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Respiratory Tract Infections Treatment

Respiratory Block

430 Pharmacology team

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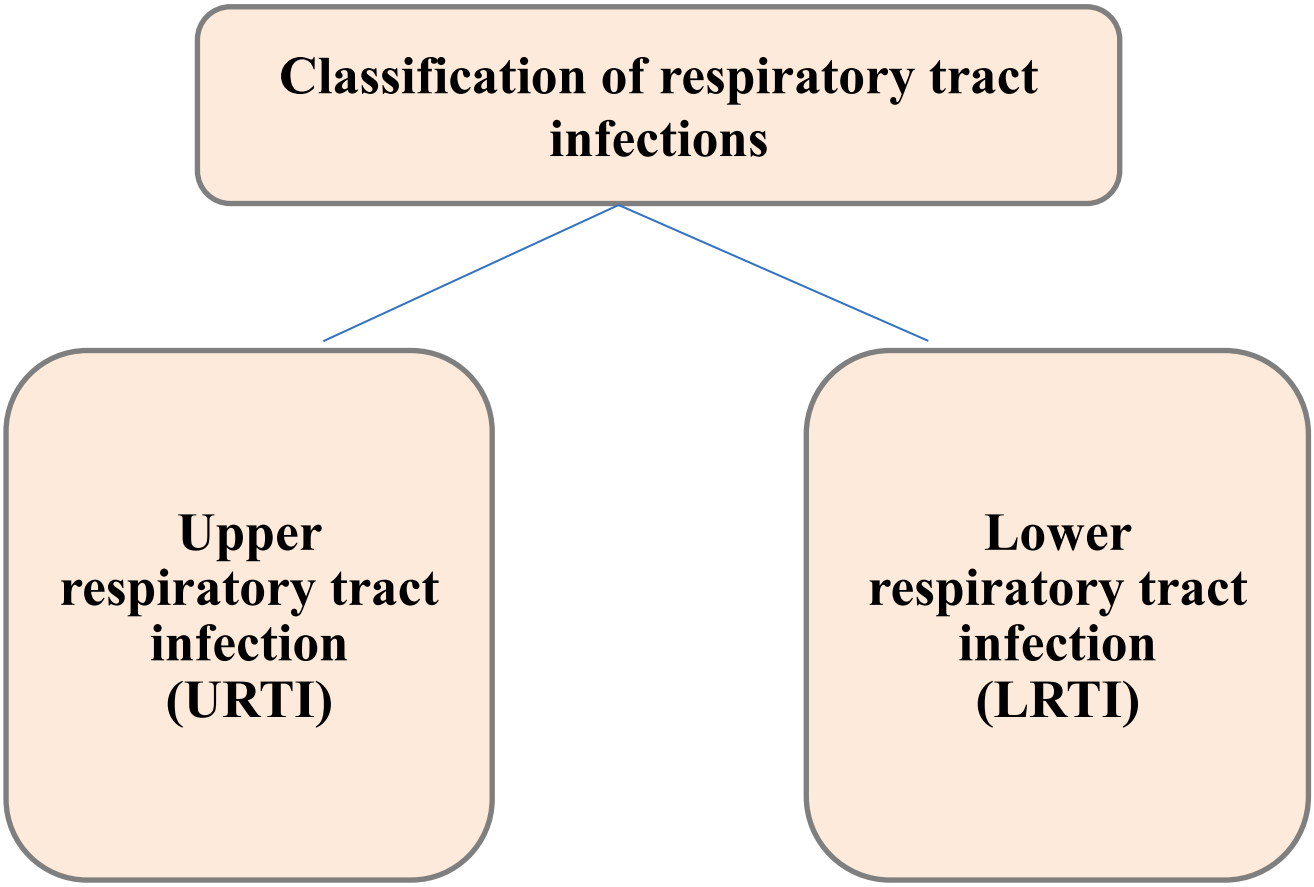


UPPER RESPIRATORY TRACT INFECTION (URTI)

- **Rhinitis :** inflammation of the nasal cavity .
- **Sinusitis :** inflammation of sinuses .
- **Pharyngitis :** inflammation of the pharynx, uvula, tonsils .
- **Laryngitis :** inflammation of the larynx .
- **Laryngotracheitis :** inflammation of the larynx & trachea .
- **Tracheitis :** inflammation of trachea .
- **Otitis media :** inflammation of middle ear .

