Pharmacology team 436

MEDICINE KING SAUD UNIVERSITY 436

Treatment of respiratory tract infection

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.

It always seems impossible until its done.
-Nelson Mandela.

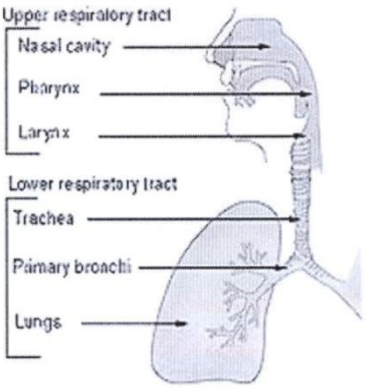
- Titles
- Very important
- Extra information
- Doctor's notes

Thnaks 435

Classification & antibiotics for respiratory tract infections

Respiratory tract infections

Upper respiratory tract infections (URTI's)



Caused by **Viruses** — 70%

- Should NOT be treated with antibiotics
- Treatment: rest and plenty of fluids, OTC cold, pain relievers.

OTC: over-the-counter cold medicines

Caused by **Bacteria** — 30%

- URTI's bacteria are mainly group A Streptococcus & H. Influenzae
- **Treatment:** Antibiotics; depending on: 1-Type of bacteria 2-Sensitivity test

Lower respiratory tract infections (LRTI's)*

Bronchitis

- Bronchitis is an **inflammation of major bronchi& trachea**
- It could be Acute, Chronic, or acute exacerbation of chronic bronchitis

- Causes: virus, or bacteria: (H.Influenzae, S.pneumonia, M.catarralis)

Pneumonia

- Pneumonia is a **serious infection of bronchioles & alveoli.** It can be:

1- Community acquired (CAP)
2- Hospital acquired (HAP)

S.pneumonia (66%), H.influenza (20%), M.catarrhalis (20%)

NOTES:

*Upper respiratory tract infections are most common due to exposure to external environment.

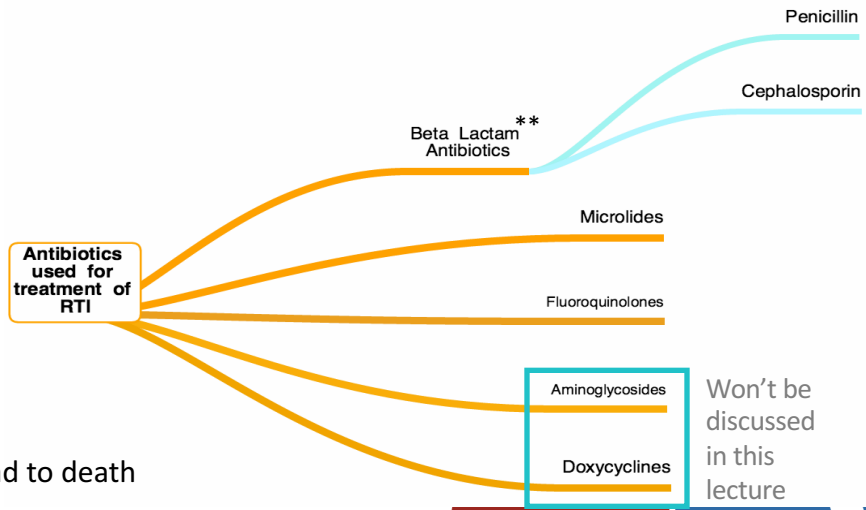
* Lower respiratory tract infections are costly & more difficult to treat.

*The air we breath will go to trachea then bronchi and finally to the alveoli then the circulation. The lower respiratory infections are the most dangerous because it will be in place that hard for antibiotics to reach and could lead to death.

* Most common routes of administration of antibiotics:

Oral for URTI's

IV Injection for LRTI's (possible hospital admission)



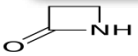
*more dangerous-difficult to treat –lead to death

** تحتوي على حلقة البيتا لاكتام

Penicillin (β-lactam)

Broad- spectrum Penicillins
(Act on both gram +ve & gram-ve microorganisms)

- Amoxicillin - Clavulanic
- Ampicillin - Sulbactam
- Piperacillin - Tazobactam

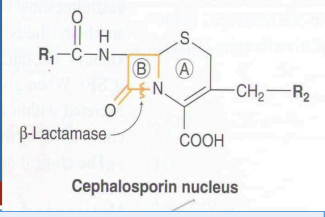


الدرق الاخر(اللي بالأحمر) وظيفته فقط حماية حلقة البيتا لاكتام(اللي في الصورة لان بعض البكتيريا تهاجم هذي الطاقة و تبطل مفعول المضاد) و ليس له أي علاقة بالبكتيريا

