بسم الله الرحمٰن الرحيم

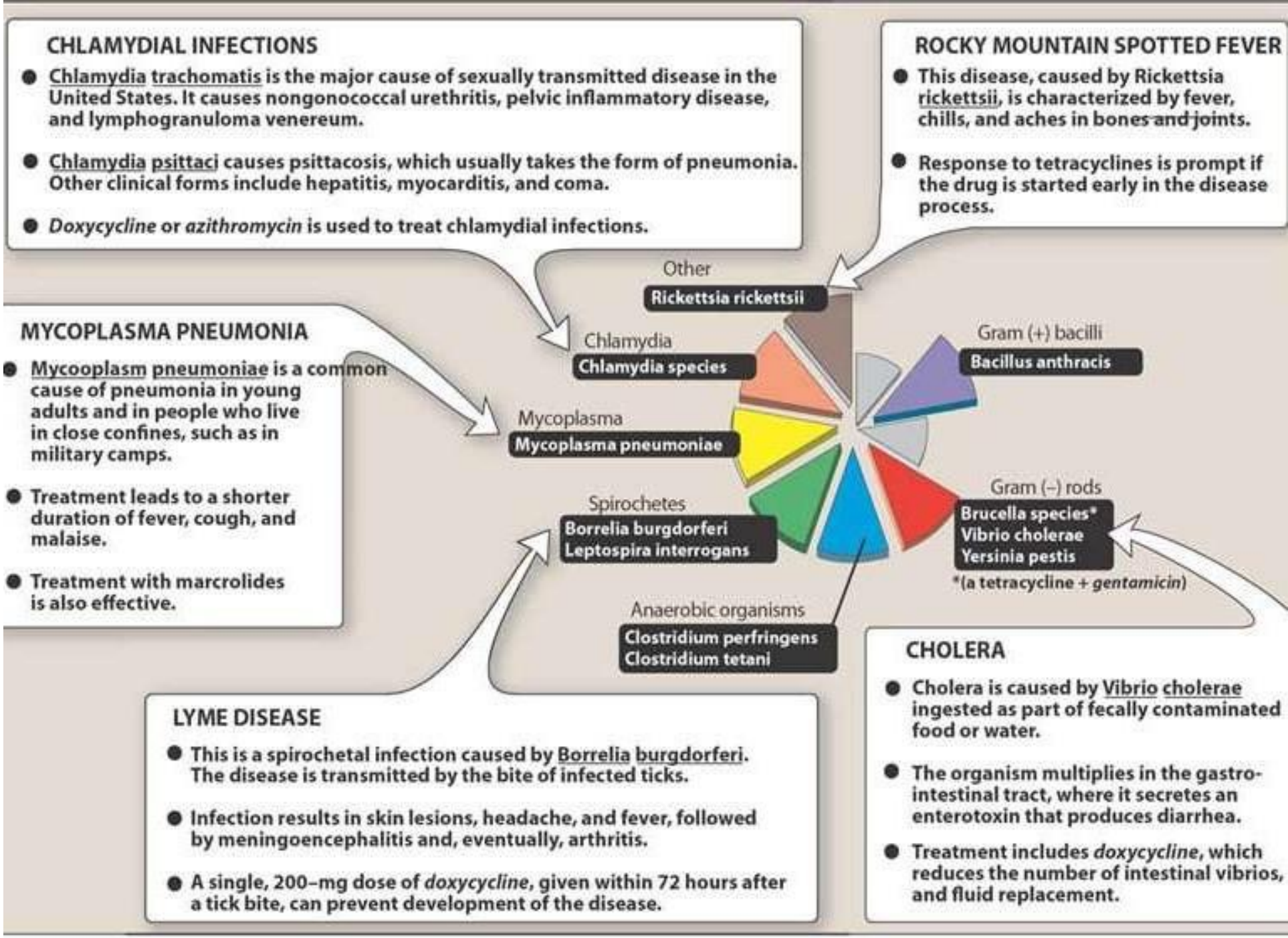
(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Pharmacology | FINAL 15

