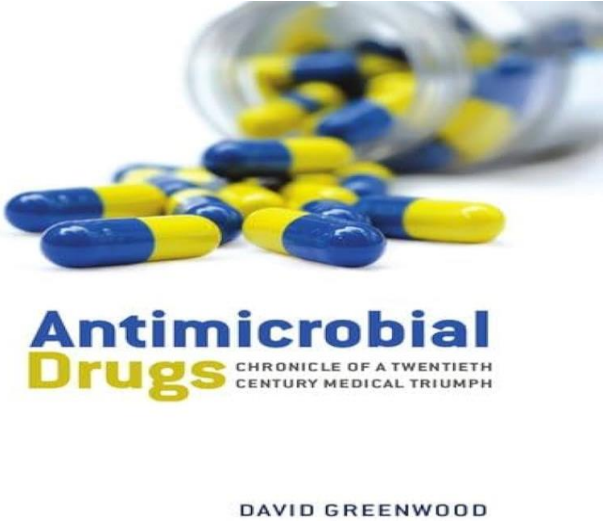


كلية التمريض – جامعة تكريت

المرحلة الثانية \ أدوية

PHARMACOLOGY FOR NURSING

أ د حسام الدين النجار

2024-2025 \ First Term

AMINOGLYCOSIDES, FLOUROQUINOLONES, METRONIDAZOL & TETRACYCLINES.

CLASSIFICATION

Systemic aminoglycosides

Streptomycin
Gentamicin
Kanamycin
Tobramycin
Amikacin
Sisomicin
Netilmicin
Paromomycin

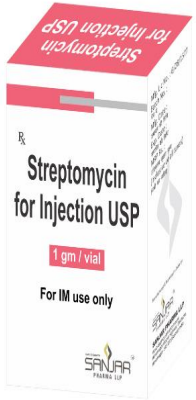
Topical aminoglycosides

Neomycin
Framycetin

Aminoglycosides

Gentamicin
Streptomycin
Tobramycin
Kanamycin
Neomycin
Amikacin
Netilmicin
Sisomicin

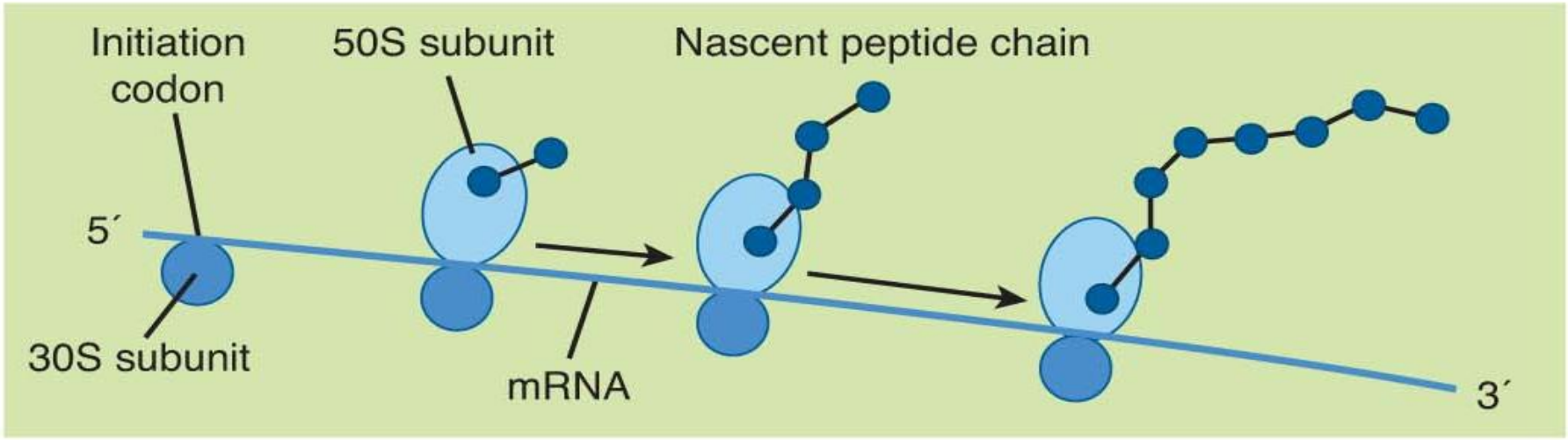
Bactericidal inhibitors of protein synthesis. Useful mainly against aerobic G-ve organisms.



