السلام عليكم ورحمة الله وبركاته
هذا تفريغ يدوي لمحاضرة 7&6 مضادات حيوية تم فيه كتابة كلام
الدكتور والسلايدات يلي مرّ عليها فقط
ينصح تحضروا المحاضرة أول
وفقكم الله
لا تنسونا بدعوة في ظهر الغيب 🌷

*Done by : Rasha Alkamra

* Antibiotics (6):

* the thing that makes MRSA resistance to: Penicillins, cephalosporines, carbapenems is that it had changed it's Penicillin binding protein structure so those drugs are now not able to act on it.

* Vancomycin:

→ it's relatively cheap

→ coming to solve our problem for MRSA

→ it have a similar shape of Peptidoglycan (a huge macromolecule)

→ it doesn't bind to penicillin binding protein

→ it's mechanism of action: vancomycin comes and set during the process of building the Peptidoglycan cell wall inside of the alanine that would be cross-linked so vancomycin inhibits the process of cross-linking by becoming part of the Peptidoglycan present on the cell → بهاي الحالة البكتيريا بتكون لسه ما وصلت لمرحلة الـ transpeptidase ، بتكون لسه في مرحلة الـ glycolasase

→ bacterocidal رح يصير loose الـ osmolarity الموجود جوا الخلية عالما بتدفع برا فتنفجر الخلية مفو

→ vancomycin is active against: - MRSA
- enterococcus
- Clostridium difficile

it has types بس بالحاضرات بكون قصدنا على الـ nosocomial MRSA ← hospital type not community

- gram +ve على الـ activity تبعية

أحسن دواء للـ enterococcus كان الـ ampicillin بس كتير استخدامه عشان هيك صرنا نعطي vancomycin على Penicillin resistant enterococcus

→ vancomycin has no activity against gram -ve

Vancomycin

- Vancomycin is bactericidal and acts by inhibiting cell wall synthesis.
- it is active only against gram-positive bacteria, particularly staphylococci.
- Its special clinical use is in treating methicillin-resistant staphylococci, resistant enterococci and *Clostridium difficile* (which causes psuedomembranous colitis).
- The main indication for parenteral vancomycin is sepsis or endocarditis caused by methicillin-resistant staphylococci.

بهاي الحالة بنستخدمه only (عشان بنا اياه يشتغل على tract GI)

remember microbiology in AIT

→ vancomycin is injectable (not absorbed orally)

عشان هيك ← during injection of vancomycin it cause thrombophlebitis (vein التهاب بال), it may enter the body and cause hestamine release as it is very irritant → anaphylaxis ممكن يؤدي لـ

أول نقطة بالصورة

Vancomycin

- Vancomycin must be administered in a dilute solution slowly, over at least 60 minutes.

This is due to the high incidence of pain and thrombophlebitis and to avoid an infusion reaction known as the red man syndrome or red neck syndrome.

- Unwanted effects are a series problem and include fever, rashes and local phlebitis.
- Ototoxicity and nephrotoxicity can occur and hypersensitivity reactions are occasionally encountered.

hypotension, broncho constriction, histamine all over the body

type of allergy mediated by histamine

إذا بالشت عند المريض لازم نوقف إعطاؤه من الدواء

عكلام الدكتور انتباهات

قصة الـ Gentamicin و الـ Ampicillin يلي بسببن صارت resistant عند الـ enterococcus عنده صار يستخدموا الـ Gentamicin مع الـ Vancomycin

very ototoxic

hearing lose بيعمل

نتيجة استخدامهم مع بعض القصة هاي العبقة بالـ Vancomycin على الرغم انه مش هيك:)

Vancomycin

لو اجاك سؤال :

- It is also valuable in severe staphylococcal infections in patients allergic to penicillins and cephalosporins.

مريض عنده حساسية الـ Penicillins و الـ cephalosporins

- Vancomycin in combination with gentamicin is aused for treatment of enterococcal endocarditis in a patient with serious penicillin allergy. and cephalosporine allergy

واصاب بـ Staph (صار عنده cellulitis) شو تعطيه

- It is not absorbed from the gut and is only given orally for treatment of GI infections. It is generally administered intravenously.

