Clinical case

- A 50-year-old man is treated for septic shock with multiple antibiotics. Seven days later, the patient is alert and oriented, and his tissue perfusion has returned to normal. However, he describes a terrible feeling that “the world is spinning.”

- **Which of the following therapeutic agents is most likely responsible for this patient’s symptom?**

  (A) Erythromycin (B) Gentamycin
  (C) Imipenem (D) Metronidazole
  (E) Piperacillin-tazobactam

- **Gentamycin is effective against:**

  a) Gram +ve aerobes b) Gram –ve anerobes
  c) Atypical bacteria d) Gram –ve aerobes

- **Common toxic adverse effects encountered with gentamycin include:**

  a) Hepatotoxicity b) Myelosuppression
  c) Nephrotoxicity d) Cardiotoxicity

Treatment of lower respiratory tract infections
Pneumonia

By Dr. Rania A. Abdel-Emam

Pneumonia

Def. Infection of the lungs' tissues.
Alveoli (air sacs of lungs) fill with fluid and pus, making breathing more difficult.

- **Pneumococcal pneumonia** Caused by bacteria called pneumococcus (*Streptococcus pneumoniae*).
- Can also be caused by other bacteria, viruses, fungi, parasites.
- Most cases of pneumonia are spread person-to-person by coughing out of tiny droplets. Some pathogens can live in nose and throat without causing disease. But when inhaled into lungs, they can cause pneumonia.

How to manage a case of pneumonia?

- **Proper diagnosis :Hx, P/E, CXR**
- **Pathogen directed antimicrobial therapy whenever possible**
- **Prompt initiation of Antibiotic therapy**
- **Decision to hospitalize based on prognostic criteria**

Outpatient treatment

- ❑ Previously healthy, no comorbidity and no risk factors for drug-resistant
- A macrolide (azithromycin, clarithromycin, or erythromycin) (strong recommendation)
- B. Doxycycline (weak recommendation)

Inpatient treatment

- ❑ Presence of comorbidities, such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; use of immunosuppressing drugs; use of antimicrobials within the previous 3 months……..
- A fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) (strong recommendation)
- A β-lactam **plus** a macrolide (strong recommendation) (High-dose amoxicillin [e.g., 1 g 3 times daily] or amoxicillin-clavulanate [2 g 2 times daily] is preferred; alternatives include ceftriaxone, cefpodoxime, and cefuroxime [500 mg 2 times daily]; doxycycline (is an alternative to the macrolide.)

Inpatient, ICU treatment ……

- A β-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **plus** either azithromycin or a fluoroquinolone (strong recommendation).
- **(For penicillin-allergic patients**, a fluoroquinolone and aztreonam are recommended.)

or

- the above β-lactam plus an aminoglycoside and azithromycin

or

- the above β-lactam plus an aminoglycoside and a fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for the above β-lactam). (Moderate recommendation)

- If MRSA is suspected, vancomycin (15 mg/kg IV every 12 hours, in seriously ill patients, a loading dose of 25 to 30 mg/kg may be given.
- For *Pseudomonas* infection, use an antipneumococcal, antipseudomonal β-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750-mg dose)

I- CELL WALL SYNTHESIS INHIBITORS

1- BETA-LACTAM ANTIBIOTICS:

Examples: I- Penicillin & Cephalosporins

II- Monobactams e.g. aztreonam

III- Carbapenems e.g. imipenem, meropenem

PENICILLINS

- **Contain β-lactam ring that mediates the anti-bacterial action.**

➢ Mechanism of action:

They inhibit cell wall synthesis in the bacteria through inhibition of transpeptidation reaction required for synthesis of peptidoglycan (main step in cell wall synthesis).

➢ ADRs:

1. Hypersensitivity reactions
2. GIT distress and superinfections

Third generation cephalosporins

e.g. ceftriaxone, cefixime

Therapeutic uses:

1- Penicillin resistant pneumococcal infection.

Most of 3rd generation cephalosporins are given parenterally.

Fourth generation cephalosporins

e.g. cefipime

Therapeutic uses:

1- Infections not responding to 3rd generation cephalosporins.

➢ ADRs:

1- Hypersensitivity reactions: as penicillins

2- Pain at injection site

MONOBACTAM e.g. Aztreonam

CARBAPENEMS e.g. Imipenem & Meropenem

- Contain β-lactam ring.

➢ **Mechanism of action:** same as penicillins

➢ **Therapeutic uses:**

1- Hospital acquired pneumonia

2- Infections caused by pseudomonas species

OTHER CELL WALL SYNTHESIS INHIBITORS

2- GLYCOPEPTIDE ANTIBIOTICS:

Examples: I- Vancomycin and Teicoplanin

➢ **Mechanism of action:**

Inhibition of cell wall synthesis through inhibition of elongation of peptidoglycan chain required for cell wall synthesis.

➢ **Pharmacokinetics:**

Not absorbed orally (given parenterally), Teicoplanin has longer half life.

➢ **Therapeutic uses:**

1- MERSA infection: pneumonia caused by MERSA

➢ **ADRs:**

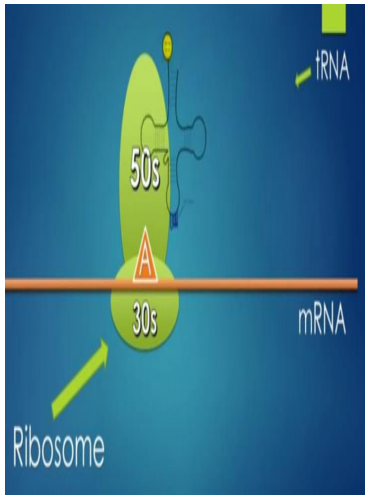
Ototoxicity and Nephrotoxicity.