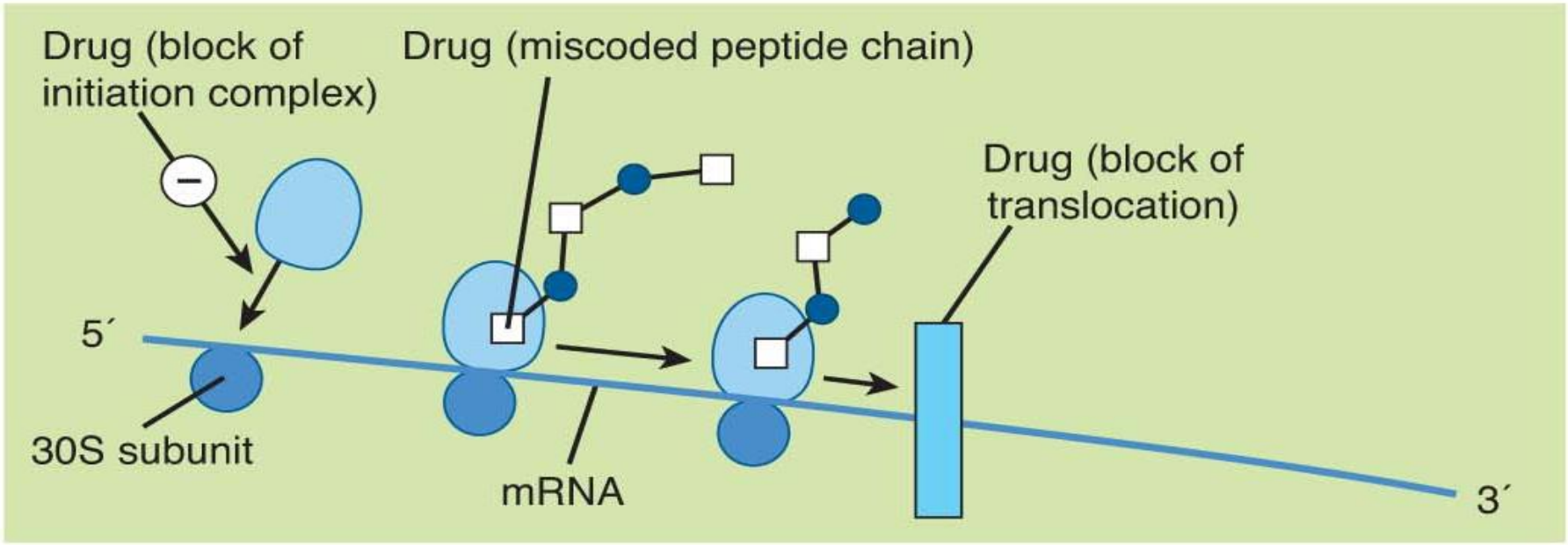
Mechanism of action:

- Bactericidal, irreversible inhibitors of protein synthesis.
- Inside the cell they bind to specific 30S-subunit:
- Block formation of the initiation complex.
- Misreading of mRNA →nonfunctional or toxic protein
- **The overall effect is irreversible and lethal for the cell (bactericidal)**

Normal bacterial cell



Aminoglycoside-treated bacterial cell



Spectrum of activity:

- **Bactericidal, broad spectrum antibiotics.**
- **Effective against aerobic G-ve bacilli, including Pseudomonas aeruginosa and some G+ve organisms**
- **Ineffective against anaerobes .**
- To achieve an additive or synergistic effect:

*Aminoglycosides are often combined with a beta-lactam antibiotic, or vancomycin.

