PHARMACOLOGY 433

King Saud University
College of Medicine
1st Year, 3rd Block

Respiratory Tract Infection Treatment

7

Respiratory Block

Objectives :

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

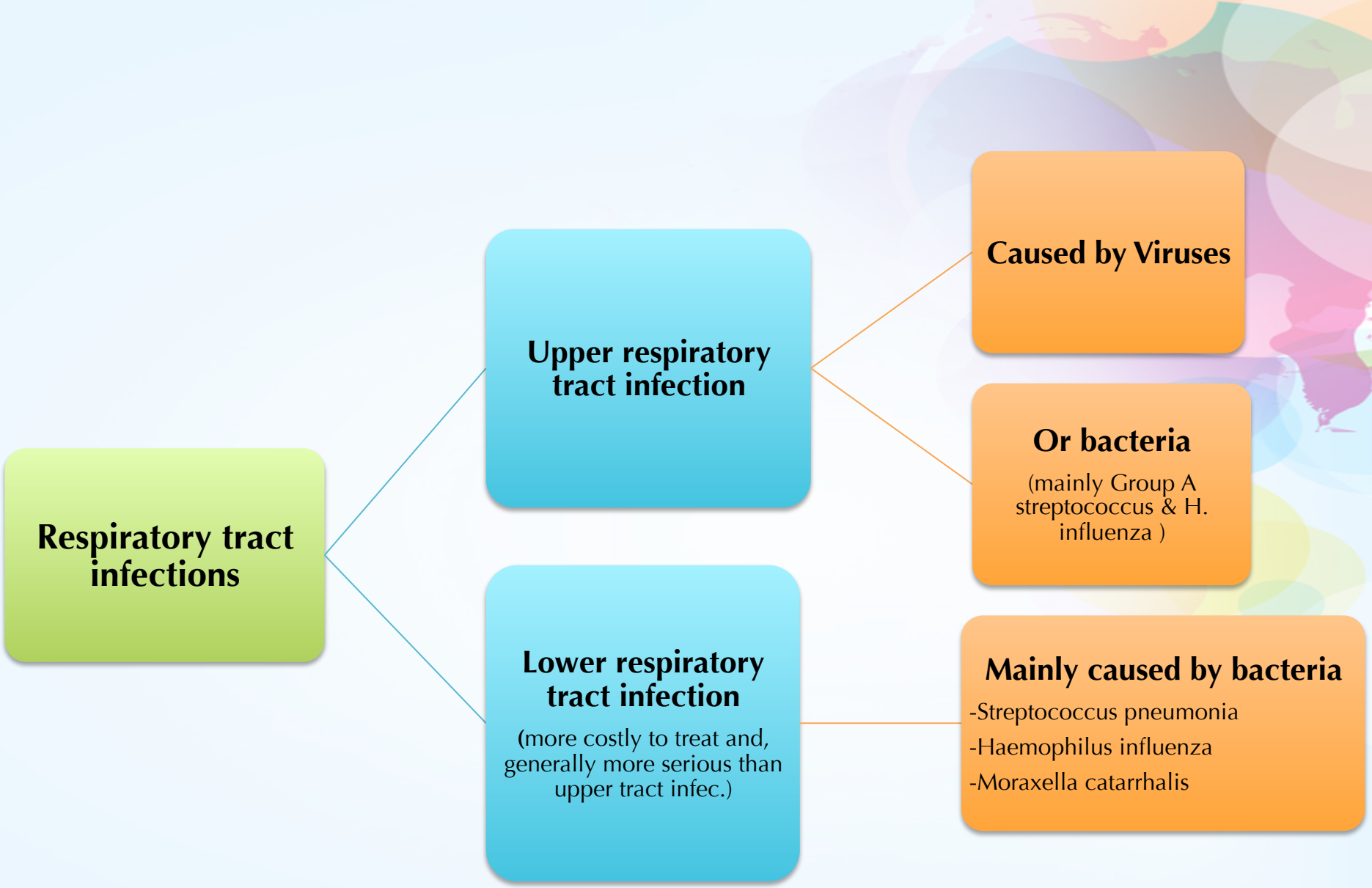
Remember :

