

Treatment of Respiratory Tract Infections

By

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Slides are adopted and modified from Dr. **Mohammad Alhumayyd**

Objectives:

❖ At the end of lecture , the students should be able to understand the following:

- The types of respiratory tract infections
- The antibiotics that are commonly used to treat respiratory tract infections and their side effects
- Understand the mechanism of action, pharmacokinetics of individual drugs

Classification of respiratory tract infections

- **Upper respiratory tract infections (URTI)**

- **Lower respiratory tract infections (LRTI)**

Upper respiratory tract

Nasal cavity

Pharynx

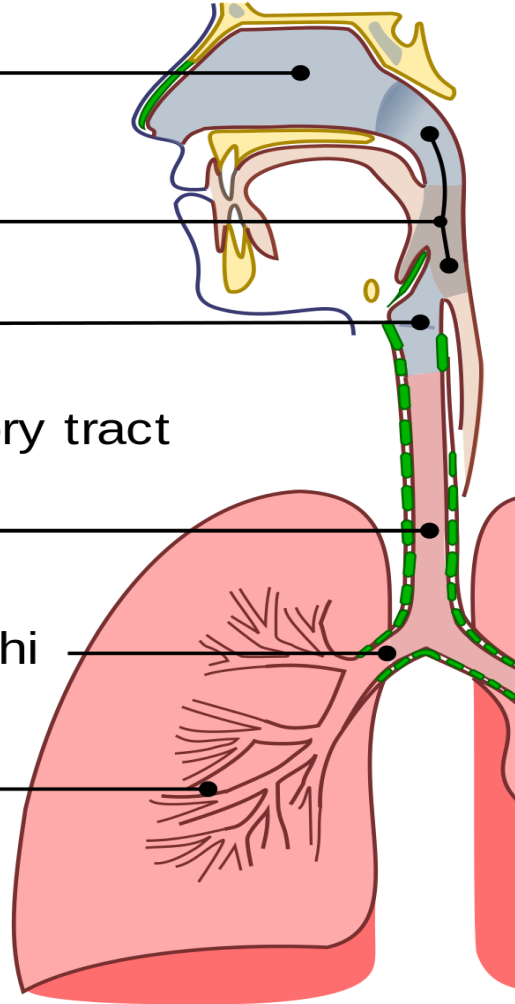
Larynx

Lower respiratory tract

Trachea

Primary bronchi

Lungs

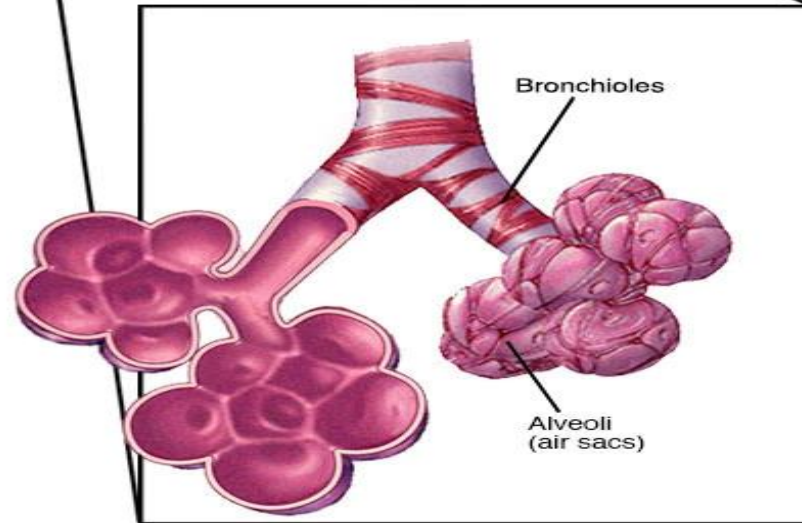
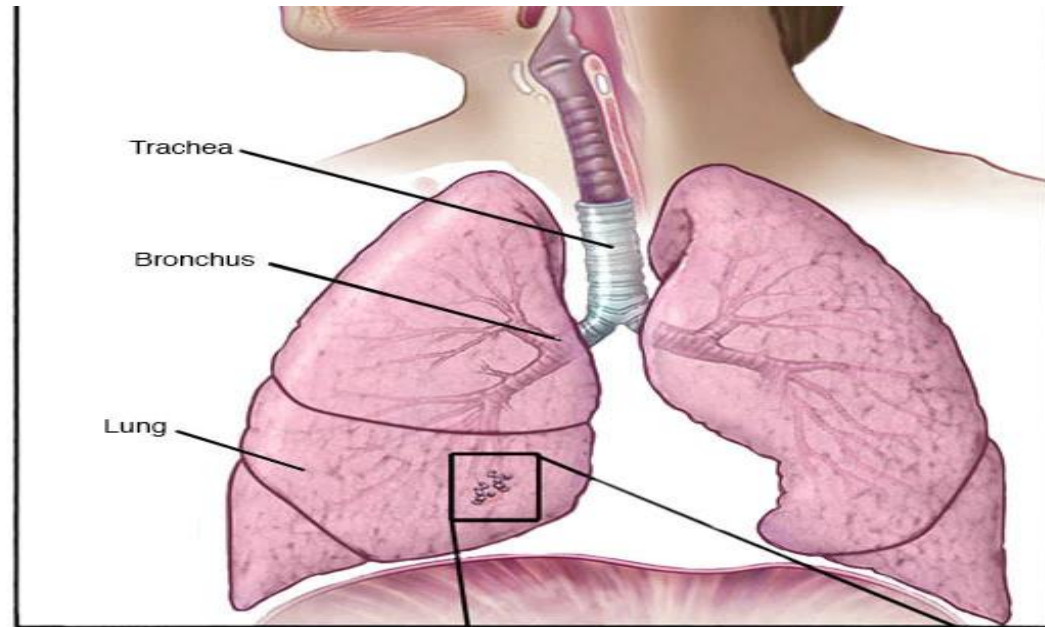


Causes of URTI's

- **Viruses** (should not be treated with antibiotics)
 - Treatment: rest and plenty of fluids, OTC cold and pain relievers.
- **Bacteria** (mainly Group A streptococcus H. influenzae)
 - Treatment: Antibiotics. The type depends on:
 - Type of bacteria
 - Sensitivity test

LRTI's (costly & more difficult to treat)