**Or combined with a drug active against anaerobic bacteria.

Adverse Effects

- Patient factors (old age, previous exposure to aminoglycosides, and renal disease) tend to predispose patients to adverse reactions.
- **Ototoxicity: (vestibular and auditory dysfunction)**
- **Nephrotoxicity**
- It is directly related to high peak plasma levels and the duration of treatment.

- **Neomycin**, **kanamycin**, and **amikacin** are the most ototoxic agents.
- **Streptomycin** and **gentamicin** are the most vestibulotoxic.
- **Neomycin**, **tobramycin**, and **gentamicin** are the most nephrotoxic.
- **Neuromuscular paralysis:**
- Occurs in very high doses
- Patients with myasthenia gravis are particularly at risk.

Clinical Uses:

- Always used in combination with B-lactams to achieve bactericidal activity as well as to shorten duration of therapy.
- **Bacterial endocarditis:**
- **Penicillin + Gentamycin** are most commonly used for enterococcal, streptococcal and staphylococcal endocarditis.
- **Tubercluosis:**
- **Streptomycin** is used as a second-line agent for treatment of tuberculosis.
- Multidrug-resistant *M. tuberculosis* are usually susceptible to **amikacin**

- **brucellosis:**
- Streptomycin + tetracycline.
- **Sepsis and pneumonia:**
- Caused by G-ve bacteria that are likely to be resistant to other drugs

- **Topical application:**

A. **Skin infections**:

- Gentamicin creams, ointments, and solutions have been used for the treatment of infected burns, wounds, or skin lesions
- Ointment of **neomycin-polymyxin-bacitracin** combination is used for **infected skin lesions**.

- **Gentamycin** and **tobramycin** are used topically as ophthalmic drops and ointments for treating **bacterial eye infections** (e.g. conjuctivitis)
- **Neomycin and kanamycin** solutions are used on infected surfaces or injected into joints, the pleural cavity, tissue spaces, or abscess cavities.

B. Preparation for elective bowel surgery:

- Neomycin + erythromycin combination is given orally to reduce the aerobic bowel flora and anaerobes.

C. Hepatic coma:

- Neomycin together with reduced protein intake is used to suppress intestinal microflora, thus reducing ammonia intoxication (supplanted by lactulose, much less toxic).

D. Meningitis:

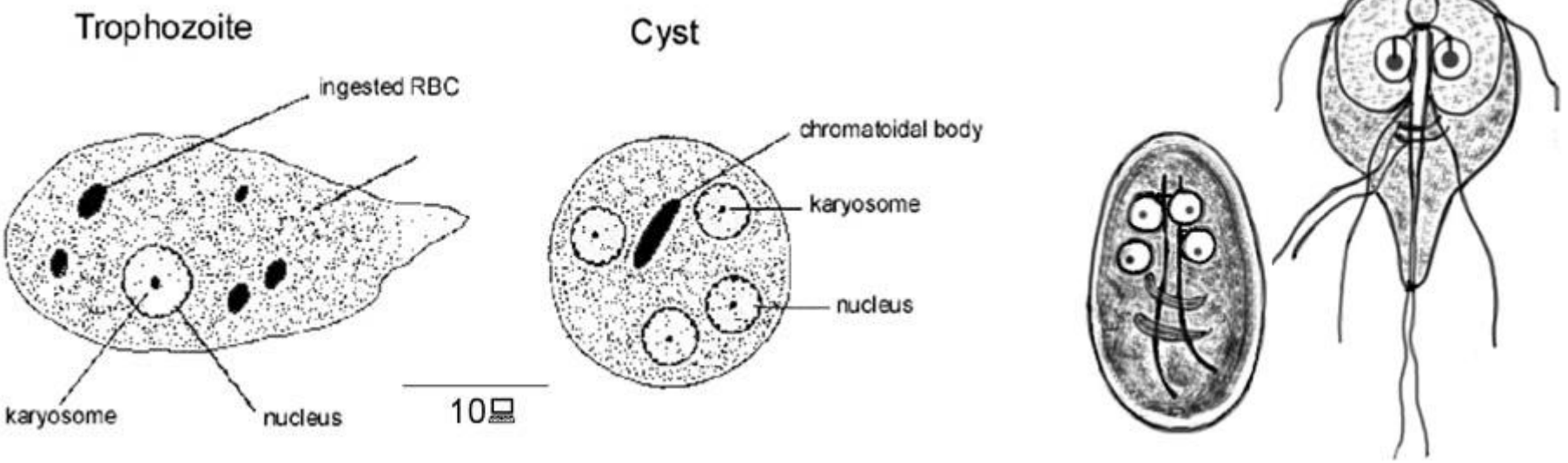
- Meningitis caused by G-ve bacteria has been treated with gentamicin given intrathecally but 3rd generation cephalosporins are preferable.