Antibiotics pt.7

Written by : NST

Chlamydia trachomatis
Causes:
Urethritis (STD)
Treatment options:
1st line: Azithromycin (Macrolide)
2nd line: Doxycycline
Note:
Due to intermediate resistance in some regions, dosing may vary



Tetracyclines (Broad-Spectrum Antibiotics)

Examples

Tetracycline

Methacycline

Doxycycline

Minocycline

Tigecycline

Mechanism of Action

Inhibit bacterial protein synthesis

Bind to the 30S ribosomal subunit

Bacteriostatic

Resistance Mechanism

Bacteria develop efflux pumps (β-glycoprotein–like pumps)

These pumps expel tetracyclines out of the bacterial cell

Variations in efflux pumps lead to variations in drug response

Known as MDR (Multi-Drug Resistance) pumps

Tigecycline

Not a substrate for MDR efflux pumps

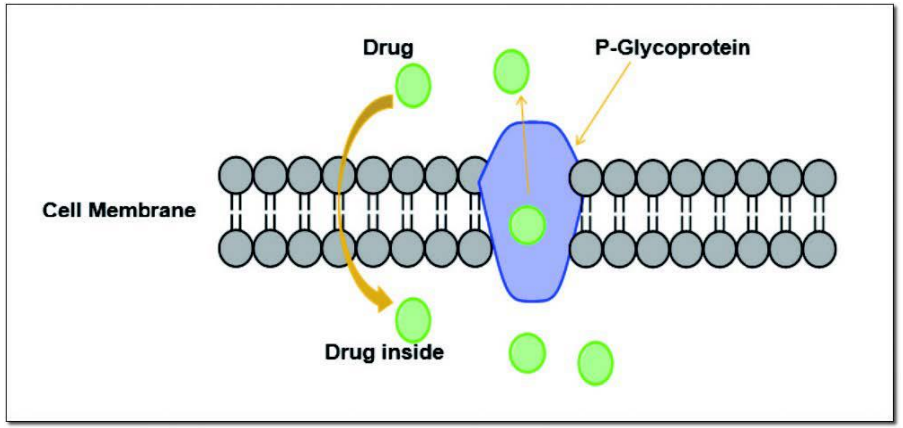
The only drug in the tetracycline family that bypasses this mechanism

Therefore:

Active against Gram-positive and Gram-negative bacteria

Effective against MDR organisms

Considered a very potent broad-spectrum antibiotic



Tetracyclines

- **Their main clinical uses are :**

(1) mycoplasma and chlamydia infections

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

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

فقدناها الآن

(4) Acne

حب الشباب

(5) syphilis Spirosheet

الزهري

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.

Tetracyclines

- **The most Common side-effects are GI disturbances, due initially to direct irritation and later to modification of gut flora.**

- **They are deposited in growing bones and teeth, causing staining and sometimes dental hypoplasia and bone deformities.**

- **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).**

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.** يعني عادة يجيبهم للأسنان مش الكم

Tigecycline

Black box
use Tigecycline as a last line

Active towards All microorganisms Except pseudonymonous Arginosa and Citrobacter

Why pseudomonas because it has agene that produce different pump (MDR) cant take the Tigecycline out

The spectrum not included

Escherichia coli, Enterococcus faecalis (vancomycin-susceptible only),
Staphylococcus aureus (MRSA and methicillin-susceptible and resistant isolates),
Streptococcus pyogenes,
Streptococcus anginosus grp,
Streptococcus agalactiae,
or Bacteroides fragilis

Complicated

E coli,
Enterococcus faecalis (vancomycin-susceptible only),
S aureus (methicillin-susceptible only),
Citrobacter freundii,
Enterobacter cloacae,
Klebsiella pneumoniae,