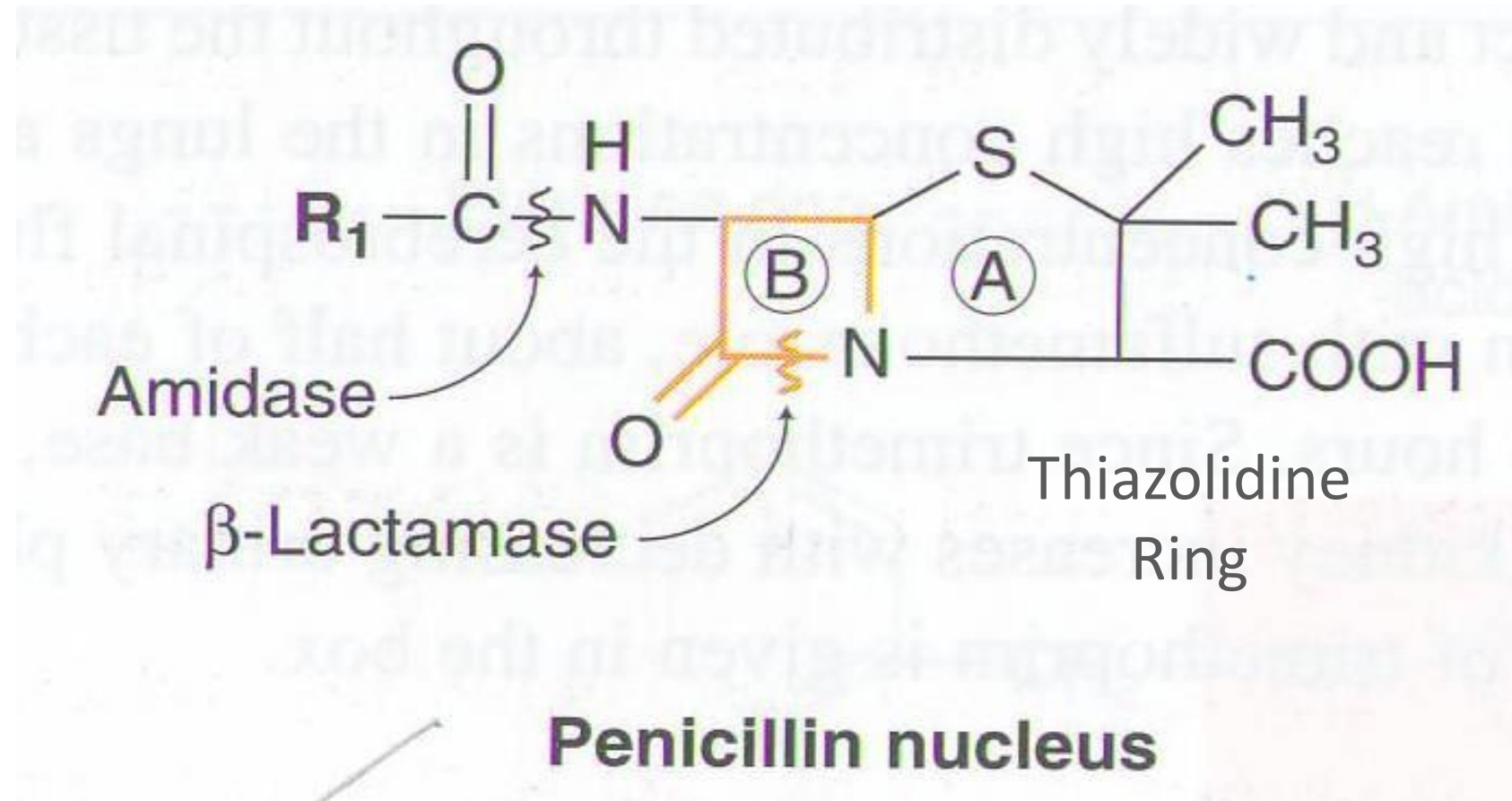
- **Bronchitis (inflammation of major bronchi & trachea)**
 - Acute
 - Chronic
 - Acute exacerbation of chronic bronchitis
 - Causes: viruses or bacteria (H. influenzae, S. pneumonia & M. catarrhalis).
- **Pneumonia (Serious infection of bronchioles & alveoli)**
 - Community –acquired (CAP)
 - Hospital-acquired
 - Causes: Bacteria S.pneumonia **** (66%)**, H.influenzae (20%), M.catarrhalis (20%)



Antibiotics used in the treatment of RTI's

- **Beta lactam antibiotics (Penicillins / Cephalosporins)**
- **Macrolides**
- **Fluoroquinolones**
- **Aminoglycosides**
- **Doxycycline**

Penicillins



Broad- spectrum penicillins

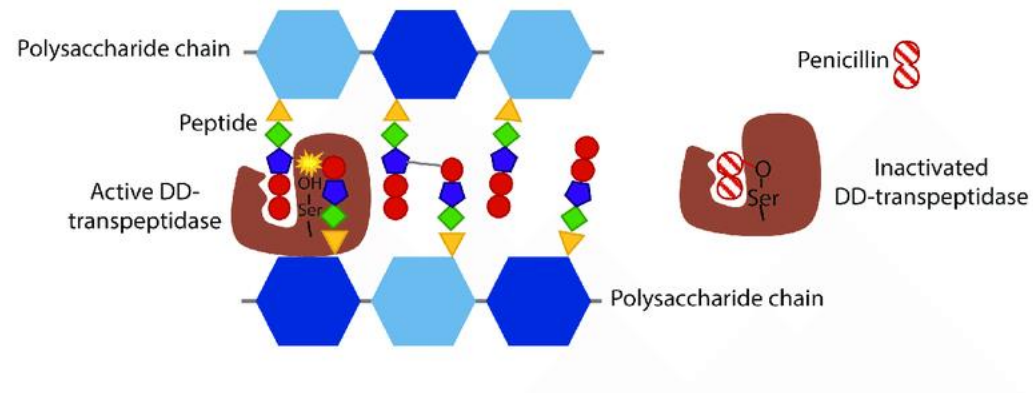
- Amoxicillin - Clavulanic acid
- Ampicillin - Sulbactam
- Piperacillin – tazobactam