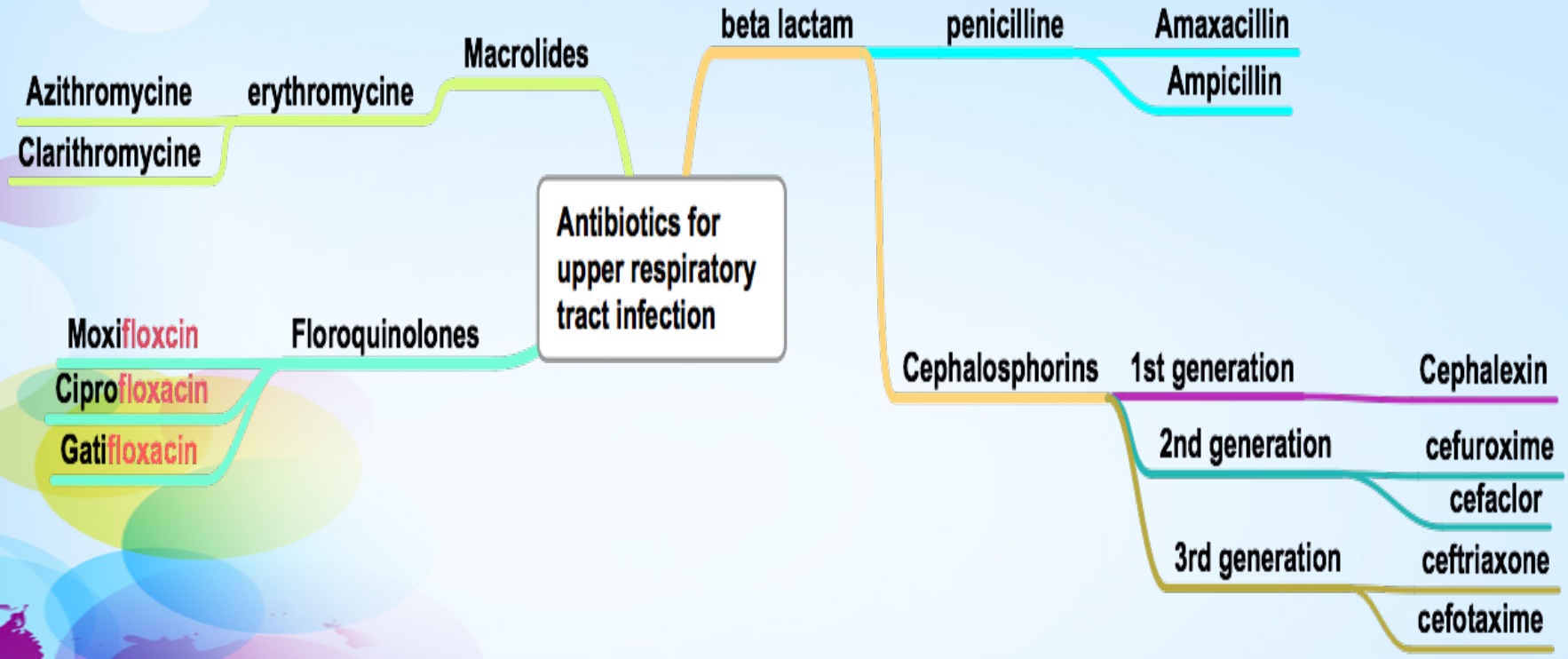
-Bactericidal: kills bacteria.

-Bacteriostatic: prevents multiplication.

-Broad spectrum: acts on gram + and gram - bacteria

-Narrow spectrum: acts only on selected organism.


