



Treatment Of Respiratory Tract Infections

- Red : important
- Black : in male / female slides
- Pink : in female's slides only
- Blue : in male's slides only
- Green : females doctor notes
- Grey: males doctor notes, extra

OBJECTIVES:

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

- ✓ The types of respiratory tract infections (RTI).
- ✓ The antibiotics that are commonly used to treat RTIs & their side effects.
- ✓ Understand the mechanism of action & pharmacokinetics of individual drugs.

Editing File

Respiratory Tract Infections Classification

Upper Respiratory Tract Infections

Viruses

most URTIs are of viral etiology.

Treatment

Should **NOT** be treated with antibiotics.
Rest and plenty of fluids, over the counter cold & pain relievers.

Bacteria

Mainly group A streptococcus and H. Influenza.

Treatment

Antibiotics.
Type depends on:
1) Type of bacteria.
2) Sensitivity test.

Lower Respiratory Tract Infections

(costly & more difficult to treat)

Bronchitis

(inflammation of major bronchi & trachea)
Acute, Chronic, or Acute exacerbation of chronic bronchitis.

Causes

Viruses or bacteria (H. Influenza, Streptococcus pneumoniae & Moraxella catarrhalis.)

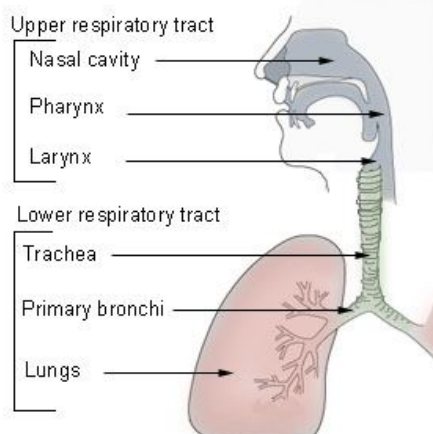
Pneumonia

(serious infection of bronchioles & alveoli)
- Community-acquired (CAP).
- Hospital-acquired. (Nosocomial)

Causes

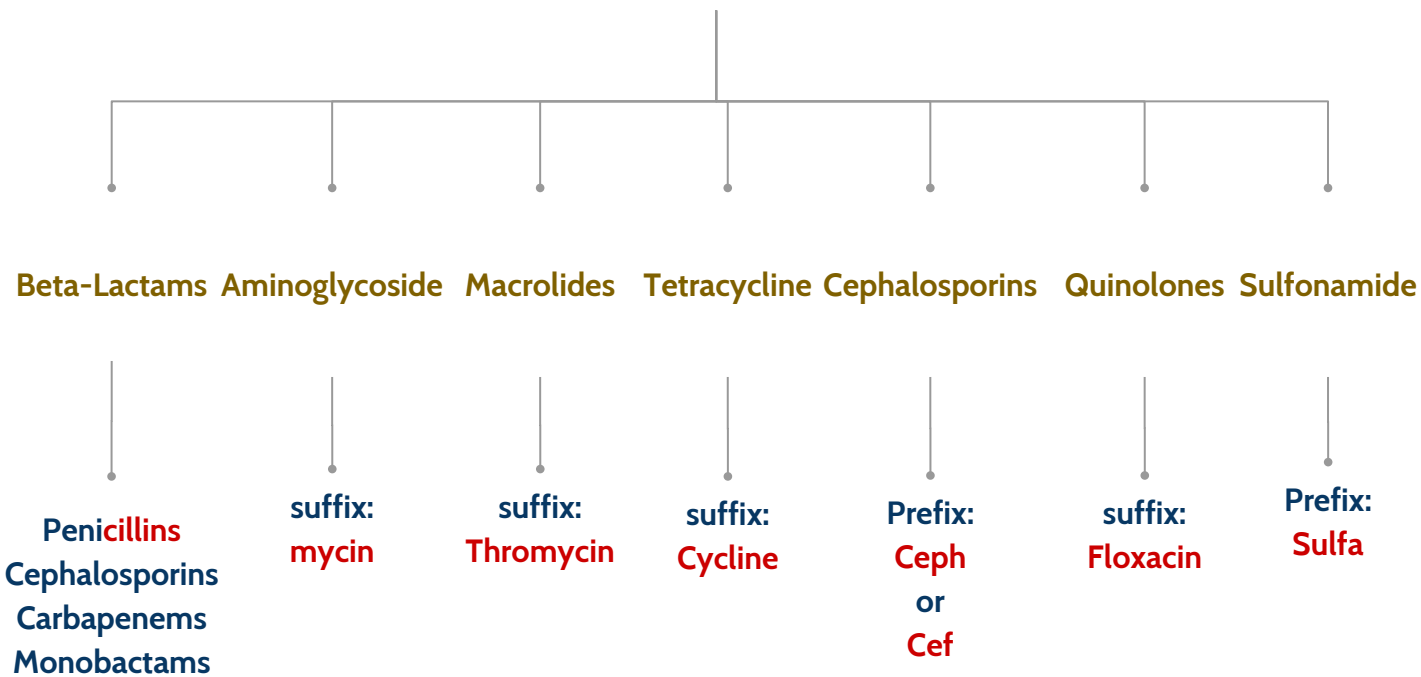
Bacteria: S. pneumoniae (66%), H. Influenza (20%), M. catarrhalis (20%)