دواء ؟ بناء "على الـ Stewardship بنعطي Vancomycin

- Resistance can be caused by changing the permeability to the drug and by decreasing the binding of Vancomycin to receptors.

extended بيغطي Carbapenem و كونه الـ Carbapenem هو spectrum

* a Patient has gram -ve nosocomial infection and Penicillin allergy and cephalosporine allergy

بهاي الحالة يا بنعطي Carbapenems أو بنعطي monobactam ← على حسب الـ Stewardship

الأحسن نعطي monobactam

* Monobactams

→ active against all gram -ve (Vancomycin عكس الـ)

→ it's a cell wall inhibitor

Monobactams
Spectrum of Activity

Penicillin binding Protein

Aztreonam bind preferentially to PBP 3 of gram-negative aerobes; has little to no activity against gram-positives or anaerobes

Gram-negative

E. coli, K. pneumoniae, P. mirabilis, S. marcescens
H. influenzae, M. catarrhalis
Enterobacter, Citrobacter, Providencia, Morganella
Salmonella, Shigella
Pseudomonas aeruginosa

مع ظهور الـ ESBL فقدنا كتير من الـ Aztreonam activity

Monobactams

Their spectrum of activity is limited to aerobic gram-negative rods (including pseudomonas). Unlike other beta-lactam antibiotics, they have no activity against gram-positive bacteria or anaerobes.

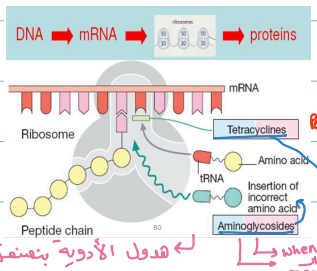
- The main monobactam is Aztreonam which is a monocyclic b-lactam resistant to most b-lactamases.
- Penicillin-allergic patients tolerate aztreonam without reaction.

In which used to treat serious infections such as pneumonia, meningitis, and sepsis caused by susceptible gram-negative pathogens.

- Its unwanted side-effects are similar to the other b-lactam antibiotics.

* Protein Synthesis inhebitors :

في أنواع بكتيريا ما عندها cell wall فمستحيل هيك بنيز الـ strategy of acting against the bacteria



extended spectrum بعيطلهم بنيزهم

كونه بيصنعوا تصنيع البن وبتبات بكل مكان

لكن إلي بتحكم بهاد الاشي اشيا كتير منهم وهو الـ Penetration

→ wheather it can get to the bacteria or not

→ blocking the coding of the codon

→ when it binds to 30s it binds irreversibly

different mechanisms of action بنيز aminoglycoside الـ Bacterocidal و Bacterostatic قبول الأدوية بنصنفهم

عبر البيضة membrane (Bactericidal)

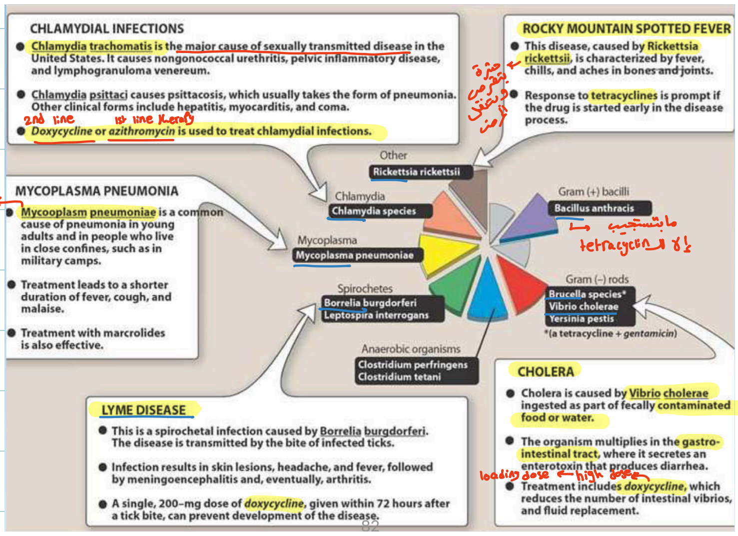
Chat gpt: protein synthesis inhibitors broad ... كل مجموعة من ال protein synthesis inhibitors الها spectrum ق فيها فرق برح يكون broad وواحد extended