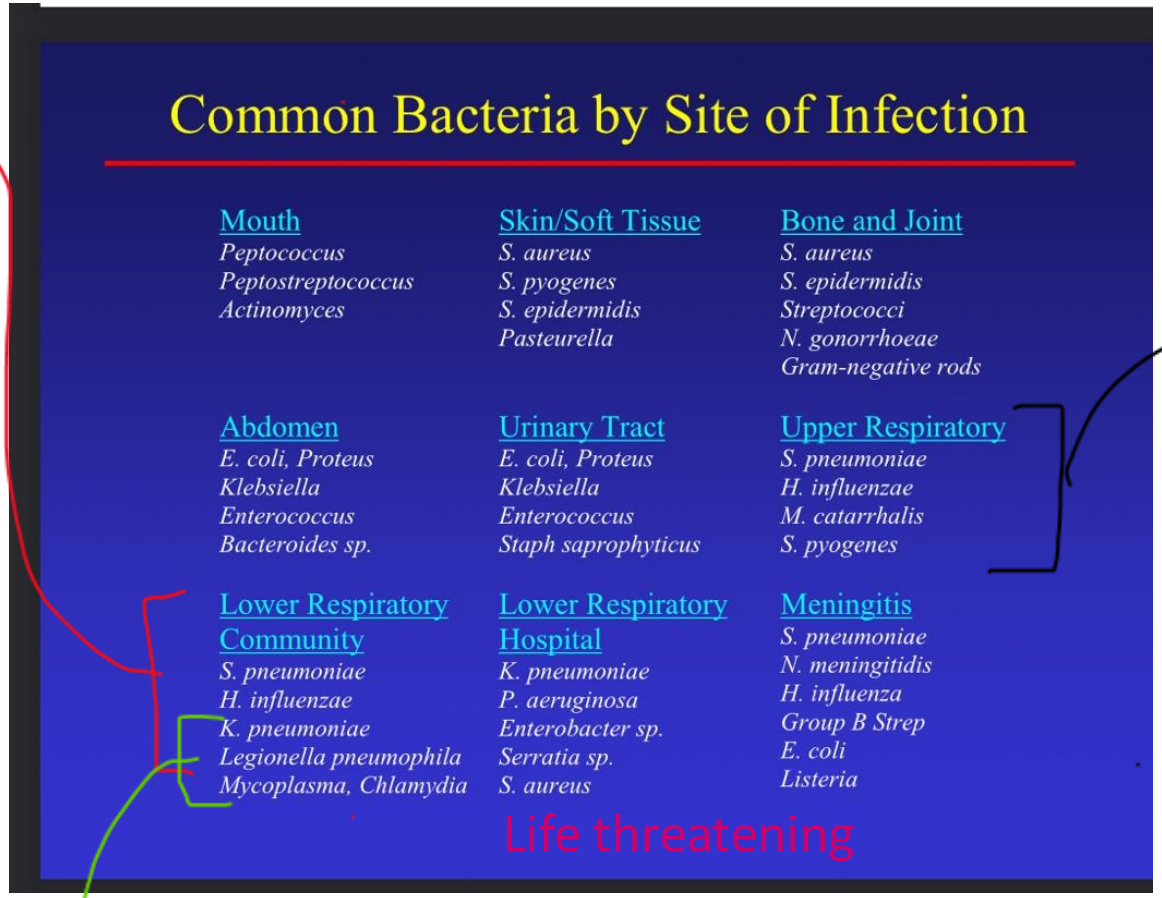
Complicated

Streptococcus pneumonia (penicillin-susceptible isolates)
Haemophilus influenzae,
Legionella pneumophila

Complicated

Tigecycline

You ask doctor that it's a Bacteriostatic so how it works?
Ok, because in community Acuierd penomonua we don't need Bactiriocidal because we don't need hospital it's not life threatening



We can use Tigecycline

Why not hospital inf because it is not active toward p.Arginosa or Enterobacter

Can be covered by Tetracycline
Methacycline
Doxycycline
Minocycline

This drug has been associated with increased mortality. In 2007, studies reported higher death rates, and in 2013, the FDA confirmed this risk. Therefore, it should be used only as a last-line option. Indications include complicated community-acquired pneumonia, complicated skin and soft tissue infections, and complicated intra-abdominal infections.