Contra-indications:

- Pregnancy
- Patient with myasthenia gravis.

Metronidazole

- *Metronidazole a nitroimidazole, is the mixed amebicide of choice for* treating amebic infections; it kills the **E. histolytica trophozoites,Giardia lamblia, Trichomonas vaginalis, anaerobic cocci, and anaerobic gram-negative bacilli (for example, Bacteroides species).**
- *Metronidazole is the drug of choice for the treatment* of pseudomembranous colitis

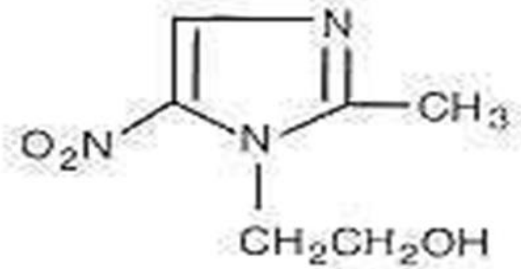

Trophozoite
ingested RBC
karyosome
nucleus
10
Cyst
chromatoidal body
karyosome
nucleus

Mechanism of action:

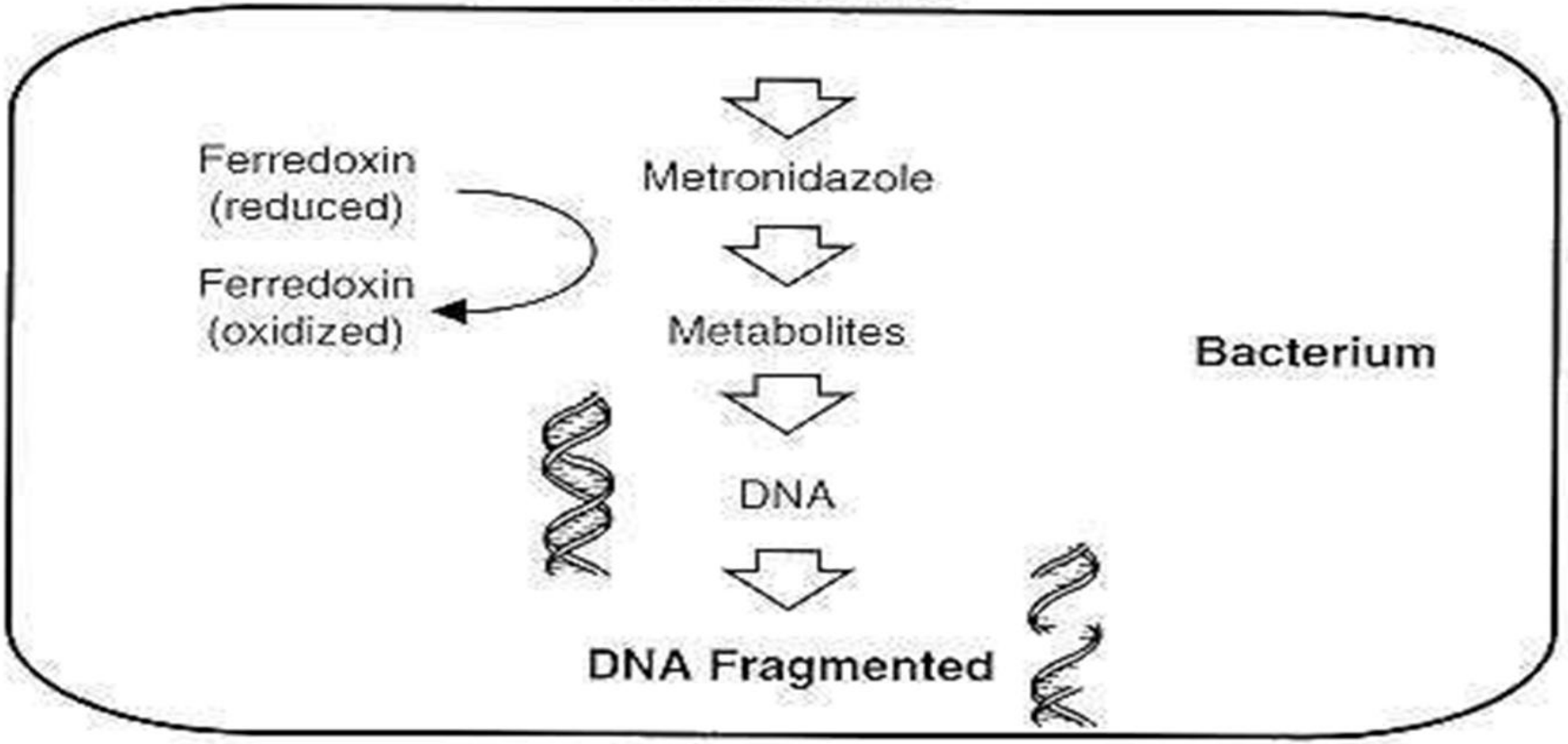
- It has selective toxicity to anaerobic microorganism and hypoxic cell.
- It is a prodrug requires reduction for activation in anaerobic bacteria and sensitive protozoans.

- The susceptible organisms derive energy from the oxidative fermentation of ketoacids such as pyruvate. Pyruvate decarboxylation, catalyzed by pyruvate:ferredoxin oxidoreductase (PFOR), produces electrons that reduce ferredoxin, which, in turn, catalytically donates its electrons to biological electron acceptors or to metronidazole.

- i.e **metronidazole acts as an electron acceptor → formation of reduced cytotoxic intermediate compounds (free radicals) → DNA damage (antimicrobial & mutagenic effect).**