Respiratory tract infections
Upper respiratory tract infection
Caused by Viruses
Or bacteria
(mainly Group A streptococcus & H. influenza)
Lower respiratory tract infection
(more costly to treat and, generally more serious than upper tract infec.)
Mainly caused by bacteria
-Streptococcus pneumonia
-Haemophilus influenza
-Moraxella catarrhalis



ANTIBIOTICS FOR UPPER RESPIRATORY TRACT INFECTION

FIRST :
BETA LACTAM → PENICILLIN

Antibiotics	Acts on :	Mechanism of action	Pharmacokinetics	Adverse effects
Penicillins	gram + & gram -	• Inhibits bacterial cell wall synthesis • Bactericidal	• orally or parentrally • Low lipid soluble. • Not metabolized in human • Excreted mostly in urine. • T1/2=30-60 min	• Hypersensitivity reactions • Convulsions • Nephritis • Diarrhea • Superinfections
Amoxicillin				
Ampicillin				

KNOW ABOUT PENICILLIN:

- Destroyed by β-lactamase enzyme. (that's why it has to bind with beta lactamase inhibitors when it works against beta lactamase producing bacteria)

THERAPEUTIC USES:

- URTIs (produced by Group A gram positive beta-hemolytic streptococci)
- LRTIs

B-LACTAMASE INHIBITORS

- have no antibacterial activity.
- They inactivate β-lactamase enzyme
- Do not affect the kinetics of the drugs

CLAVULANIC ACID	SULBACTAM
+Amoxicillin (**augmentin**)	+Ampicillin

FIRST :
BETA LACTAM → CEPHALOSPRINS

Antibiotics	effective against:	Mechanism of action	Pharmacokinetics	Adverse effects
Cephalosprins		• Inhibit bacterial cell wall synthesis • Bactericidal	• Given parentrally or orally • Relatively lipid insoluble • Excreted Mostly unchanged in the urine. • Half-life 30-90 min (increased in renal failure)	• Hypersensitivity reactions • Thrombophilibitis (blood clot When it occurs repeatedly in different locations) • • Superinfections • Diarrhea
1st Generation • Cephalexin	• Gram +ve, and some gram –ve, • effective in URTI • Given orally			
2nd Generation • Cefuroxime axetil • cefaclor	• mainly against Gram-gative bacteria. • Active against β-lactamase – producing bacteria • absorbed orally			
3rd Generation • Ceftriaxone • Cefotaxime	• against gram-negative bacilli • Given by IV route • Effective treatment in pneumonia			

SECOND MACROLIDES

Antibiotics	Acts on :	Mechanism of action	Pharmacokinetics	Adverse effects
MACROLIDES		• Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes • Bacteriostatic		• GIT disturbance • Hypersensitivity Reactions
Erythromycin				
Clarithromycin	• effective on G+ bacteria. • Stable at gastric acidity		1. **Inhibits** cytochrome P450 system 2. **Metabolized** to active metabolite 3. **Excreted** in urine 20-40%unchanged or metabolite & 60% in bile 4. **Half-life** 6-8 hours	
Azithromycin	• effective on Gram negative bacteria. • Stable at gastric acidity		1. Undergo hepatic **metabolism** 2. Biliary route is the major **route of elimination** Only 10-15% excreted unchanged in the urine 3. **Half- life** (3 days) Once daily dosing No effect on cytochrome P-450	

THIRD: FLUOROQUINOLONES

Antibiotics	effective against:	Mechanism of action	Pharmacokinetics	Adverse effects
Fluoroquinolones		Inhibit DNA synthesis by inhibiting **DNA Gyrase enzyme**	1. Well **absorbed** orally (available i.v) 2. Di & tri- valent cations **interfere with its absorption**(examples: iron and calcium) 3. Concentrates in many tissues (kidney, prostate, lung & bones/ joints) **4. Does not** cross BBB **5. Excreted** mainly through the kidney 6. **Half-life** 3.3 hrs	• Nausea , vomiting , diarrhea • CNS effects (confusion, insomnia,headache, anxiety). • Damage growing cartilage (arthropathy) • Phototoxicity (avoid excessive sunlight)
Moxifloxacin				
Ciprofloxacin	Mainly effective against G – bacteria			
Gatifloxacin				