These medications are considered Reserves (Last-line drugs), meaning they are "hidden" and used only as a last resort when other medications fail to work.

Doxycycline serves as an alternative to Benzathine penicillin for treating Syphilis.

It is the drug of choice (primary treatment) for Acne, Rickettsia, and Lyme disease.

Additionally, it is used as a definitive treatment for Mycoplasma, a second-stage therapy for Chlamydia, and is the necessary choice for treating Brucella.

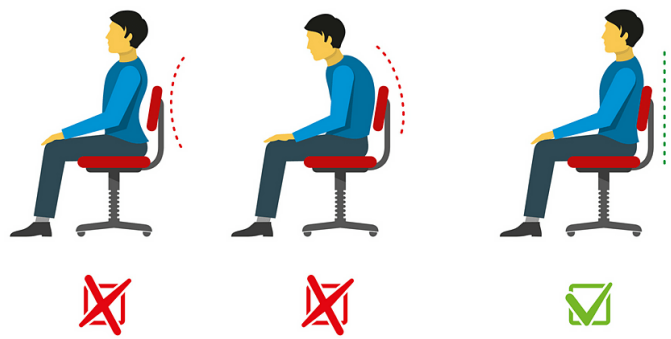
Administration Instructions for Doxycycline

To avoid a heavy gastric burning effect, the following precautions must be followed:

The patient must remain in an upright sitting or back upright posture for half an hour after taking the medication.

It should be taken on an empty stomach (without food).

The drug must be taken with two cups of water.



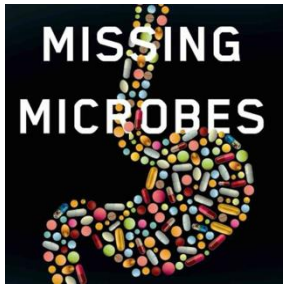
COUNCIL FOR DISABILITY AWARENESS

Tetracyclines have a high affinity for calcium. They chelate (bind to) divalent and trivalent metal ions:
Growing Bones/Teeth: Because they bind to calcium, they deposit in areas of new bone and tooth formation.
Consequences: This leads to permanent yellow-brown staining of teeth, dental hypoplasia (underdeveloped enamel), and potential bone growth retardation or deformities.
Important Contraindication: Due to these risks, they are strictly avoided in children (usually under 8 years old).

Drug & Food Interactions

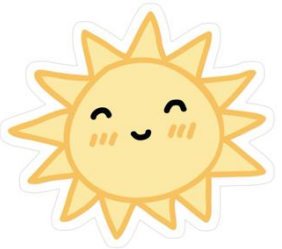
The chelation property also affects how the body absorbs the medicine:
Interaction with Diet: Absorption is significantly decreased if taken with milk (calcium), antacids (magnesium/aluminum), or iron preparations.

Mechanism: The drug binds to these minerals in the gut to form an insoluble complex that the body cannot absorb, making the antibiotic ineffective.



Phototoxicity:

• Skin Sensitivity: Tetracyclines can cause severe sunburn-like reactions when the patient is exposed to UV light.



• Advice: Patients should use sunblock and avoid direct sunlight while on this medication.

Pregnancy and Hepatotoxicity

Tetracyclines are generally avoided in pregnant or nursing women for two main reasons:

• Teratogenicity: They can cross the placenta and affect the developing fetus's skeletal system and teeth.

• Hepatotoxicity (Liver Damage): pregnant women are at a higher risk for severe liver damage when taking these drugs.

• Mechanism: Because Tetracyclines are lipophilic, they can accumulate in hepatocytes (liver cells). This leads to "fatty liver" changes, swelling of the cells, and potential obstruction of the bile duct (cholestasis).