❖ **Acts on both gram +ve & gram -ve microorganisms**

Mechanism of action

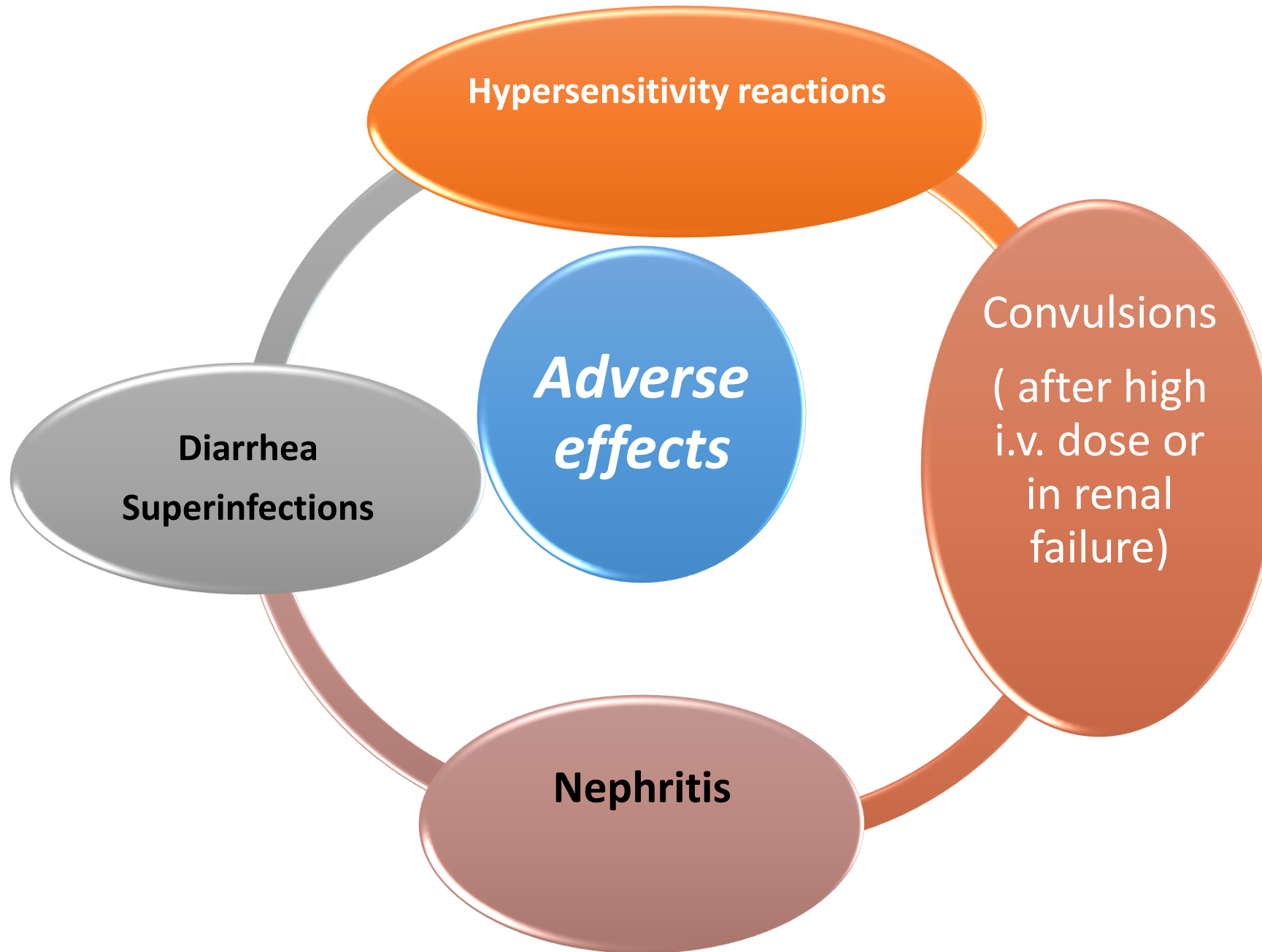
- Inhibits bacterial cell wall synthesis through inhibition of peptidoglycan layer of the cell wall