CONTRAINDICATIONS

1. Is preferred to be avoided in adolescents (under 18 years because of arthropathy)
1. Pregnancy
2. Breast feeding women

CLINICAL USES

1. Acute exacerbation of chronic obstructive pulmonary disease
2. Community acquired pneumonia
3. Legionella pneumonia

SUMMARY

Drug	Upper \lower	spectrum	Mechanism of action	activity	Side effects	Notes
Penicillins: Amoxicillin and Ampicillin)	both	Broad	Inhibit bacterial cell wall senthysis	bactericidal	Hypersensitivity	Destroyed by b-latamase enzymes → should be given in combination with b-lactamase inhibitors
1st generation: Cephalexin	upper	+				
2nd : Cefaclor, Cefuroxime axetil		-				Active against b-lactamase bacteria
3rd: ceftriaxone, cefotaxime	lower	-				Strongest, given I.V
Clarithromycin		+	Inhibit protein synthesis by binding to 50 S subunit of bacterial ribosomes		GI upset	Stable at gastric acidity
Azithromycin		-				
Ciprofloxacin		-	Inhibit DNA synthesis		Damage cartilage growing	Not given to younger than 18, pregnant and breast feeding

Cephalosprins Macrolides (Erythromycin) Floroquinolones

MCQS

1- A patient came to the hospital with respiratory tract infection and after investigations we found that the cause of infection is bacteria producing β-lactamase enzyme .. which one of the following antibiotic should we give to the patient :

A. Amoxicillin
B. Augmentin
C. Ampicillin
D. Sulbactam

2- The most safe group of antibiotic in case of pregnant and Breast feeding women is :

A. Penicillins
B. Fluoroquinolones
C. Macrolides
D. Aminoglycoside

3- A patient came with upper respiratory tract infection causes by gram positive bacteria .. which one of the following antibiotic should we give to the patient :

A. Cefaclor
B. Cephalexin
C. Azithromycin
D. Ciprofloxacin

4- The main route to give 3rd generation Cephalosporins (Ceftriaxone/Cefotaxime) is :

A. Orally
B. I.M
C. I.V
D. Inhalation

5- Pregnant women came with lower respiratory tract infection caused by gram negative bacilli .. which one of the following antibiotic should we give to her :

A. Ceftriaxone
B. Cephalexin
C. Clarithromycin
D. Ciprofloxacin

1-B 2-A 3-B 4-C 5-A 6-D 7-A 8-C 9-D 10-D

6- which one of the following antibiotic has bacteriostatic effects in mechanism of action :

A. Penicillins
B. Fluoroquinolones
C. Cephalosporins
D. Macrolides (Azithromycin / Clarithromycin)

7- The mechanism of action in Macrolides (Azithromycin / Clarithromycin) is :

A. Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes
B. Inhibit protein synthesis by binding to 30 S subunit of the bacterial ribosomes
C. Inhibit DNA synthesis by inhibiting DNA Gyrase enzyme .
D. Inhibit bacterial cell wall synthesis

8- A patient came with lower respiratory tract infection causes by gram negative bacteria .. which one of the following antibiotic should we give to the patient :

A. Cephalexin
B. Clarithromycin
C. Ciprofloxacin
D. Vancomycin

9- The most contraindication of ciprofloxacin is :

A. Renal fleur
B. Heart fleur
C. Old person
D. Adolescents (under 18 year)

10- Which one of the following is one of the adverse effects of Fluoroquinolones :

A. Hypertension
B. Nephritis
C. Thrombophilibitis
D. Damage growing cartilage (arthropathy)

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We hope that we made this lecture easier for you
Good Luck !