- The toxic intermediate products then decay into inactive end product.



Metronidazole



Clinical Uses:

1. **Amebiasis:**
- Metronidazole or tinidazole is the drug of choice in the treatment of intestinal and extraintestinal amebiasis.
2. **Giardiasis:**
- Treatment of choice for giardiasis.
3. **Trichomoniasis**
- Metronidazole is the treatment of choice.
4. **Anaerobic infection** (endocarditis, dentistry).
- Metronidazole is the drug of choice for the treatment of pseudomembranous colitis caused by C difficile
- Prophylaxis of postsurgical abdominal and pelvic infections.
- In multi-drug regimen for treatment of peptic ulcer due to H.pylori.
- Tissue nematode infections
- Tetanus (with diazepam + tetanus immunogloulin)

Adverse Effects and Cautions :

- GIT disturbance: nausea, vomiting, epigastric distress, and abdominal cramps (most common).
- Dry mouth and unpleasant metallic taste.
- Oral moniliasis (yeast infection of the mouth
- CNS disturbance:Dizziness, vertigo, numbness or paresthesias and rarely encephalopathy, convulsion and ataxia. Should be used with caution in patients with CNS disease
- Urine discoloration: Reddish-brown urine.
- Disulfiram-like reactions: when taken with alcohol.
- Metronidazole potentiates the anticoagulant effect of warfarin.
- Chronic administration of large doses led to tumorigenicity in mice.