- Bactericidal



Pharmacokinetics

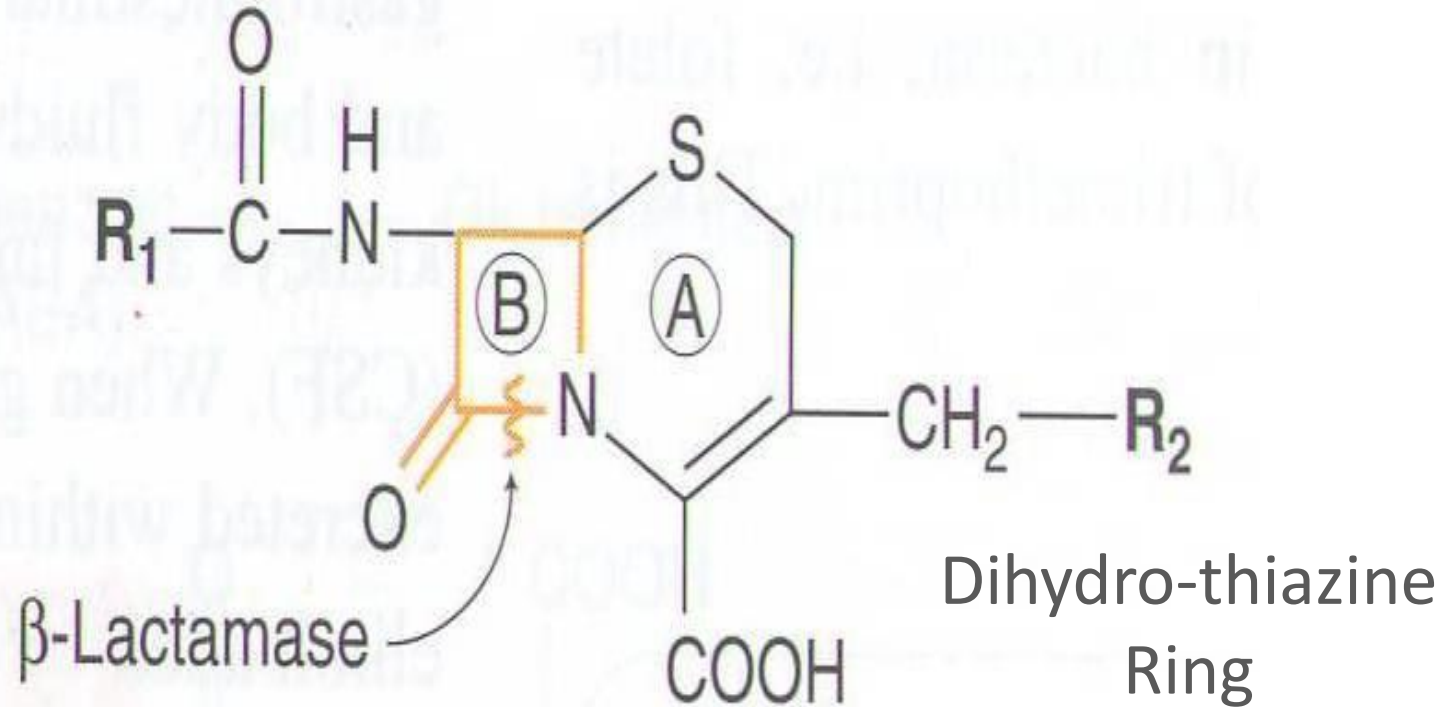
- **Given orally or parenterally**
- **Not metabolized in human**
- **Relatively lipid insoluble**
- **Excreted mostly unchanged in urine**
- **Half-life 30-60 min (increased in renal failure).**