Why Tetracycline in Pregnancy?

Hemodynamics: Different hemodynamic status (changes in blood flow and volume).

Water Retention: They accumulate more water and may experience edema.

Physiological Changes: Different cycles, constipation, and vomiting.

Pharmacokinetics: Longer drug half-life in the body.

Pharmacological Properties (tetracycline)

Penetration: High tissue penetration.

Metabolism: Hepatic cycle (enterohepatic circulation).

﴿وَوَصَّيْنَا الْإِنسَانَ بِوَالِدَيْهِ حَمَلَتْهُ أُمُّهُ وَهْنًا
عَلَىٰ وَهْنٍ وَفِصَالُهُ فِي عَامَيْنِ أَنِ اشْكُرْ لِي
وَلِوَالِدَيْكَ إِلَيَّ الْمَصِيرُ ﴿١٤﴾﴾ [لقمان]

Macrolides

- The best known example is Erythromycin, modern clinical member s being Clarithromycin , Azithromycin, Telitromycin.
- They bind to the 50S ribosomal subunit and inhibit protein synthesis.
- 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.**

Macrolides:

1- Old Generation (Erythromycin):

- Active against Gram-positive bacteria.
- Low activity against Gram-negative bacteria.

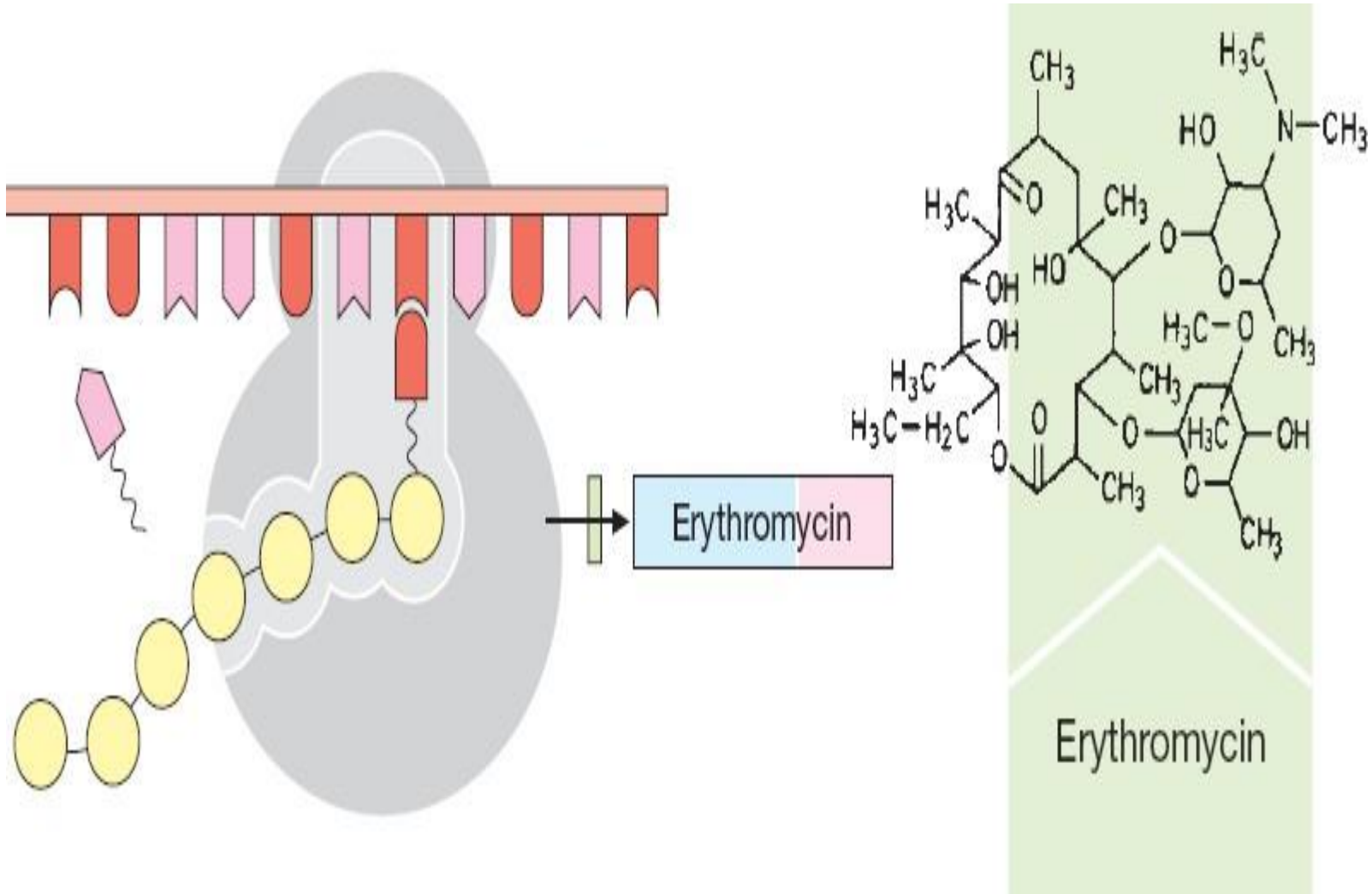
2- Newer Generation (Clarithromycin & Azithromycin):

