Pharmacology Team

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Red	Important
Purple	Extra Notes
Orange	General Explanation
Black	From the slides

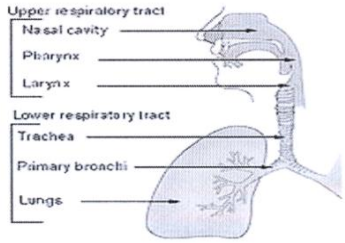
7th lecture: Treatment of URTIs

OBJECTIVES

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

- **Types of respiratory tract infections**
- **Antibiotics commonly used to treat tract infections respiratory and their side effects.**
- **Understand the mechanism of action, pharmacokinetics of individual drugs.**

Respiratory Tract Infections has two types:



1-URTI's (Upper respiratory tract infections)

2-LRTI's (Lower respiratory tract infections)

NOTE: Most common infections in Out Patient Clinics and ER are URTI's.

LRTI's is dangerous and most admitted to Hospital

URTI'S

1- Rhinitis
2- Sinusitis
3- Pharyngitis/ tonsilitis
4- Laryngitisz

Causes

1-Viruses: mainly;
H. influenzae 90% of URTI's infections
2- **Bacteria** , mainly; Group A streptococcus

Treatment

Bacteria (Antibiotics)

Decongestants,eg: pseudoephedrine

Antihistamines,e.g: diphenhydramine ,vit.c, Plenty of fluids, analgesics

LRTI'S

Bronchitis:

Acute, Chronic, Acute exacerbation of chronic bronchitis

Pneumonia

Community - acquired

Hospital- acquired

Causes

Bacteria mainly:

S. pneumonia

H. influenza

M. catarrhalis

Treatment

1- Broad- spectrum penicillins

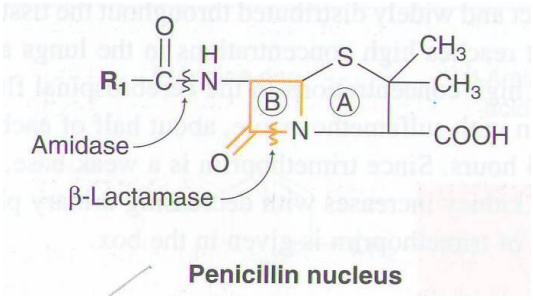
Amoxicillin, Ampicillin

2- Cephalosporins

3- Macrolides

4- Flouroquinolones

1) Penicillins



- **Penicillins has β-lactam ring which destroyed by β-lactamase of the bacteria.**

Mechanism of action	Pharmacokinetics	Adverse effects	Therapeutic uses
• Inhibits bacterial cell wall synthesis. • Bactericidal.	• orally or parentally • Not metabolized in human. • Excreted mostly unchanged • Relatively lipid insoluble. • ½ life 30-60 min (increased in renal failure). *we must assess renal function before give penicillin	• Hypersensitivity reactions (anaphylactic shock) • Superinfections • Diarrhea • Convulsions (after high dose by IV or in renal failure) • Nephritis	• URTI'S, especially those produced by Group A gram positive beta-hemolytic streptococci. • Lower respiratory tract infections

*β-Lactamase inhibitors *organic substances

1- Clavulanic acid. 2-Sulbactam 3-tazobactam

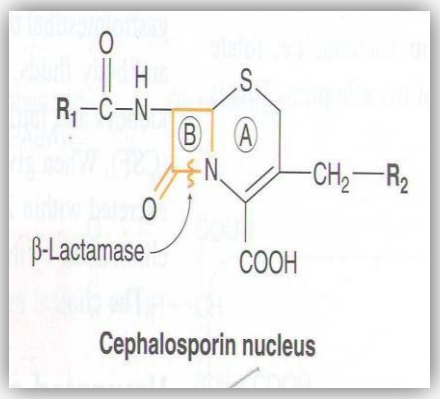
Themselves have no antibacterial activity.

They inactivate β-lactamase enzyme.