Tetracyclines

* Tetracyclines : → Broad spectrum drugs

- Tetracycline, Methacycline, Moxycycline, doxycycline, minocycline and Tigecycline.
  (substrates of multi-drug resistant pump — not a substrate of multi-drug resistant pump; حفظ)
- They bind to both mRNA and the ribosomal 30S subunit where they prevent the binding of aminoacyl-tRNA.
- They are bacteriostatic not bacteriocidal.
- Their spectrum of activity is very wide and includes Gram-positive and Gram-negative bacteria, some spirochaetes and some protozoa (eg amoebae).

Atypical type of bacteria :



Tetracyclines

- Resistance is common and is mainly due to a plasmid-mediated energy-dependent efflux pump, (typical of the multiple drug resistance type). Mutations in the tetracycline target site are also found.
- The Tetracyclines are usually administered orally but can be given parenterally.
- Absorption from the gut is irregular and better in the absence of food.
- Since Tetracyclines chelate di- and trivalent metal ions, forming insoluble complexes, absorption is decreased in the presence of milk, certain antacids and iron preparations.

ل← البكتيريا طورت اشي اسمه multi-drug resistant pump ضد ال tetracyclin مضخات تطرده ، بجسم البكتيريا يلي كان active عليها زي ال gram +ve and gram -ve

Tetracyclines

- **Their main clinical uses are :**

(1) mycoplasma and chlamydia infections

(2) A tetracycline—usually in combination with an aminoglycoside—is indicated for brucellosis → اسمه activity لحاله

(3) They are used in combination regimens to treat gastric and duodenal ulcer disease caused by *Helicobacter p* → فقدنا ال activity لحاله

(4) Acne

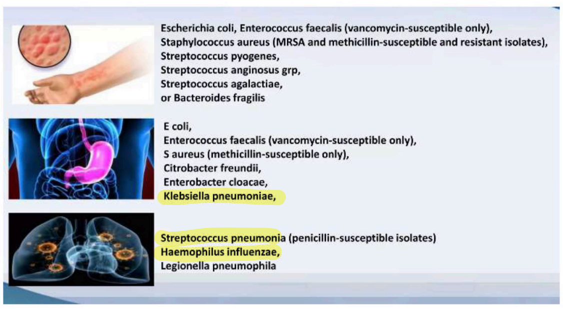
(5) syphilis

and Q-fever

* Antibiotics (7) :

Tigecycline

→ this drug is active as a bacteriostatic against all microorganisms except Pseudomonas. aurgenosa and citrobactor, (they have different genes that encode the MDR pump which have the ability to pump Tigecycline in addition to other tetracyclins)



Lower Respiratory
Community
- S. pneumoniae
- H. influenzae
- K. pneumoniae
- Legionella pneumophila
- Mycoplasma, Chlamydia

Tigecyclin covers all these organisms + organisms causes infections in the upper respiratory tract

→ له coverage على ال lower-rispiratory hospital ← كونه مش active against ← Psedumonas, enterobactor

* important note:

- Tigecyclin is used as the last drug resort (بنعطيه للمريض كخيار أخير إذا ما استجاب للأدوية الثانية)
- it's indications: - complicated acquired Pneumonia
  - complicated skin and extra abdominal infections

هاد الكلي صار بسبب ظهور حالات وفاة بعد استخدام هذا الدواء

Tetracyclines

من الأدوية الـ contraindicated للأطفال

عشان هيك لازم يتاخد على معدة فاضية

- The most Common side-effects are GI disturbances, due initially to direct irritation and later to modification of gut flora. → it has an epigastric burning effect
- They are deposited in growing bones and teeth, causing staining and sometimes dental hypoplasia and bone deformities. → it leads to deposition and can't chelation leading to
- Phototoxicity: for example, severe sunburn, occurs when the patient receiving a tetracycline is exposed to sun or ultra-violet rays.
- They shouldn't be given to children, pregnant women or nursing mothers. (may causes hepatotoxicity in pregnant women).