LOWER RESPIRATORY TRACT INFECTION (LRTI)

- **Bronchitis :**
  Acute .
  Chronic .
  Acute exacerbation of chronic bronchitis .
- **Pneumonia :**
  Community - acquired or Hospital – acquired .

Are more costly to treat and generally more serious than URTIs

- **Causes of URTI,s :**
  - **Viruses :** (over 200 different types have been isolated) .
  - **Bacteria :** mainly Group A streptococcus & H. influenzae .

- **Causes of LRTI,s :**
  - **Bacteria mainly:**
    Streptococcus pneumonia
    Haemophilus influenza
    Moraxella catarrhalis

LINES OF TREATMENT :

Analgesics (NSAIDs) , Nasal decongestant , Vitamin C , Drinking plenty of fluids , Antiviral , Antibiotics .

ANTIBIOTICS

- **First-line treatment (given for 3-10 days) :**

  For the treatment of moderate to severe infections
  Broad spectrum penicillins

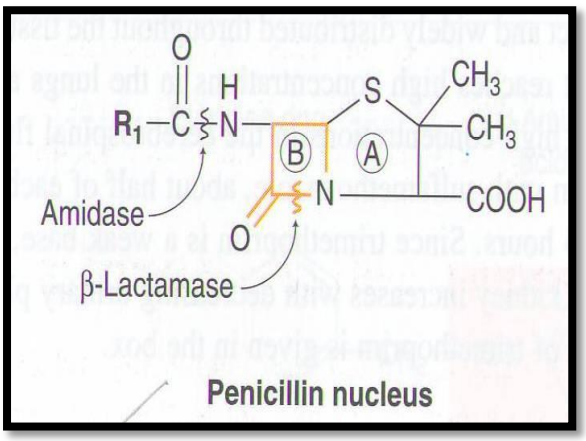
- **Second-line treatment :**

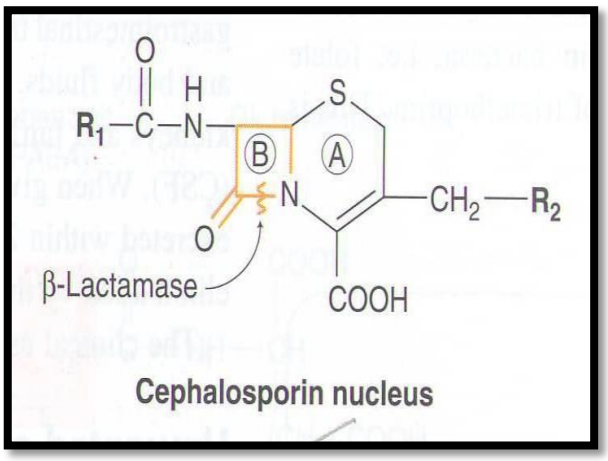
  Used in allergic patients to drugs of first –line or in antibiotic – resistant organisms

  - **Macrolides**
  - **Cephalosporins**
  - **Fluoroquinolones**

❖ Beta-Lactam Antibiotic

Group of antibiotic share a common **β-lactam ring**
include *penicillin* & *cephalosporin*





β-Lactam antibiotics work by **inhibiting cell wall synthesis** by the bacterial organism

Bacteria often develop resistance to β-lactam antibiotics by synthesizing **beta-lactamase**

(An enzyme that attacks the β-lactam ring and make the drug unfunctional)

▪ Penicillins *(β-Lactam Antibiotics)*

- All penicillins are Beta-lactam antibiotics and are used in the treatment of lower &upper respiratory tract infections, especially those produced by **Group A gram positive beta-hemolytic streptococci**.
- For both Gram-positive (+) & Gram-Negative(-) that's why they call it **Broad spectrum drugs** (Amoxicillin- Ampicillin**)** which are Sensitive to β-lactamase enzyme

○ MOA:

- Act by inhibition of cell wall synthesis.
- Bactericidal antibiotics. *(Which kills the bacteria not only inhibits their growth as bacteriostatic antibiotics do)*

○ 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)

○ Adverse Effects:

- Hypersensitivity reactions (Urticarial rash- Exfoliative dermatitis- Anaphylaxis).
- Super infections.
- Diarrhea.
- Convulsions after high doses by I.V or in renal failure.
- Nephritis.