Conducting Passages



This page is for your understanding only, but we **HIGHLY RECOMMEND** that you read it

Antibiotics Classification:



Antibiotics
Mechanism of Action:

- **Bactericidal (kills the bacteria)** by either:
 - 1- Destroying the cell wall
 - 2- Destroying the Nucleic Acid (DNA or RNA)
- **Bacteriostatic (stops the growth)** by:
 - 1- Affecting the protein synthesis

EXCEPTION: Aminoglycoside affects the protein synthesis but is considered Bactericidal

Cell wall synthesis	Nucleic acid synthesis	Protein synthesis
- Beta Lactams Note: Beta Lactams are sometimes combined with beta lactamase inhibitors such as: clavulanic acid, sulbactam, tazobactam, this is because some strains of bacteria have evolved into species that can cleave beta lactam ring through an enzyme called beta lactamase.	DNA: Quinolones RNA: Rifampin, Rifabutin Folate synthesis: Sulfonamide, TMP-SMX	30S: - Aminoglycoside -Tetracycline 50S: - Macrolides (Erythromycin) - Clindamycin - Chloramphenicol - Linezolid

buy **AT 30** **CCEL** (sell) at 50:

AT: Aminoglycoside, Tetracycline **CCEL:** Clindamycin, Chloramphenicol, Erythromycin, Linezolid

Antibiotics commonly used in the treatment of RTIs:

1 Beta-lactam antibiotics
(Penicillins/Cephalosporins)

3 Fluoroquinolones

2 Macrolides

4 Aminoglycosides

5 Tetracycline

Penicillins

Broad-spectrum penicillins

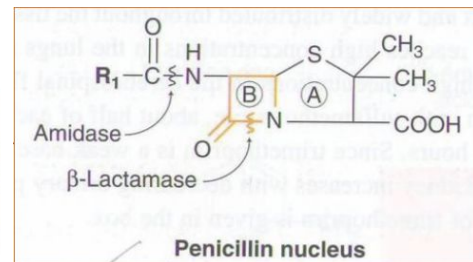
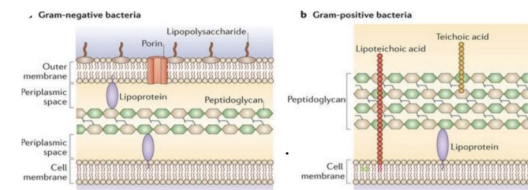
- **Amoxicillin**-Clavulanic acid
- **Ampicillin**-Sulbactam
- **Piperacillin**-Tazobactam

Note: Beta Lactams are sometimes combined with beta lactamase inhibitors such as: clavulanic acid, sulbactam, tazobactam, this is because some strains of bacteria have evolved into species that can cleave beta lactam ring through an enzyme called beta lactamase.

Act on both gram +ve and gram -ve microorganisms.

Mechanism of action

- Inhibit bacterial wall synthesis through inhibition of peptidoglycan layer on the cell wall.
- Bactericidal



Pharmacokinetics

- Given orally or parenterally
- Not metabolized in human
- Relatively lipid insoluble
- Excreted mostly unchanged in urine
- Probenecid slows their elimination and prolongs their half life by inhibiting the renal excretion of penicillin.
- Half-life: 30-60 min (increased in renal failure)

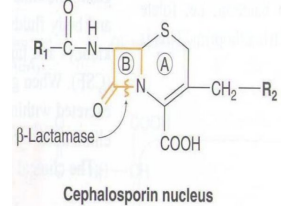
Adverse effects

- Hypersensitivity reactions nausea and vomiting as a start , followed by urticaria, laryngeal edema, and finally anaphylactic shock and cardiovascular collapse.
- Diarrhea
- Superinfections an infection that occurs as a result of killing the normal flora along with the pathogen after using antibiotics
- Nephritis (especially broad spectrum antibiotics)
- Convulsions (after high I.V dose or in renal failure)