- **Examples:**

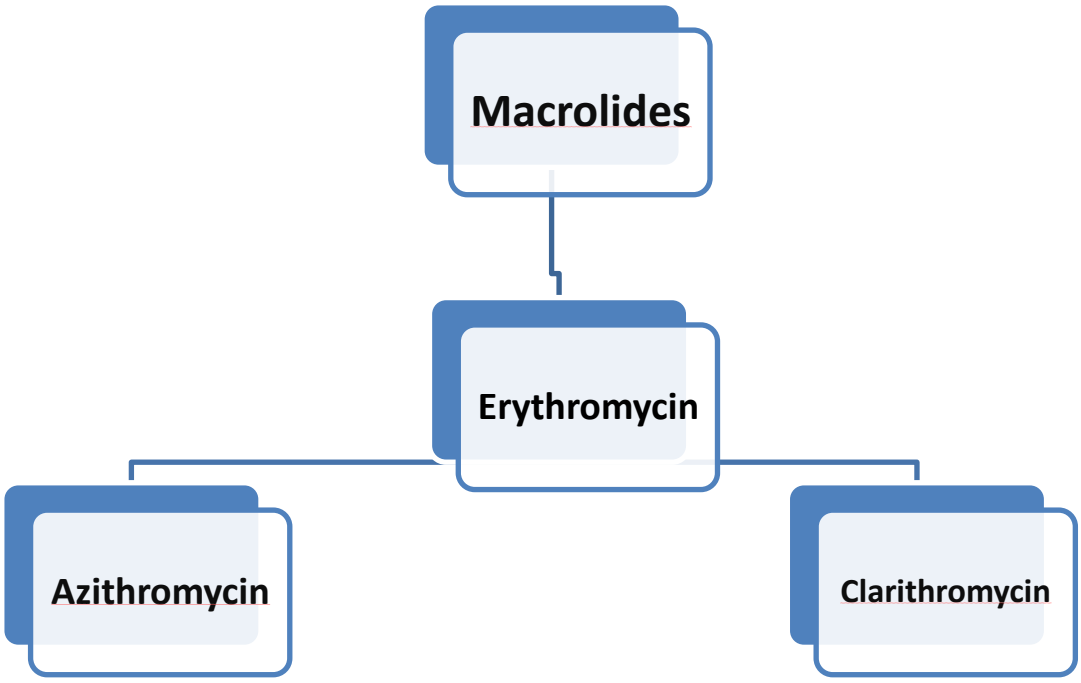
1-Amoxicillin/clavulanic acid (augmentin)	2- Ampicillin/ sulbactam

2) Cephalosprins



Mechanism of action	1st Generation	2nd Generation	3rd Generation	Pharmacokinetics	Adverse effects
● Inhibit bacterial cell wall synthesis ● Bactericidal	Cephalexin ● Given orally ● against G+ve & to some G-ve bacteria ● Effective in URTI's	Cefuroxime axetil "zinnat" + cefaclor ● Mainly against G-ve bacteria. ● Well absorbed orally ● Active against β-lactamase • Good for H. influenza • Cefuroxime – for adult • Cefaclor – for children	Ceftriaxone/Cefotaxime ● Against G-ve bacilli ● Given IV ● treatment in pneumonia produced by β-lactamase ● good for LRTI'S	✓ parentrally or orally ✓ Relatively lipid insoluble ✓ Excreted Mostly unchanged ✓ ½ life 30-90 min (increased in renal failure)	☒ Hypersensitivity reactions ☒ Thrombophilibitis ☒ Superinfections ☒ Diarrhea

3) MACROLIDES



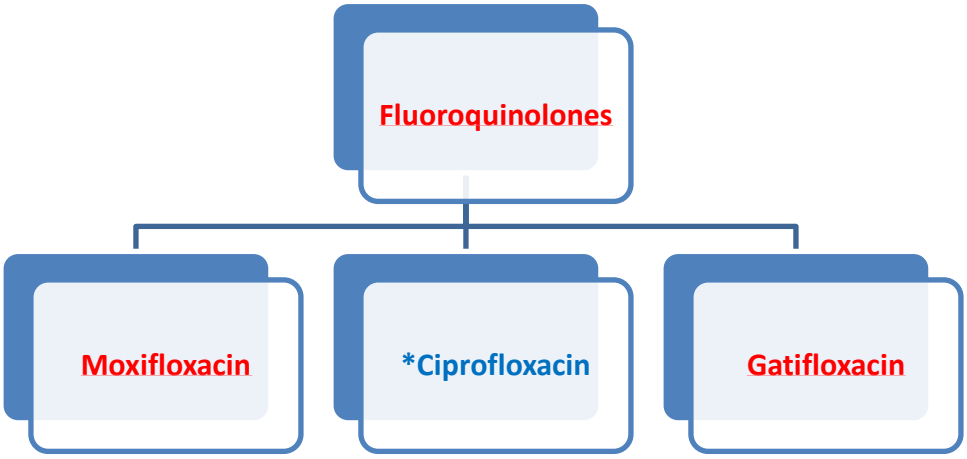
Mechanism of action	Clinical Uses	Adverse effects
✓ Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes ✓ Bacteriostatic ✓ Bactericidal at high concentration	1- Community acquired pneumonia(CAP) 2- Legionella pneumonia	☒ GI disturbances ☒ Hypersensitivity