Therapeutic uses

- Upper respiratory tract infections, Acute otitis media especially those produced by Group A gram positive beta-hemolytic streptococci
- Lower respiratory tract infections

Cephalosporin

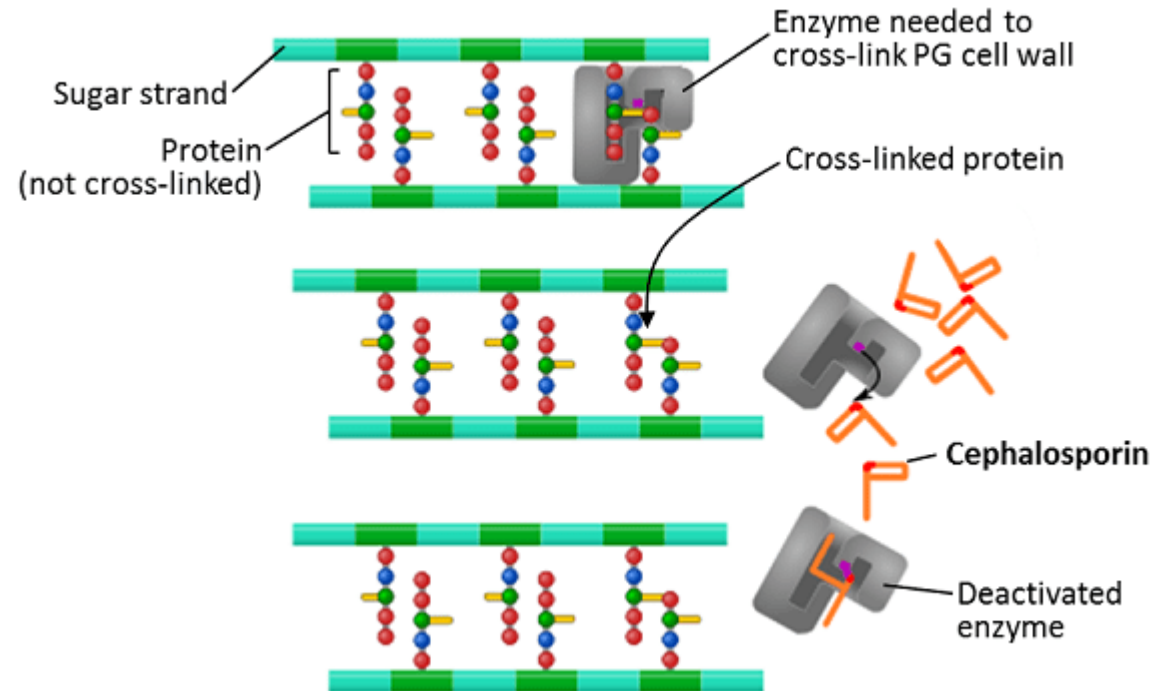


Cephalosporin nucleus

Mechanism of action

- Inhibit bacterial cell wall synthesis

- Bactericidal



1st Generation Cephalosporins

- Cephalexin
- Given orally
- Effective against **gram positive** bacteria
- Effective in URTI's

2nd Generation Cephalosporins

- Cefuroxime axetil , cefaclor
- Effective mainly against Gram-negative bacteria.
- Well absorbed orally
- Active against β -lactamase –producing bacteria
- Uses:
- Upper and lower respiratory tract infections
- Sinusitis, otitis media

3rd Generation Cephalosporins

- Ceftriaxone / Cefotaxime / Cefixime
- Given by intravenous route
- More effective against gram-negative bacilli
- Effective treatment in pneumonia produced by β -lactamase bacteria

Pharmacokinetics

- Given mainly parenterally
- Oral preparation (**Cefixime**)
- Penetration into CSF
- Excreted Mostly unchanged in the urine.
- Long Half-life (4-7h) (**ceftriaxone**)