كيتي بيعمل diarrhea ٦ لدرجة انه مشهور جدًا بموضوع الـ superinfection كونه بيقدر يقتل كميّة من البكتيريا الموجودة بالـ normal flora تبعت الـ GI tract على الرغم من وجود الـ MDR pump في كميّة من البكتيريا الأخرى

عشان هيك ما بنعطيه للأطفال

لبسن لون السن بني

لـ بيعمل حجم السن

سؤال: ليش الـ tetracyclin بيعمل hepatotoxicity أكتر بالـ pregnant lady من النساء العاديين؟

- مشكلة الـ tetracyclin الرئيسية انه كميّة lipophilic فبضل بيرجع enterohepatic circulation ٦ لذلك إذا الجرعة كانت عالية رح يتراكم الدواء في الكبد بالتالي رح يصير في destruction أو swelling بالتالي رح تسكر على الـ bile duct ورح يصير في Cholestic Jaundice ومرّات كمان بيعمل destruction لـ hepatocytes فبصير في عنا إفراز لـ ALT و الـ AST (liver enzymes) لـ رجوع لنقطة ليش عند الحوامل أكتر: عندهم homodynamics مختلفة، بصير عندهم تجمع أكبر للسوائل (more edema) الـ blood circulation عندهم مختلفة فعندهم ثبات وبقاء الدواء في الجسم بتكون أكتر

- Since Tetracyclines chelate di- and trivalent metal ions, forming insoluble complexes, absorption is decreased in the presence of milk, certain antacids and iron preparations.

aluminum hydroxid and magnesium hydroxid مع بعض لـ بهم تبعت basic فبيعادلوا الحموضة المعدة فبتتشكل الحرقة

إذا اتناولوا مع الـ tetracyclin مارح يصير في امتصاص لأي منهم كون الـ 2 بيعملوا عمل بعض

Tetracyclines

- Tetracycline is a broad spectrum antibiotic that is occasionally used in Dentistry to treat bacterial infections.
- This antibiotic has a natural tendency to concentrate in the gingival fluids around the teeth so it is often used to treat gingivitis and gum disease.
- It is one of the first choices for the treatment of ANUG.
- Acute Necrotizing Ulcerative Gingivitis appears with stress. College students can get it during finals and people breaking up can get it.

this is sort of inflammation, that's why we give a very little dose

* Important note about Tetracycin:

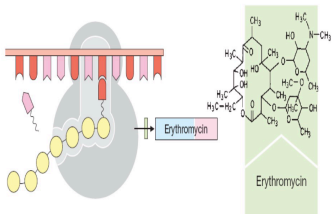
it has a good Pentration

entrahepatic circulation

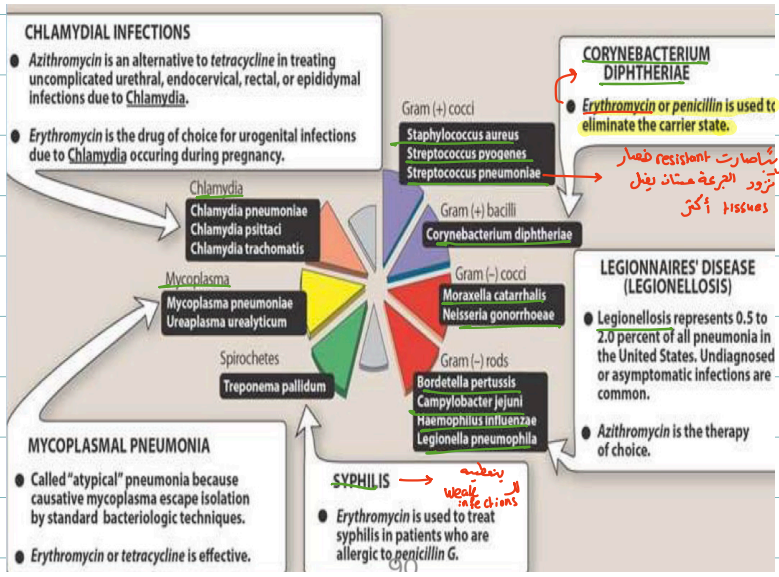
Macrolides → 3 types

weak gram negativity — القديم

- The best known example is Erythromycin, modern clinical member s being Clarithromycin , Azithromycin, Telitromycin.
  - Clarithromycin, Azithromycin: good gram negativity and Positivity
  - Telitromycin: أجيد واحد → atypical, عشان نعالج strep. Pneumonia
- They bind to the 50S ribosomal subunit and inhibit protein synthesis. → inhibits the Process of elongation of Peptides
  - bacteriostatic
- Erythromycin is active against Gram-positive bacteria and spirochaetes but not against most Gram-negative organisms.
- **Azithromycin far more active against respiratory infections due to Haemophilus influenzae and Ecoli.**



* the drug spectrum (Azithromycin إذا كان)
↓ من erythromycin لأنه ما بشتغل منيح على الـ gram-ve



تقريباً صارت resistant فصار لازم نزود الجرعة شوي بقل بالـ tissues أكثر

↓ upper respiratory tract infections بيغطي

↓ lower respiratory tract infections بيغطي الـ

Klebsella Pneumonia ← tigecycline بغطيها

they are the drug of choice ↓
for a Patient with upper respiratory tract with allergy toward Penicillins and cephalosporienes

Azithromycin → it also enters nuetrophiles with addition of tissues, so the nuetrophiles will Produce the drug as a reservoir

- **azithromycin penetrates into most tissues (except cerebrospinal fluid), with tissue concentrations exceeding serum concentrations by 10- to 100-fold.**
- **The drug is slowly released from tissues (tissue half-life of 2–4 days) to produce an elimination half-life approaching 3 days.**

الـ ← Serum half-life ما بتتعدى الـ 4-5 hours ← يعني لو سحبنا دم من الريض بالي اخذ الدواء بعد ٥ ساعات مارح نلاقيه بالدم

Macrolides clinical uses

- Its antibacterial spectrum is very similar to that of penicillins and it has proved a very useful penicillin substitute in penicillin-sensitive patient
- drug of choice in corynebacterial infections (diphtheria, corynebacterial sepsis);
- Azithromtcin drug of choice in respiratory, neonatal, ocular, or genital chlamydial infections; and
- Azithromycin drug of choice in treatment of community-acquired pneumonia because its spectrum of activity includes pneumococcus, mycoplasma, and legionella. and strep. Pneumonia

عشان نعالج klebsella Pneumonia (الوحيدة اللي ما بيشتغل Azithromycin عليها) رح نستخدم:

cefuroxime, cefdinir, cefixime, Augmantin

allergy ← بدون ما ننسى موضوع الـ

narrowest possible ← لازم هدول الأدوية يكونوا الـ

Macrolides

- The macrolides are administered orally, although they can be given parenterally.
- Azithromycin differs from erythromycin and clarithromycin mainly in pharmacokinetic properties
- Gastrointestinal disturbances are common side effects, but not serious. The newer agents seem to have less GI effects. Erythromycin has been reported to cause skin rashes and fever, transient hearing disturbances.

Macrolides

- Ototoxicity: Transient deafness has been associated with erythromycin, especially at high dosages.
- Cholestatic jaundice especially with the estolate form of erythromycin

الـ Azithromycin ما بيعمل هدول الـ effects

شرحنا الـ Process فوق عند الـ Tetracyclins

*erythromycin also has enterohepatic circulation

«أرجو من الله
أن تثمر جميع محاولاتنا
أن نصل إلى ما نود
وأن تلك المساعي لن تخيب» .

لا تنسونا من دعواتكم ...