Pharmacokinetics and characteristics

Clarithromycin& Azithromycin

1- Clarithromycin	2- Azithromycin
✓ Stable at gastric acidity	✓ More effective on G- Bacteria. ✓ Stable at gastric acidity
✓ Inhibits cytochrome P450 system	✓ Undergo some hepatic metabolism (inactive metabolite) ✓ Biliary route is the major route of elimination
✓ Metabolized to active metabolite	✓ Only 10-15% excreted unchanged
✓ Excreted in urine 20-40% unchanged or metabolite ▪ Bile approx. 60%	✓ ½ life (3 days) ✓ Advantage over clarithromycin :Once daily dosing ✓ No effect on cytochrome P-450
✓ ½ life 6-8 hours	✓ Given orally over 3 days ✓ Once daily dosing"dr.azza"

4) FLUOROQUINOLONES



***CIPROFLOXACIN Mainly effective against G – bacteria**

Mechanism of action	Pharmacokinetics	ADRS	Contraindications	Clinical Uses
Inhibit DNA synthesis by inhibiting DNA Gyrase enzyme	✓ Well absorbed ✓ Given orally or I.V ✓ Di & tri- valent cations interfere with its absorption ✓ Concentrates in many tissues, esp. kidney, prostate, lung & bones/ joints ✓ Does not cross BBB ✓ Excreted mainly through the kidney ✓ ½ life 3.3 hrs	✓ Nausea , vomiting & diarrhea ✓ CNS effects (confusion, insomnia, headache, dizziness & anxiety). ✓ Damage growing cartilage (arthropathy) ✓ Phototoxicity(avoid execessive sunlight)	✓ Is preferably avoided in adolescents (under 18 years because of arthropathy) ✓ Pregnancy ✓ Breast feeding women	• Acute exacerbation of COPD • Community acquired pneumonia • Legionella pneumonia

NOTES by the doctor:

- **Cephalosprins have the same β-lactam ring and function of Penicillin.**

- **Superinfections + Diarrhea are the ADRS for all antibiotics.**

- **In Fluoroquinolones, Di & tri- valent cations like Ca+2 interfere with its absorption. So, we don't use milk with these antibiotics**

	Mechanism of action	Pharmacokinitcks	ADRS	Clincal uses	Contaciationids
1- Penicillin e.g: Amoxicillin Ampicilin	● Inhibits bacterial cell wall synthesis.	orally or parentrally. Not metabolized. Excreted unchanged. ½ life ↑ with renal failure.	Hypersensitivity + Superinfection + Diarrhea + Convulsions + Nephritis	1) URTI'S by Group A gram positive beta-hemolytic streptococci. 2)LRTI'S	Don't use without <u>β-Lactamase inhibitors</u>
Cephalosphorins 3 gernarations	● Inhibits bacterial cell wall synthesis.	orally or parentrally. Not metabolized. Excreted unchanged. ½ life ↑ with renal failure.	Hypersensitivity Thrombophilibitis Superinfections Diarrhea	1st generation : URTI'S 2nd generation: LRTI'S	—
Macrolides Erythromycin: 1 -Clarithromycin 2-Azithromycin	Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes	<u>Clarithromycin:</u> Inhibits cytochrome P450 Excreted in urine 20-40% unchanged. ½ life 6-8 hrs <u>Azithromycin:</u> Biliary route is the major route of elimination. Only 10-15% excreted unchanged. Half- life (3 days). No effect on cytochrome P-450	GIT disturbances + Hypersensitivity	1- CAP + 2- Legionella pneumonia	—
Flouroquinolones Ciprofloxacin	Inhibit DNA synthesis by inhibiting DNA Gyrase enzyme	Di & tri- valent cations interfere with its absorption + Does not cross BBB + Excreted by kidney	GIT effects CNS effects arthropathy Phototoxicity	COPD+ CAP+ Legionella pneumonia	avoided in adolescents + Pregnancy + Breast feeding women

MCQ'S

Q1: Which of the following used with β-Lactamase inhibitors:

a) Clarithromycin

b) Ciprofloxacin

c) Ampicillin

d) Moxifloxacin

Q2: Which of the following NOT for Pregnancy:

a) Clarithromycin

b) cefaclor

c) Azithromycin

d) Ciprofloxacin

Q3: Which of the following work by Inhibit cytochrome P450:

a) Clarithromycin

b) Ciprofloxacin

c) Ampicillin

d) Moxifloxacin

Question	Answer
1	c
2	d
3	a