  Data on teratogenicity are inconsistent. Metronidazole is thus best avoided in pregnant or nursing women.

ANTIBIOTICS: FLUOROQUINOLONES

~ NURSING PHARMACOLOGY ~

OSMOSIS.org

Quinolones and Fluoroquinolones

Fluoroquinolone FQs are synthetic fluorinated analogs of nalidixic acid (quinolone)

➢ Mechanism of action:

Quinolones block bacterial DNA synthesis that is required for normal transcription and replication into the respective daughter cells during cell division.

- First-generation.
- cinoxacin
- nalidixic acid
- rosoxacin

- Second-generation
- ciprofloxacin
- enoxacin
- fleroxacin
- lomefloxacin
- norfloxacin
- ofloxacin

Third generation:

Gatifloxacin, gemifloxacin, and moxifloxacin. have improved activity against G+ve organisms, particularly S pneumoniae and some staphylococci.

3RD GENERATION: Unlike the first- and second-generations, the third-generation is active against streptococci as

grepafloxacin ,levofloxacin

- **fourth generation** fluoroquinolones act at DNA gyrase and topoisomerase IV. This dual action slows development of resistance. As gemifloxacin ,moxifloxacin

- Ciprofloxacin is the most active agent of this group against G-ve organisms especially Pseudo. aeruginosa.

- Levofloxacin (L-isomer of ofloxacin) has superior activity against G+ve organisms, including Streptococcus pneumoniae.

Spectrum of activity:

- They are bactericidal, broad spectrum.
- Effective against aerobic G-ve bacteria.
- Limited activity against G+ve organisms, but newer members have improved activity against G+ cocci.

- Ciprofloxacin is the most active agent of this group against G-ve organisms especially Pseudo. aeruginosa.

- Levofloxacin has superior activity against G+ve organisms, including Streptococcus pneumoniae.

- **Clinical Uses:**

1-Urinary tract infections: FQs (excep moxifloxacin) are effective in UTIs even when caused by multidrug-resistant bacteria, eg, pseudomonas.

2- GIT infections: FQs are also effective for bacterial diarrhea caused by shigella, salmonella, E coli, and campylobacter.

3- S**oft tissue and bone infections:**FQs (except norfloxacin) are effective in infections of the soft tissues, bones, and joints and in intra-abdominal infection, including those caused by multidrug-resistant organisms such as pseudomonas and enterobacter.

- Osteomyelitis and diabetic foot infections require prolong therapy with FQs plus anti-anaerobic agent

4-Ciprofloxacin is a drug of choice for prophylaxis and treatment of anthrax.

5-Sexually transmitted disease: Gonorrhea, chlamydial urethritis or cervicitis.

6-Ciprofloxacin, levofloxacin, or moxifloxacin is occasionally used for treatment of tuberculosis and atypical mycobacterial infections.

7-Eradication of meningococci from carriers or for prophylaxis of infection in neutropenic patients.

8-Respiratory tract infections: Levofloxacin, gatifloxacin, gemifloxacin, and moxifloxacin (respiratory FQs):

- Enhanced activity against G+ve and atypical pneumonia agents (eg, chlamydia, mycoplasma, and legionella), are effective and used increasingly for treatment of upper and lower respiratory tract infections.

➢ Adverse Effects

FQs are extremely well tolerated.

1-The most common effects are nausea, vomiting, and diarrhea.

2-Occasionally, headache, dizziness, insomnia, skin rash, or abnormal liver function tests develop.