Therapeutic uses

- URTIs
- LRTIs

Cephalosporins

Features (MOA)	<ul style="list-style-type: none"> - Inhibit bacterial cell wall synthesis - Bactericidal (similar to Penicillins) more stable than penicillins to β-lactamase. - Classified into 3 generations: 			 <p>Cephalosporin nucleus</p>
Generation	1st	2nd	3rd	
Drug	Cephalexin	Cefuroxime, Cefaclor	Ceftriaxone, Cefotaxime, Cefixime	
Route of administration	Orally	Orally well absorbed	I.V	
Spectrum	Gram +ve bacteria (mild infection)	Gram -ve bacteria (active against β-lactamase-producing bacteria)	Gram -ve bacilli	
Uses	Effective in URTIs	Upper & lower RTIs	Effective in treatment of pneumonia	
P.K of Cephalosporins	<ul style="list-style-type: none"> - Given parenterally & orally. - Relatively lipid insoluble (like penicillins). - Do not penetrate cells or the CNS except for 3rd generation. - Mostly excreted unchanged by the kidney (glomerular & tubular secretion). - Probenecid slows their elimination & prolongs their half lives. - Half-life: 30-90 min except ceftriaxone (4-7 hr). 			
A.D.R of Cephalosporins	<ul style="list-style-type: none"> - Hypersensitivity reactions. - Thrombophlebitis <small>an inflammation that forms a blood clot which blocks a vein therefore injections are given slowly</small> - Superinfections. - Diarrhea. 			

Macrolide

	Erythromycin	
Drugs	Clarithromycin	Azithromycin
MOA	<ul style="list-style-type: none"> Inhibits bacterial protein synthesis by binding to 50S subunit of the bacterial ribosomal RNA. They are bacteriostatic, But when used at higher concentration → bactericidal 	
Antibacterial spectrum	<ul style="list-style-type: none"> More effective on G+ve bacteria 	<ul style="list-style-type: none"> More effective on G-ve bacteria
Pharmacokinetics	<ul style="list-style-type: none"> Stable at gastric acidity Inhibition cytochrome P450 system Metabolized in liver to active metabolites Biliary route is the major route of elimination Only 10-15% excreted unchanged in the urine (good for kidney problems) 	<ul style="list-style-type: none"> Stable at Gastric Acidity No effect on cytochrome P-430 Undergo Some Hepatic Metabolism (inactive metabolite) Biliary route Is The major route of elimination Only 10-15% excreted unchanged the urine
Half-life	<ul style="list-style-type: none"> Half-life 6-8 hours 	<ul style="list-style-type: none"> Half-life 3 days
Dose	Twice a day	<ul style="list-style-type: none"> Once Daily Dosing
Clinical Uses	<ol style="list-style-type: none"> Chlamydial Pneumonia Legionella Pneumonia 	
Adverse effects	<ul style="list-style-type: none"> GI Disturbances (Nausea, Vomiting, abdominal cramps, diarrhea) Hypersensitivity Reaction 	

Fluoroquinolones

Drugs	Ciprofloxacin	Moxifloxacin Gatifloxacin
Antibacterial spectrum	<p>G -ve bacteria</p> <p>highly active against Pseudomonas species</p>	<p>G -ve & G +ve</p> <p>highly active against Pseudomonas species</p>
P.K	<ul style="list-style-type: none"> Given orally or parenterally Di & tri-valent cations interfere with its absorption. (divalent cation is a cation with +2 charge, like calcium, trivalent with +3 like aluminium) Concentrate in many tissues (kidney, prostate, lung & bones/joints) <i>which means it can treat infections in these organs.</i> Excretion mainly through the kidney. Long half-life 	
Dose	twice-daily	Once daily
MOA	<p>Block bacterial DNA synthesis by inhibiting DNA Gyrase enzyme (an enzyme involved in DNA supercoiling).</p>	
Clinical Uses	<ol style="list-style-type: none"> Acute exacerbation of chronic obstructive pulmonary disease Community-acquired pneumonia. Legionella pneumonia 	
ADRs	<ul style="list-style-type: none"> Nausea, vomiting and diarrhea CNS effects (confusion, insomnia, headache and anxiety) Damage of growing cartilage (arthropathy) (for <18 years old) Phototoxicity (avoid excessive sunlight) <i>causes skin irritation</i> 	
Contraindications	<ul style="list-style-type: none"> Not recommended for patients younger than 18 years Pregnancy Breastfeeding Women 	

