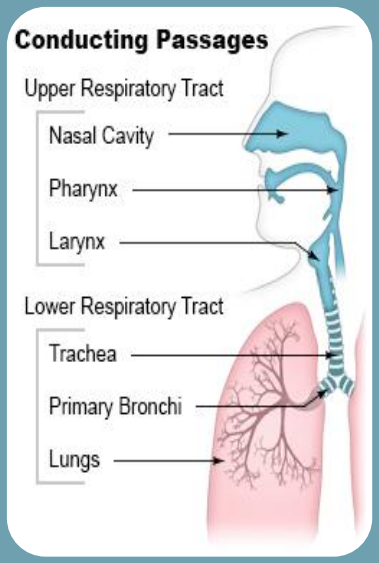
RESPIRATORY TRACT INFECTIONS

Objectives

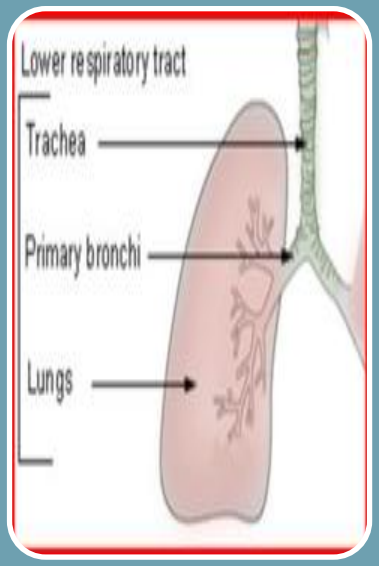
- At the end of lecture , the students should be able to understand the following:
- The types of respiratory tract infections
- The antibiotics that are commonly used to treat respiratory tract infections and their side effects.
- Understand the mechanism of action, pharmacokinetics of individual drugs.



Upper respiratory tract infections (URTI)

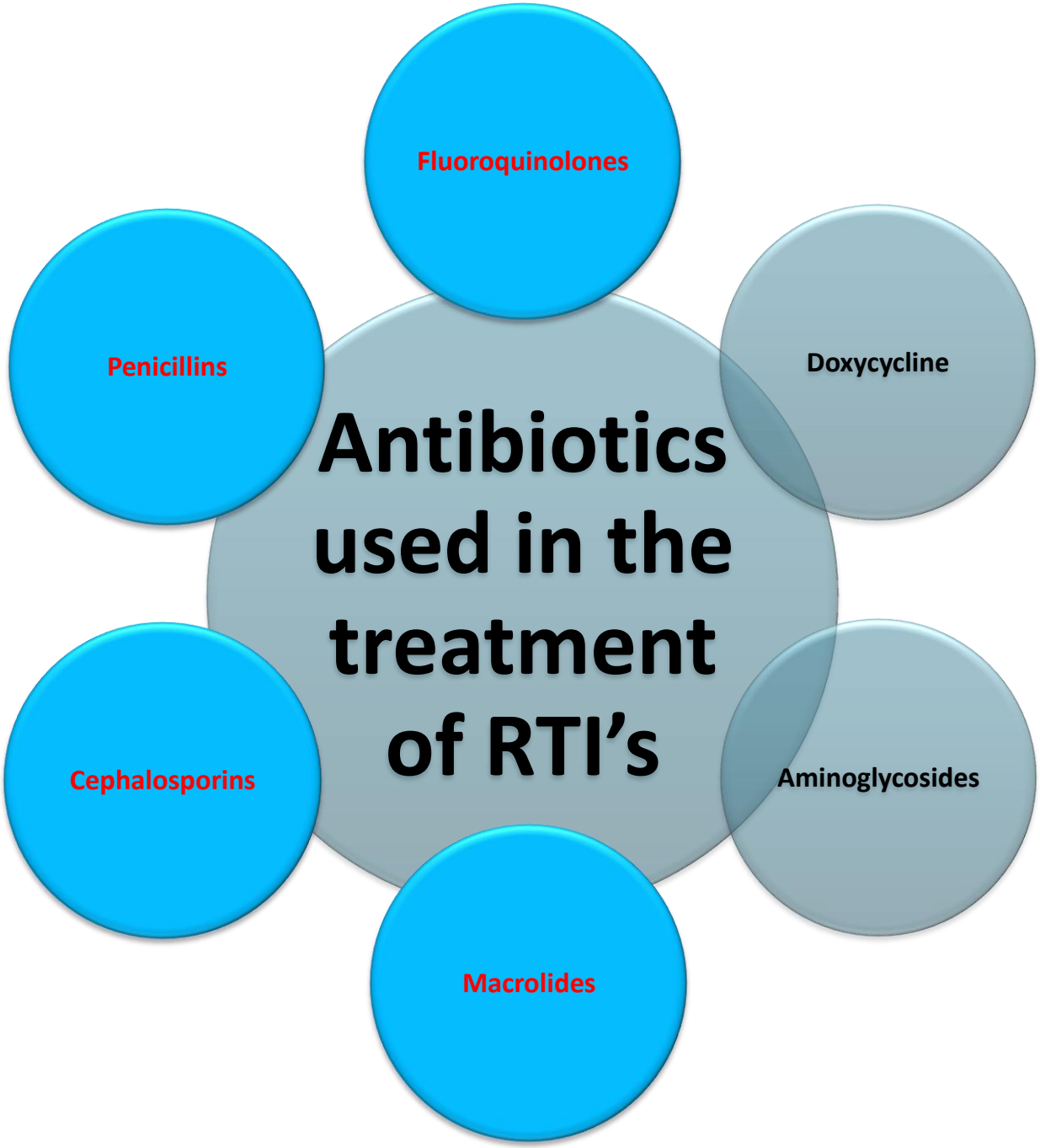
- **Viruses** (over 200 different types have been isolated) :-
- (Should not be treated with antibiotics)
- Treatment: rest and plenty of fluids, OTC cold, pain relievers.