Red man syndrome [with RAPID I.V. infusion] due to diffuse flushing

II- PROTEIN SYNTHESIS INHIBITORS

❑ AMINOGLYCOSIDES:

Gentamycin, Tobramycin, Amikacin, Streptomycin and Neomycin.



➢ Mechanism of action:

Inhibition of protein synthesis through binding to 30S ribosomal subunit causing misreading of the codon on mRNA.

➢ Therapeutic uses:

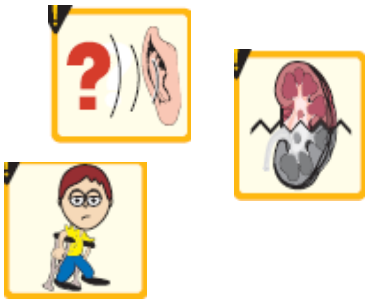
1- Pneumonia caused by gm –ve bacilli, in combination with β-lactams

➢ ADRs:

1- Ototoxicity

2- Nephrotoxicity.

3- Neuromuscular blockade.



❑ **MACROLIDES:** Erythromycin, Azithromycin and Clarithromycin

** **KETOLIDES:** Telithromycin

➢ **Mechanism of action:**

Inhibition of protein synthesis

↓

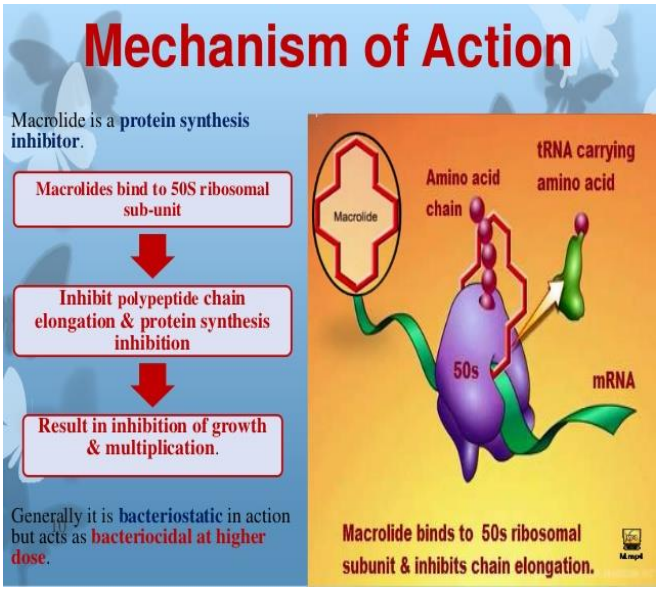
binding to 50S ribosomal subunit

↓

Inhibiting the **translocation** of the growing (nascent) polypeptide chain [temporarily residing] at the acceptor (A) site of the peptidyl-transferase

↓

fail to move to the peptide (P) site.



➢ **Antimicrobial activity**

Clarithromycin & Azithromycin are active against atypical bacteria as chlamydia, mycoplasma.

❑ MACROLIDES: Erythromycin, Azithromycin, Clarithromycin

➢ **Therapeutic uses:**

1- ***Erythromycin is alternative to penicillin in cases of hypersensitivity.***

2- **Lower respiratory tract infections caused by susceptible organisms**

➢ **ADRs:**

1- **GI irritation: *diarrhea & abdominal cramps* *(erythromycin is motilin receptor agonist).* Less with new macrolides.**

2- **Acute cholestatic hepatitis (hypersensitivity reaction).**

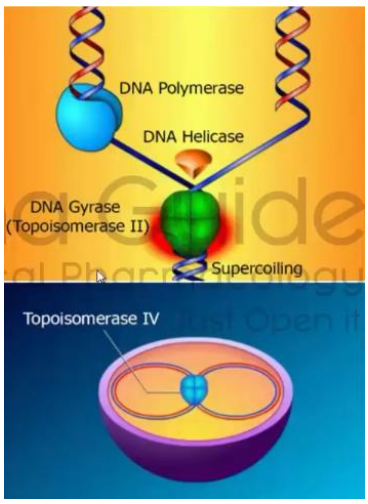
3- **Cardiac toxicity: erythromycin, clarithromycin and telithromycin [but not azithromycin] may cause cardiac arrhythmias (prolonged QT interval).**

4- Drug interactions: macrolides except azithromycin are CYP3A4 inhibitors. Interaction with carbamazepine, corticosteroids, cyclosporine and valproate.

III- Nucleic Acid Synthesis Inhibitors

Fluoroquinolones → **Mechanism of Action**

- Bactericidal
- Block bacterial DNA synthesis by inhibiting bacterial Topoisomerase II (DNA gyrase) & Topoisomerase IV.



Clinical Uses

1.Resp. tract Infections e.g. pneumonia caused by S. aureus, H. influenza, chlamydia.

What vaccines will help protect you from pneumonia?

- **In the United States, there are several vaccines available for preventing pneumonia:**
  - 2 pneumococcal vaccines
  - vaccines against *Haemophilus influenzae* type b (Hib), whooping cough, chickenpox, measles, and flu
- **Adults should check with their doctors – they may need vaccines or boosters to vaccinations that they got as children.**

Clinical case

- Gentamycin acts by:

  a) Inhibition of bacterial wall synthesis.

  b) Inhibition of nucleic acid synthesis.

  c) Interfere with folic acid synthesis within the bacteria.

  d) Inhibition of bacterial protein synthesis.

- Gentamycin is often combined with β-lactam antibiotics because they act synergistically. (True – False)

- Enumerate the value of combination of aminoglycosides with β-lactam antibiotics.

thanks for listening!