Aminoglycosides

e.g. Gentamicin, Neomycin, Streptomycin

Drugs	Gentamicin
Antibacterial spectrum	Only active against Gram -Ve Aerobic organisms
M.O.A	<ul style="list-style-type: none">● bactericidal antibiotics● inhibits protein synthesis by binding to 30S ribosomal subunits.
P.K	<ul style="list-style-type: none">● Given parenterally (IM, IV) poorly absorbed orally (highly charged).● Cross placenta contraindicated in pregnancy, may cause hearing loss.● Excreted unchanged in urine● Half-life: 2-3 h & increased to 24-48 h in renal impairment
ADR for all types of Aminoglycosides	<ul style="list-style-type: none">● Ototoxicity● Nephrotoxicity● In very high doses → neuromuscular blockade that results in respiratory paralysis
Clinical uses	<ul style="list-style-type: none">● Severe infection caused by gram -ve organisms

Tetracyclines

e.g. Doxycycline, **Minocycline**, **Chlortetracycline**

Drugs	Doxycycline
Antibacterial spectrum	<p>Broad Spectrum Bacteriostatic Active against many gram +ve and gram -ve bacteria (Anaerobes, Rickettsiae, Chlamydiae and Mycoplasma).</p>
M.O.A	<ul style="list-style-type: none"> ● It inhibit protein synthesis by binding reversibly to 30-S subunit of the bacterial ribosome.
P.K	<ul style="list-style-type: none"> ● long acting ● Usually given orally ● Absorption is 90-100% ● Absorbed in the upper s.intestine & best in absence of food ● Food & di & tri-valent cations (Ca, Mg, Fe, AL) impair absorption <small>it binds with Ca decreasing the absorption, patients should avoid dairy products</small> ● Protein binding 40-80 % ● Distributed well, including CSF ● Cross placenta and excreted in milk <small>contraindicated in pregnancy and breastfeeding. causes bone deformities in newborns</small> ● Largely metabolized in the live
ADR	<ul style="list-style-type: none"> ● nausea, vomiting ,diarrhea & epigastric pain (given with food <small>that doesn't contain dairy products</small>) ● Thrombophlebitis – I.V ● Hepatic toxicity (prolonged therapy with high dose) ● Brown discolouration of teeth in children ● Deformity or growth inhibition of bones in children ● Phototoxicity <small>in sun or light exposure</small> ● Vertigo ● Superinfections.
Contraindication	<ul style="list-style-type: none"> ● pregnancy ● breastfeeding ● Children (below 10 years)
Clinical uses	<ul style="list-style-type: none"> ● Treatment of URTIs caused by S.pyogenes, S.pneumonia & H.influenza.

QUIZ

MCQs:

1- Amongst those antibiotics that act by inhibiting protein synthesis, this drug are known to produce side effects related to drug interactions caused by inhibition of cytochrome P-450?

A-Gentamicin B-Doxycycline C-Clarithromycin

2-Most of the upper respiratory tract infections are caused by?

A-Viruses B-Bacteria C-Fungi

3-A 6 year old patient came to the hospital with his mother, he was presented with brown teeth discoloration after taking a medication to treat his upper respiratory tract infection. What could be the possible drug that is responsible for this discoloration?

A-Doxycycline B-Cephalexin C-Ciprofloxacin

4-A pregnant woman came to the hospital and was diagnosed with legionella pneumonia, the doctor prescribed an antibiotic to treat her. What antibiotics is contraindicated in her condition?

A-Clarithromycin B-Azithromycin C-Moxifloxacin

5-What type of cephalosporins is used for treatment of both upper and lower respiratory tract infections ?

A-Cephalexin B-Cefuroxime C-Cefotaxime

Answers: 1)C -2)A -3)A -4)C -5)B

SAQ:

Q1.What is the drug that can be use in both LRTIs & URTIs ?

Q2.Mention 3 adverse effects of Cephalosporins ?

Q3.What drug is effective against G–ve bacteria only and suitable for treating acute exacerbation of chronic obstructive pulmonary disease?

Q4.Which antibiotic is consider as (Bacteriostatic) and (Bactericidal at high doses)?

Q5.Mention three antibiotics that commonly used in in the treatment of RTIs?

Q1.Penicillin

Q2.Hypersensitivity reactions - Thrombophlebitis - Superinfections - Diarrhea

Q3.Ciprofloxacin

Q4.Macrolides

Q5.Beta-lactam antibiotics (Penicillins/ Cephalosporins) - Macrolides - Fluoroquinolones -Aminoglycosides - Doxycycline



GOOD LUCK

Team Leaders:

Nouf Alshammari

Zyad Aldosari

Team sub-leader:

May Babaeer

Team Members:

Deana Awartani

Waad Aldajani

Njoud Almutairi

Shahad Alsa Hil

Noura Almazrou

Najla Alkilani

Sources:

Team 435