- Formulation;

with a β-lactamase inhibitor, such as clavulanic acid or sulbactam,protects amoxicillin or ampicillin, respectively, from enzymatic hydrolysis and extends their antimicrobial spectra. For example, without the β-lactamase inhibitor, MSSA is resistant to ampicillin and amoxicillin.

# 3. Antistaphylococcal penicillins

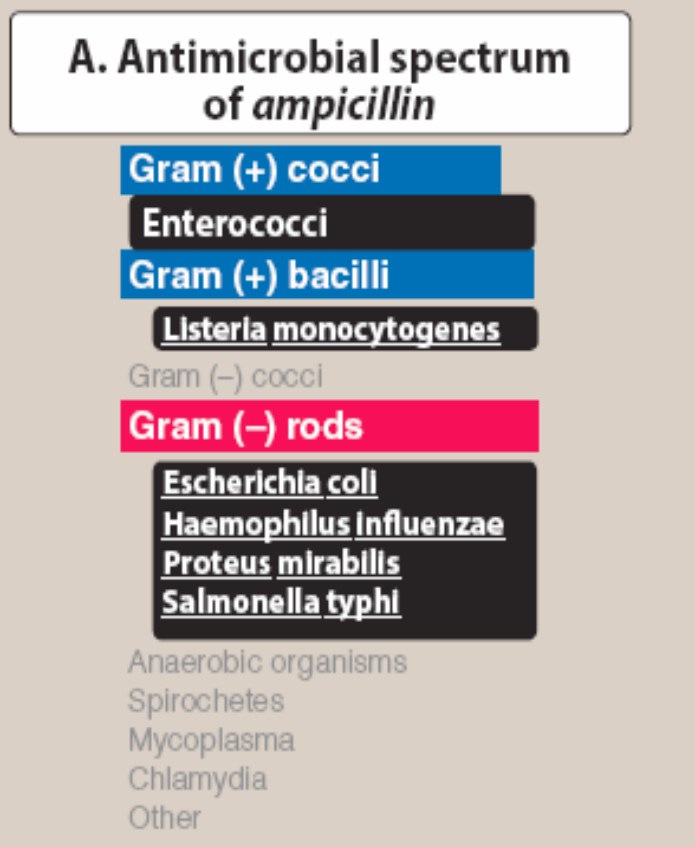
- **-narrow spectrum**
- **1)Nafcillin, 2)Oxacillin**, and 3)**Dicloxacillin** are penicillinase-resistant penicillins.
- Their use is restricted to the treatment of infections caused by penicillinase-producing staphylococci, including methicillin sensitive S. aureus (**MSSA**)
- **4) Methicillin** withdrawn from market because of interstitial nephritis +neurotoxicity
- MRSA is currently a source of serious community and nosocomial (hospital-acquired)

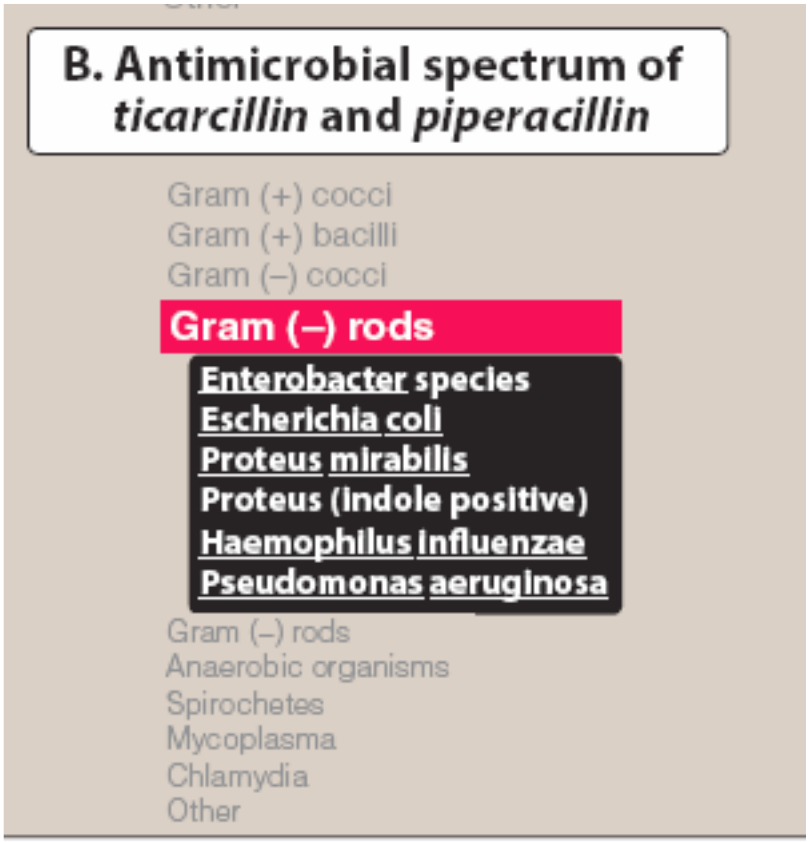
#

- **MRSA**:methicillin resistance S.aureus
- 4)Used only for lab tests to determine if these drugs are effective against the sample or not(MSSA or MRSA) ,we don’t use methicillin for treatment
- **Antistaphylococcal penicillins are not affected by penicillinase (their B lactam ring isn't effected)**

# 4. Antipseudomonal penicillins

- **Piperacillin Carbenicillin Ticarcillin** active against *Pseudomonas . Aeruginosa* and gram-negative bacilli
- They re effective against many gram-negative bacilli, but not against Klebsiella because of its constitutive penicillinase.
- Formulation of ticarcillin or piperacillin with clavulanic acid or tazobactam, respectively, extends the antimicrobial spectrum of these antibiotics to include penicillinase-producing organisms
- These agents are available in parenteral formulations only.
- Formulation of *ticarcillin or piperacillin with clavulanic acid* or *tazobactam, respectively, extends the antimicrobial spectrum* of these antibiotics to include penicillinase-producing organisms


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


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

#

- RULE:
  - اذا خلطنا اي دواء مع clavulanic acid ← can be given orally
  - اذا خلطنا اي دواء مع tazobactam,sulbactam ← can not be given orally (IV)
- Given IV
- Not for G+

# THE END

DONE BY :MUSTAFA TAWAHA & AYAH OBEIDAT

if you come by any mistake , please kindly report it to shaghafbatch@gmail.com