- **Bacteria** (mainly Group A streptococcus H. influenzae)
- Treatment: Antibiotics. The type depends on: Type of bacteria &Sensitivity test



Lower respiratory tract infections (LRTI)

- **Bronchitis**
- Acute(Mostly due to viruses) ,Chronic & Acute exacerbation of chronic bronchitis.
- **Pneumonia**
- Community –acquired(CAP)
- Hospital-acquired
- LRTI's are more costly to treat and generally more serious than URTI's
- Causes of LRTI's :-Bacteria mainly:
- Streptococcus pneumonia**,Haemophilus influenza,Moraxella catarrhalis


Fluoroquinolones
Penicillins
Doxycycline
Antibiotics used in the treatment of RTI's
Cephalosporins
Aminoglycosides
Macrolides

Broad- spectrum penicillins

Amoxicillin
Ampicillin

Mechanism of action

Inhibits bacterial cell wall synthesis

Through inhibition of transpeptidase enzyme.

Bactericidal.

Adverse effects

Diarrhea

Superinfections

Nephritis

Hypersensitivity reactions

Convulsions (after high dose by IVI or in renal

Pharmacokinetics

Given orally or parentrally

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

- Acts on both gram + ve & gram – ve microorganisms .
- Destroyed by β-lactamase enzyme

β-Lactamase inhibitors e.g.Amoxicillin/ clavulanic acid
Ampicillin/ sulbactam

- Themselves have no antibacterial activity.
- They inactivate β-lactamase enzyme

Cephalosporin

Cephalosporin	1st Generation	2nd Generation	3rd Generation
drugs	Cephalexin	Cefuroxime axetil , cefaclor	Ceftriaxone / Cefotaxime / Cefixime
Effect on	○ Given orally ○ Effective against gram positive microorganisms ○ Effective in URTI's	○Effective mainly against Gram-negative bacteria. ○Well absorbed orally ○Active against β-lactamase –producing bacteria ○Uses:-URTI&LRTI ○Sinusitis, otitis media.	○More effect on gram-negative bacilli ○Effective treatment in pneumonia produced by β-lactamase bacteria

Pharmacokinetics

- Given mainly parentrally
- Oral preparation : Cefixime
- Penetration into CSF
- Excreted Mostly unchanged in the urine.
- Eliminated via biliary excretion (ceftriaxone)
- Long Half-life (ceftriaxone)

Adverse effects of cephalosporins

1. Hypersensitivity reactions
2. Thrombophilibitis
3. Superinfections
4. Diarrhea

Drug	Macrolides		
	Erythromycin		
	Clarithromycin		Azithromycin
Mechanism of action	• Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes • Bacteriostatic • Bacteriocidal at high concentration		
Bacteria	More effective on Gram+ve bacteria.		More effective on Gram-ve bacteria
gastric acidity	• Stable at gastric acidity		
Pharmacokinetics	**cytochrome P-450**	Inhibits cytochrome P450	No effect on cytochrome P- 450
	Metabolism	Metabolized to active metabolite	hepatic metabolism (inactive metabolite)
	Excretion	In urine 20-40%unchanged or metabolite & 60% in bile .	Biliary route is the major route of elimination, Only 10-15% excreted unchanged in the urine.
	Half-life	Half-life 6-8 hours	3 days, Once daily dosing
Clinical uses	• Chlamydial pneumonia • Legionella pneumonia		
Adverse effects	• GIT disturbances • Hypersensitivity Reaction		

Drug	Fluoroquinolones		
	Ciprofloxacin	Moxifloxacin	Norfloxacin
Mechanism of action	Inhibit DNA Gyrase enzyme (an enzyme involved in DNA supercoiling)		
Bacteria	Mainly effective against Gram–ve bacteria		
Distribution	Concentrates in many tissues (kidney, prostate, lung & bones/ joints)		
Routes of drug administration	Well absorbed orally (available i.v)		
Half-life	Long Half-life, twice-daily dosing		
Excretion	Excreted mainly through the kidney		
Contradiction	• Not recommended for patients younger than 18 years • Pregnancy • Breast feeding women		
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 growing cartilage(arthropathy) • Phototoxicity(avoid excessive sunlight)		

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)

Good luck!

Done by pharmacology team 434

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