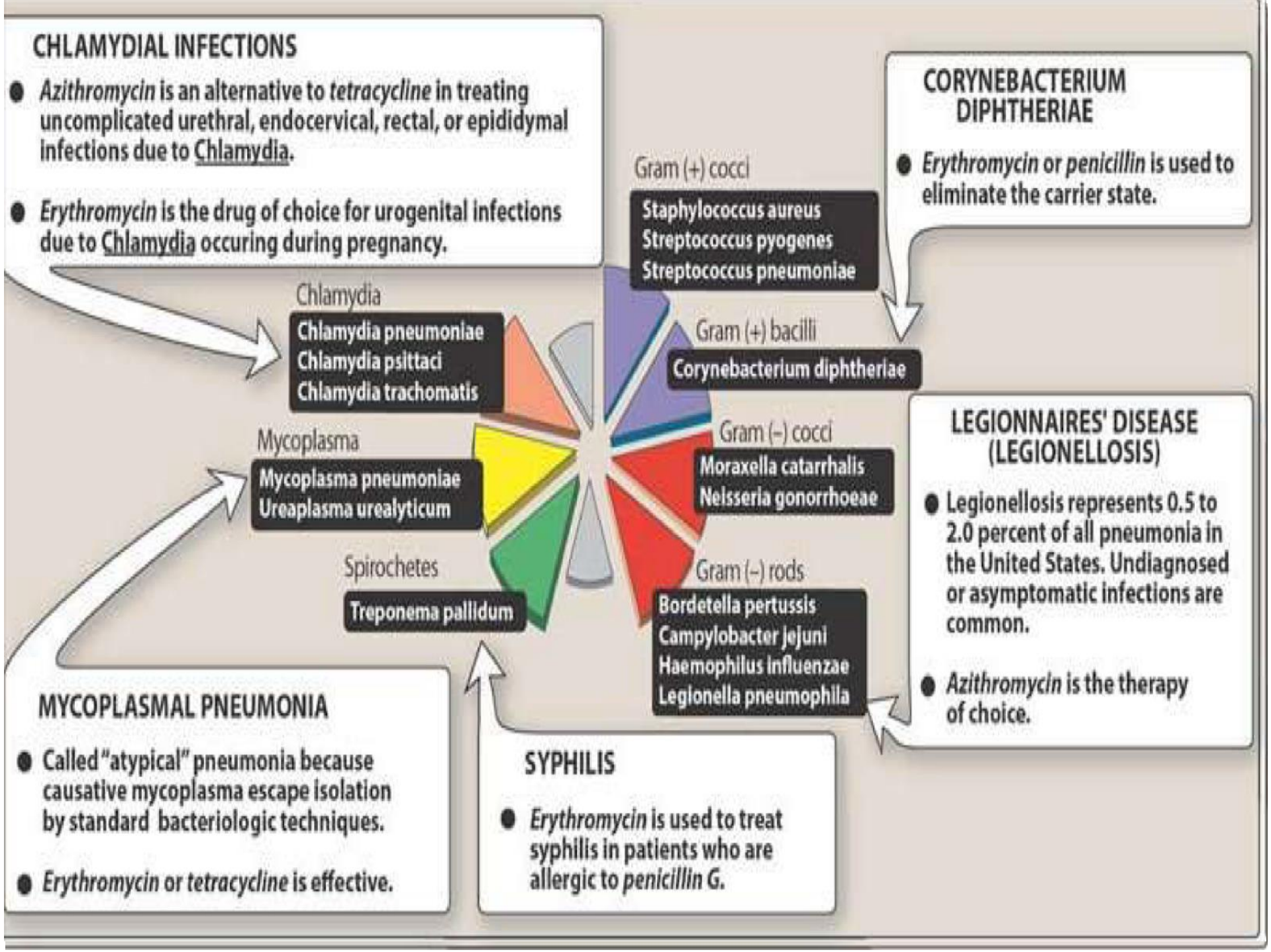
- Good activity against both Gram-positive and Gram-negative bacteria.
- Active against Atypical bacteria (e.g., Mycoplasma).
- **Note:** Azithromycin is effective against H. influenzae and E. coli.