Adverse effects of cephalosporins

- Hypersensitivity reactions
- Thrombophlebitis
- Superinfections
- Diarrhea

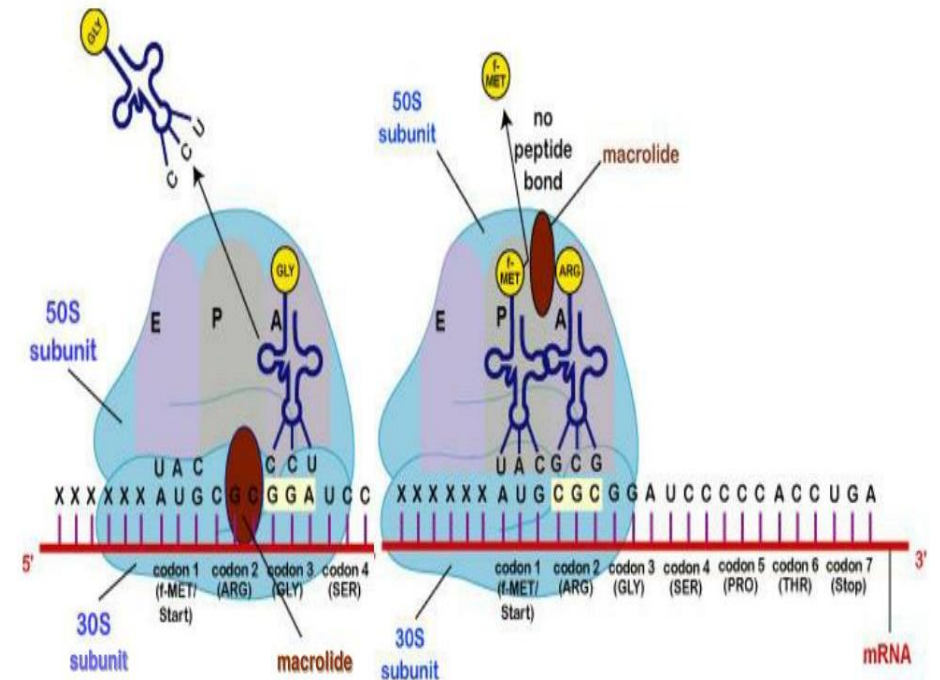
Macrolides

- Erythromycin
- Azithromycin
- Clarithromycin



Mechanism of action

- Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes
- Bacteriostatic
- Bactericidal at high concentrations



Clarithromycin

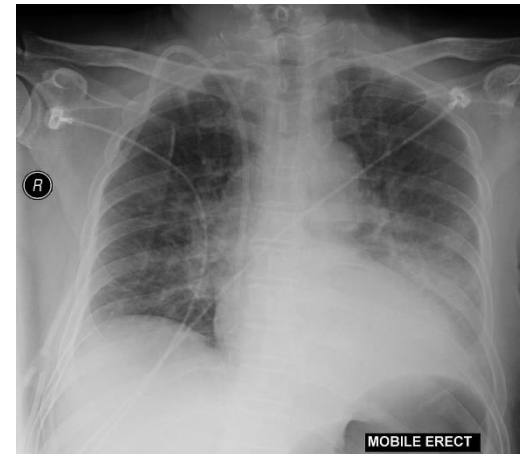
- More effective on **G +ve bacteria**
- Stable at gastric acidity
- **Inhibits cytochrome P450 system**
- Metabolized to **active metabolite**
- Excreted in urine 20-40% unchanged or metabolite & 60% in bile
- Half-life 6-8 hours

Azithromycin

- More effective on **G -ve bacteria**
- Stable at gastric acidity
- Undergo some hepatic metabolism (**inactive metabolite**)
- Biliary route is the major route of elimination. Only 10-15% excreted unchanged in the urine
- Half- life (3 days)
- Once daily dosing
- **No effect on cytochrome P- 450**