❖ β-Lactamase Inhibitors *(Clavulanic acid- Sulbactam- Tazobactam)*

- They inactivate β -lactamase enzyme.
- Have no antibacterial activity.
- Given in combination with β -lactamase sensitive antibiotics: Augmentin (Amoxicillin + Clavulanic Acid), (Ampicillin + Sulbactam)

▪ Cephalosprins

○ MOA:

- Bactericidal (kills bacteria)
- Inhibit bacterial cell wall synthesis

○ Classification

- First Generation Cephalosporins
- Second Generation Cephalosporins
- Third Generation Cephalosporins

1st Generation Cephalosporins:

- Example : ***Cephalexin***
- Given orally
- Effective against Gram positive(+) microorganisms *more than* Gram-negative(-)
- Effective in upper respiratory tract infections

2nd Generation Cephalosporins:

- Example : ***Cefuroxime Axetil***
- Effective against Gram negative bacteria(-) more than Gram positive bacteria(+)
- Well absorbed orally
- *Active against **β -lactamase** (producing by bacteria)
  *That means that the drug is resistant to **β -lactamase***

3rd Generation Cephalosporins:

- Examples : ***Ceftriaxone / Cefotaxime***
- Resistant to **β -lactamase**.
- Mostly against Gram-negative bacilli (-)
- Given by **Intravenous route**
- *Effective treatment in **pneumonia**

1st Generation Cephalosporins	2nd Generation Cephalosporins	3rd Generation Cephalosporins
Cephalexin	Cefuroxime axetil	Ceftriaxone Cefotaxime
Given orally	Given orally	Intravenous Route
Effective against Gram positive(+) microorganisms *more than* Gram-negative(-)	Effective against Gram negative bacteria(-) more than gram positive bacteria(+)	Mostly against gram-negative bacilli(-)
Effective in URTIs	_____	Effective in pneumonia

Pharmacokinetics	Adverse Effects
Given Parentrally Or Orally	Hypersensitivity Reactions (Like Skin Rash,Edema)
Relatively Lipid Insoluble	Thrombophilibitis (Mostly With 3rd Genration) وهي بسبب الاليه عن اعطاء الابره
Excreted Mostly Unchanged In The Urine.	Superinfections
Half-Life 30-90 Min (Increased In Renal Failure)	Diarrhea

❖ MACROLIDES

1\ ***Azithromycin*** **(Prototype)**
2\ ***Clarithromycin***

○ MOA:

Inhibit protein synthesis by binding to the 50 s subunit

Azithromycin:-

○ Clinical Uses

Upper & lower respiratory tract infections like (Pneumonia, Otitis media, pharyngitis).

○ Side effects

Nausea, vomiting, abdominal pain & diarrhea(AAC)
Allergic reactions- (urticaria), mild skin rashes Sore mouth.

○ Pharmacokinetics

1. Rapidly absorbed except if taken with food.
2. Widely distributed except CSF (cerebrospinal fluid)
3. Protein binding 51% (which makes the duration last longer)
4. Undergo some hepatic metabolism (some will get inactivated)
5. Biliary route is the major route of elimination
6. Only 10-15% excreted unchanged in the urine
7. Half- life approx. 3 days (which considered long T ½)

So this is an Advantage over erythromycin & clarithromycin because the dose is once daily

8. No inhibition of cytochrome P- 450

❖ FLUOROQUINOLONES

1\ Ciprofloxacin
2\ Moxifloxacin
3\ Gatifloxacin

○ Mechanism Of Action

Inhibit DNA synthesis by inhibiting DNA gyrase.

Ciprofloxacin:-

(Antibacterial spectrum)
Mainly effective against G – bacteria **BUT Not** against G+ and Anaerobes

○ Pharmacokinetics

1. Orally or I.V.
2. Di & Tri- valent cations interfere with its absorption
3. Concentrates in many tissues, esp. kidney, prostate, lung & bones/ joints
4. Do not cross BBB
5. Excreted mainly through the kidney so it'll Accumulate when renal insufficiency
6. Up to 20% metabolized by liver
7. T ½ = 3.3 hrs (which considered short T ½)

Gatifloxacin:-

- Is a new Fluoroquinolones
- Has extended gram-positive activity
- Given once daily (long half-life)
- 1st line treatment of LRTI
- It is effective against community acquired pneumoniae

○ Adverse Effects:

- Nausea , Vomiting & Diarrhea
- CNS effects – confusion, insomnia, headache,
- Dizziness & Anxiety.
- May damage growing cartilage
- Phototoxicity – avoid excessive sunlight

○ Contraindications

Children / adolescents (under 18), pregnancy and lactation

○ Clinical Uses

1. Respiratory infections due to P.aeruginosae.
2. Community- acquired pneumoniae
3. Legionnaires disease