3- Newest Generation (Telithromycin)

Macrolides Mechanism of Action (Bacteriostatic):

Macrolides bind to the **50S ribosomal subunit**, preventing the elongation of the amino acid polypeptide chain, which will inhibit protein synthesis.


Erythromycin
Erythromycin

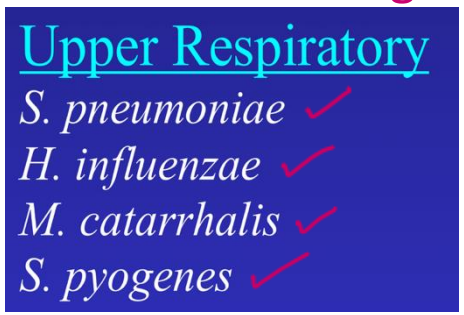

CHLAMYDIAL INFECTIONS
Azithromycin is an alternative to tetracycline in treating uncomplicated urethral, endocervical, rectal, or epididymal infections due to Chlamydia.
Erythromycin is the drug of choice for urogenital infections due to Chlamydia occuring during pregnancy.
CORYNEBACTERIUM DIPHTHERIAE
Erythromycin or penicillin is used to eliminate the carrier state.
Gram (+) cocci
Staphylococcus aureus
Streptococcus pyogenes
Streptococcus pneumoniae
Chlamydia
Chlamydia pneumoniae
Chlamydia psittaci
Chlamydia trachomatis
Gram (+) bacilli
Corynebacterium diphtheriae
Mycoplasma
Mycoplasma pneumoniae
Ureaplasma urealyticum
Gram (–) cocci
Moraxella catarrhalis
Neisseria gonorrhoeae
LEGIONNAIRES' DISEASE (LEGIONELLOSIS)
Legionellosis represents 0.5 to 2.0 percent of all pneumonia in the United States. Undiagnosed or asymptomatic infections are common.
Azithromycin is the therapy of choice.
Spirochetes
Treponema pallidum
Gram (–) rods
Bordetella pertussis
Campylobacter jejuni
Haemophilus influenzae
Legionella pneumophila
MYCOPLASMAL PNEUMONIA
Called "atypical" pneumonia because causative mycoplasma escape isolation by standard bacteriologic techniques.
Erythromycin or tetracycline is effective.
SYPHILIS
Erythromycin is used to treat syphilis in patients who are allergic to penicillin G.