Clinical uses of Macrolides

- Chlamydial pneumonia
- Legionella pneumonia



Adverse effects

- Hypersensitivity
- GI disturbance

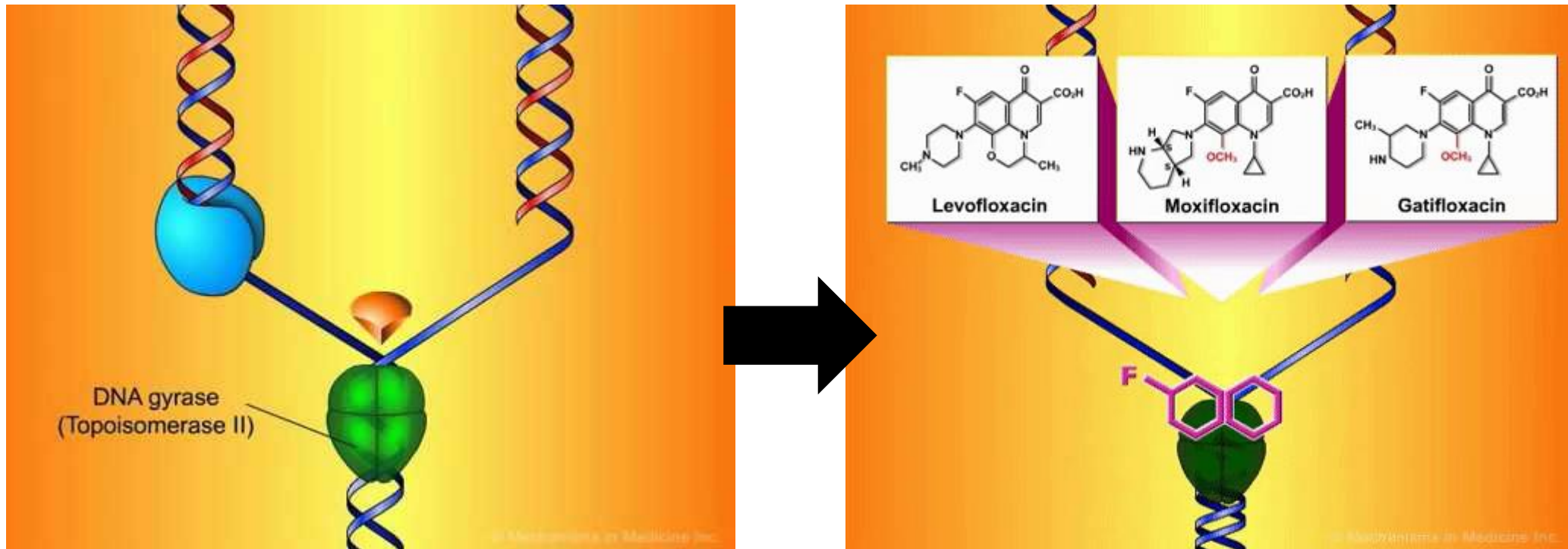


Fluoroquinolones

- **Ciprofloxacin**
- **Moxifloxacin**
- **Gatifloxacin**

Mechanism of action

Inhibit DNA Gyrase enzyme (an enzyme involved in DNA supercoiling)



Antibacterial spectrum

- Ciprofloxacin, mainly effective against G -ve bacteria
- Moxifloxacin, and Gatifloxacin G -ve & G +ve & given once daily. (highly active against *Pseudomonas* species)

Pharmacokinetics

- Given orally or parenterally.
- Concentrates in many tissues (kidney, prostate, lung & bones/ joints)
- Excreted mainly through the kidney
- Their relatively long Half-life allows once daily (moxifloxacin & Gatifloxacin) & twice-daily (ciprofloxacin) dosing.

Clinical Uses

- **Acute exacerbation of chronic obstructive pulmonary disease**
- **Community acquired pneumonia**
- **Legionella pneumonia**

Adverse effects

- Nausea , vomiting , diarrhea
- CNS effects (confusion, insomnia, headache, anxiety)
- Damage of growing cartilage (**arthropathy**)
- Phototoxicity (avoid excessive sunlight)

Contraindications

- Not recommended for patients younger than 18 years
- Pregnancy
- Breast feeding women

Questions???