Mechanism	1. Inhibits bacterial cell wall synthesis through inhibition of peptidoglycan layer of the cell wall. Penicillin inhibits transpeptidase enzyme which is a bacterial enzyme that cross-links peptidoglycan chains to form rigidcell walls. 2. Bactericidal (kills bacteria) all act one gram +ve and –ve.
Pharmaco-kinetics	1. Given orally or parenterally 2. Not metabolized in human, thus excreted mostly unchanged in urine. 3. Relatively lipid insoluble. Doesn't cross placental barrier nor BBB, but yet used in meningitis because inflamed meninges are more permeable to the penicillins. (inflammation = ↑ permeability) 4. Half-life=30-60 min (increased in renal failure). 5. Probenecid slows their elimination and prolonged their half life.
Adverse effects	1. Hypersensitivity reactions. Most serious ADR! Penicillins could cause Anaphylactic shock, so it is important to do skin test before prescribing the drug 1. Convulsions (due to increased concentration in plasma, either after high IV dose or in renal failure) 2. Nephritis 3. Diarrhea (اغلب المضادات تسبب الاسهال لأنها تقتل النورمال فلورا) 4. Superinfections (superinfection is a second infection superimposed on an earlier one, mostly due to healthy normal flora eradication by antibiotics)
Therapeutic uses	1. Upper respiratory tract infections 2. used in treatment of Acute otitis media especially those produced by GroupA streptococci, which is gram positive (beta-hemolytic). 3. Lower respiratory tract infections

From the first generation to the third generation of cephalosporins, there is:
—A decrease in gram-positive coverage
—An increase in gram-negative coverage
—An increase in CNS penetration
—An increase in resistance to β-lactamase

Cephalosporins



Mechanism of Action	Inhibit bacterial cell wall synthesis → Bactericidal		
Generation	1st	2nd	3rd
Drugs	*Cephalexin*	*Cefuroxime axetil*, *Cefaclor*	*Ceftriaxone*, *Cefotaxime*, *Cefixime*
Route	Orally	Orally (well absorbed)	I.V.
Spectrum	Gram +ve	Mainly Gram -ve (β-Lactamase – producing Bacteria)	(wide selection of Gram -ve Bacilli (no effect on Gram +ve)
Uses	Upper Respiratory Tract Infections (URTI) (Post-operative)	Upper and Lower Respiratory Tract Infections	• Effective in treating Pneumonia • (Emergency) • Meningitis (due to CNS Penetration)
Pharmacokinetics	• Relatively lipid insoluble → do not penetrate cells or the CNS. Except 3rd generation • Mostly excreted unchanged by the kidney(glomerular & tubular secretion) • Half-life 30-90 min; except ceftriaxone 4-7 hr • Probenecid ↑ half life (slows elimination)		
ADRs	• Hypersensitivity reactions • If allergic to Penicillin → don't give cephalosporins (cross reactivity) • Thrombophlebitis* • Superinfections* • Diarrhea		

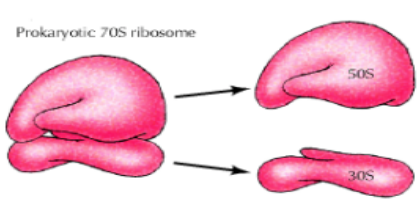
Glossary

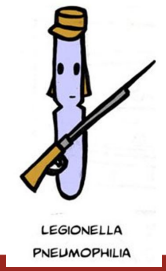
Thrombophlebitis: Inflammation of veins

Superinfections: an infection that develops during drug treatment for another infection, caused by a different microorganism that is resistant to the treatment used for the first infection

Macrolides

		Erythromycin	
		Azithromycin	*Clarithromycin*
Mechanism of Action		Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes → Bacteriostatic At high doses: Bactericidal	
Spectrum		Gram -ve	Gram +ve
Route		Stable at gastric acidity → Orally	
Drug Interaction		No effect on cytochrome P-450	Inhibit cytochrome P-450 → increase duration & toxicity of co-administered drugs
Pharamacokinetics	**Metabolism**	Undergo some hepatic metabolism (inactive metabolite)	Metabolized to active metabolite
	Excretion	• Biliary route is the major route of elimination • 0-15% excreted unchanged in the urine	
	Half-life	3 days	6-8 hours
Dose		Once daily	Twice daily
Uses		• Chlamydial pneumonia • Legionella pneumonia	
ADRs		• GI disturbance • Hypersensitivity reactions	
Notes		Hepatic metabolism → not given to patients with Liver failure. Vomiting may require re-dosage of Azithromycin	





Fluoroquinolones

Drug	Ciprofloxacin	Moxifloxacin	Gatifloxacin
Dose	Given twice-daily	given once-daily	
Spectrum	• Mainly effective against gram – ve. • Has high activity against pseudomonas species.	• Effective against gram-ve and gram +ve. • Has high activity against pseudomonas species.	
Mechanism of action	inhibits DNA gyrase enzyme, which is an enzyme involved in DNA supercoiling.		
Pharmacokinetics	• Given orally or parentally. • Concentrates in many tissues (kidney, prostate, lung, bones and joints). • Excreted mainly trough the kidney. • Has long half life.		
Clinical uses	• Acute exacerbation of chronic obstructive pulmonary disease. • Community acquired pneumonia. • Legionella pneumonia.		
Adverse effects	• Nausea, vomiting and diarrhea. • CNS effects (confusion, insomnia, headache and anxiety). • Damage of growing cartilage (arthropathy). • Phototoxicity. Avoid excessive sunlight		
Contraindications	• Not recommended for patients under 18 years. • Pregnancy. • Breast feeding women.		

Boys	Girls
عبدالرحمن ذكري	غادة المهنا
عبدالعزيز رضوان	اللولو الصليهم
مؤيد أحمد	روان القحطاني
فيصل العباد	درة الحمدي
فارس النفيسة	شروق الصومالي
خالد العيسى	سما الحربي
عبدالرحمن العريفي	انوار العجمي
عبدالرحمن الجريان	وتين الحمود
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