3- Photosensitivity (lomefloxacin and pefloxacin).

4-QT prolongation may occur with gatifloxacin, levofloxacin, gemifloxacin, and moxifloxacin).

5-Gatifloxacin has been associated with hyperglycemia in diabetic patients and with hypoglycemia in patients also receiving oral hypoglycemic agents.

6-FQs may damage growing cartilage and cause an **arthropathy.**

7-Tendinitis : a rare but serious complication that may cause tendon rupture in adult. Risk factors for tendonitis include:

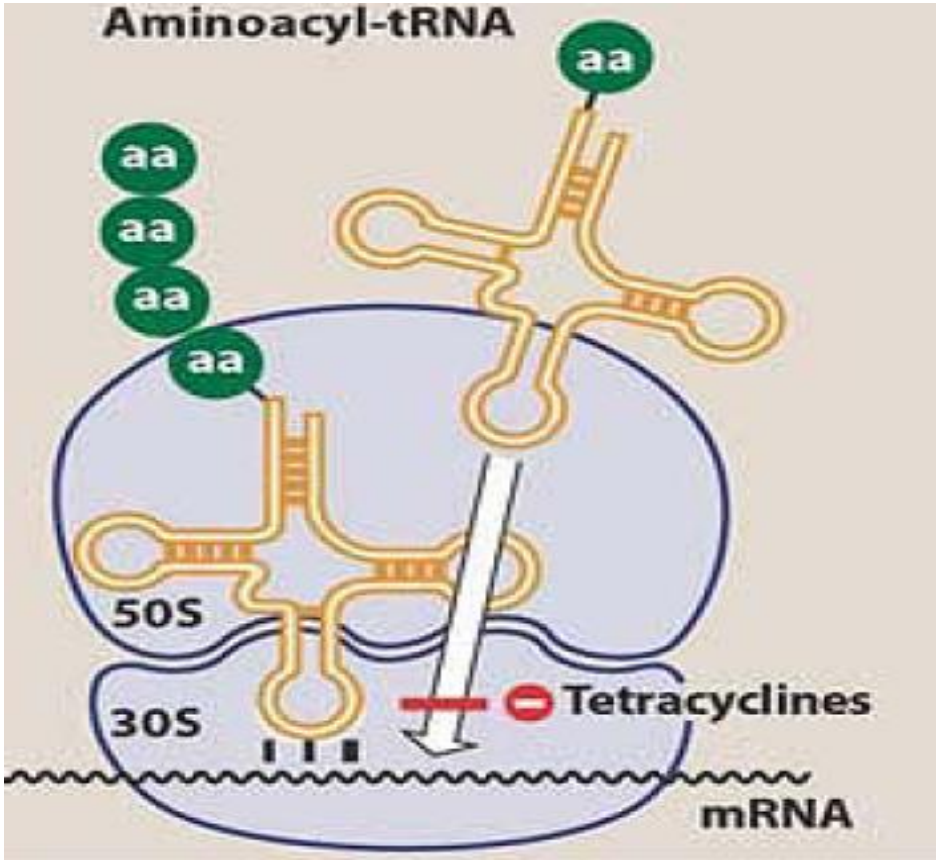
- Advanced age (> 60)
- Renal insufficiency.
- Concurrent steroid use.
- Diabetes mellitus, and a history of musculoskeletal disorders.

Achilles tendinitis or rupture is among the most serious side effects associated with FQs (90% with ciprofloxacin) also been noted with norfloxacin, pefloxacin, ofloxacin, and reccently levofloxacin

Tetracyclines

- **Chlortetracycline, tetracycline**, **oxytetracycline** (short acting, 6-8 hrs)
- **Demeclocycline** and **methacycline** (intermediate, 12 hrs)
- **Doxycycline** and **Minocycline** (16-18 hrs. long acting).
- **Tigecycline** (36 hrs)
- **Mechanism of action:**

  Tetracyclines binds reversibly to the 30S subunit of the bacterial ribosome, thereby blocking access of the amino acyl-tRNA to the mRNA-ribosome complex at the acceptor site (A site) resulting in inhibition of bacterial protein synthesis (bacteriostatic)



Tetracyclines binds to the 30S ribosomal subunit, thus preventing the binding of aminoacyl-tRNA to the ribosome. aa = amino acid.