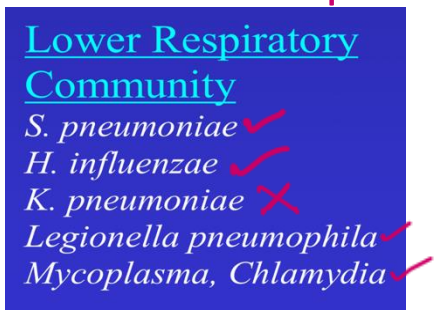
Macrolides Spectrum:

Macrolides are generally active against a broad range of bacteria, including Staphylococcus, Streptococcus, Corynebacterium diphtheriae, Moraxella, mycoplasma, syphilis, Neisseria, and H. influenzae.

Respiratory Tract Infections (The Newer Generation):

Unlike Erythromycin, the **newer drugs (Azithromycin and Clarithromycin)** are **effective against most upper and lower respiratory tract infections, except for K.pneumonia.** They specifically target Streptococcus pneumoniae, Moraxella catarrhalis, H. influenzae, and Streptococcus pyogenes **(Respiratory Tract Bacteria).** Because of this coverage, Macrolides are the drug of choice for upper respiratory infections in patients who are allergic to Penicillin and Cephalosporins.





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.

Community Acquired Pneumonia (CAP) Treatment:
Azithromycin and Clarithromycin are considered drugs of choice for treating Community Acquired Pneumonia. However, they have a gap in their spectrum: they are **ineffective against Klebsiella pneumoniae.** So**,** to ensure the treatment covers all potential pathogens, we combine the **Macrolide with a Beta-lactam antibiotic**. This second drug must be active against Klebsiella pneumoniae and other typical bacteria.

Empiric Therapy Strategy:
Common antibodies for this combination include **2nd or 3rd generation Cephalosporins, or Augmentin**. By using this combination, we successfully treat **all common Upper and Lower Respiratory System infections.** This dual approach is the standard **empirical treatment** to ensure Klebsiella pneumoniae is not missed.

Macrolides clinical uses

- **Clarithromycin is effective against *Mycobacterium avium cellulare* which can cause chronic lung disease in elderly or immunologically compromised individuals.**

- **Clarithromycin : Adjunct in treatment of duodenal ulcer (H. pylori)**

- **Azithromycin shows particularly good activity against chlamydial urethritis**

  Except for its cost, it is now the preferred therapy for urethritis

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.**

Azithromycin

- azithromycin penetrates intomost 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. See next slide fore more explanation:

Tissue Penetration and Half-Life:

Azithromycin has excellent penetration into most body tissues, with the exception of the Cerebrospinal Fluid (CSF). It accumulates in the tissues and releases very slowly, resulting in a long tissue half-life of 2 to 4 days. This allows the drug to remain active against bacteria hiding in tissue reservoirs for much longer than drugs that only stay in the serum.

Targeted Delivery via Neutrophils:
This antibiotic is unique because it enters neutrophils (white blood cells). When these neutrophils are recruited to an infection, they carry the Azithromycin with them, delivering the drug directly to the site of inflammation.

Advantage in Chlamydia Treatment:
Because of its long half-life and tissue concentration, Azithromycin is often preferred over Tetracyclines for treating Chlamydia. Instead of taking Doxycycline (100 mg) twice daily for a full week, a patient can be treated with a single 2-gram dose of Azithromycin. We also can kill the resistant streptococcus pneumonia by increasing the dose.

Macrolides

- **Ototoxicity:** Transient deafness has been associated with erythromycin only. especially at high dosages.

- **Cholestatic jaundice** especially with the estolate form of erythromycin only.

Important Note: Erythromycin might cause ototxicity and cholestatic jaundice, by closing the bile duct.

Additional Resources:

رسالة من الفريق العلمي:

اذكرونا بدعوة صادقة بظهر الغيب.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			