- **Spectrum of activity:**
- Broad spectrum bacteriostatic agents.
- Active against aerobic, anaerobic G+ve, G-ve bacteria, Rickettsia, Chlamydia, Mycoplasma, Spirochetes and some protozoa (amoeba).
- **Pharmacokinetics:**
- All tetracyclines are adequately absorbed after oral ingestion, except Tigecycline (administered I.V)
- Chelate with metal ions (diary products, antacids and iron preparations decrease tetracycline absorption)
- Doxycycline and minocycline absorption is not affected by food.

- Distribute throughout the body fluids but with poor penetration to CSF (except for minocycline).
- Minocycline enters the brain in the absence of inflammation and also appears in tears and saliva (useful in eradicating the meningococcal carrier state)
- Accumulate in the liver, kidney, spleen , bone marrow and bones(accumulation in bones and teeth can damage the growing bones and teeth).
- All tetracyclines cross the placental barrier and concentrate in fetal bones and also excreted in breast milk.

Clinical Uses:

- **Rickettsial Infections:**
- Rocky mountain spotted fever, rickettsial pox.
- **Mycoplasma Infections.**
- *Mycoplasma pneumoniae*
- **Chlamydial Infections:** Pneumonia, bronchitis, or sinusitis, psittacosis, Trachoma, urethral infection
- **Syphilis**: Non pregnant, penicillin-allergic patients
- **Anthrax.** Doxycycline, for prevention or treatment
- **Bacillary Infections:**
- Brucellosis: Tetracyclines in combination with rifampin or streptomycin
- **Cholera**
- Infections caused by *Shigella, Salmonella*

- They are used in combination regimens to treat **H. pylori-associated ulcer**.
- Sometimes used in the treatment of **protozoal infections** (E. histolytica or P. falciparum).
- Treatment of **acne**
- **Eradication of meningococcal carrier state:** Minocycline, but rifampin is preferred.
- Treatment of **inappropriate secretion of ADH (ISADH):**
  - Demeclocycline
- **Tigecycline (I.V only):**
  - Tigecycline is FDA-approved for treatment of skin and intra-abdominal infections

Adverse effects:

- **GIT disturbance:**
- Epigastric distress, nausea, vomiting, anorexia and diarrhea.
- **Secondary infections:**
- Candidiasis or p*seudomembranous colitis caused by overgrowth of* Clostridium difficile
- **Effects on bony structures and teeth:**
- Permanent brown discoloration and hypoplasia of the teeth, and bone deformity or growth inhibition (contraindicated during pregnancy and for children below 8 years).
- **Liver Toxicity:**
- Especially during pregnancy, in patients with hepatic insufficiency and with ↑ I.V doses.
- Oxytetracycline and tetracycline are the least hepatotoxic

- **Kidney Toxicity**
- Doxycycline has fewer renal side effects than other tetracyclines
- Renal tubular acidosis and other renal injury have bee reported after administration of outdated tetracycline preparations (**Fanconi syndrome**).
- Demeclocycline: induces nephrogenic diabetes insipidus.
- **Phototoxicity:**
- Especially demeclocycline.
- **Vestibular problems:**
- Minocycline and doxycycline at doses above 100 mg.
- **Pseudotumor cerebri:**
- Benign intracranial hypertension in young infants. Occurs rarely in adults.
- **Contra-indication:**

1. Children
2. Pregnant & nursing woman.
3. Patient with renal failure (except doxycycline.


Thank you