Pharmacology team

Treatment of Respiratory Tract infections

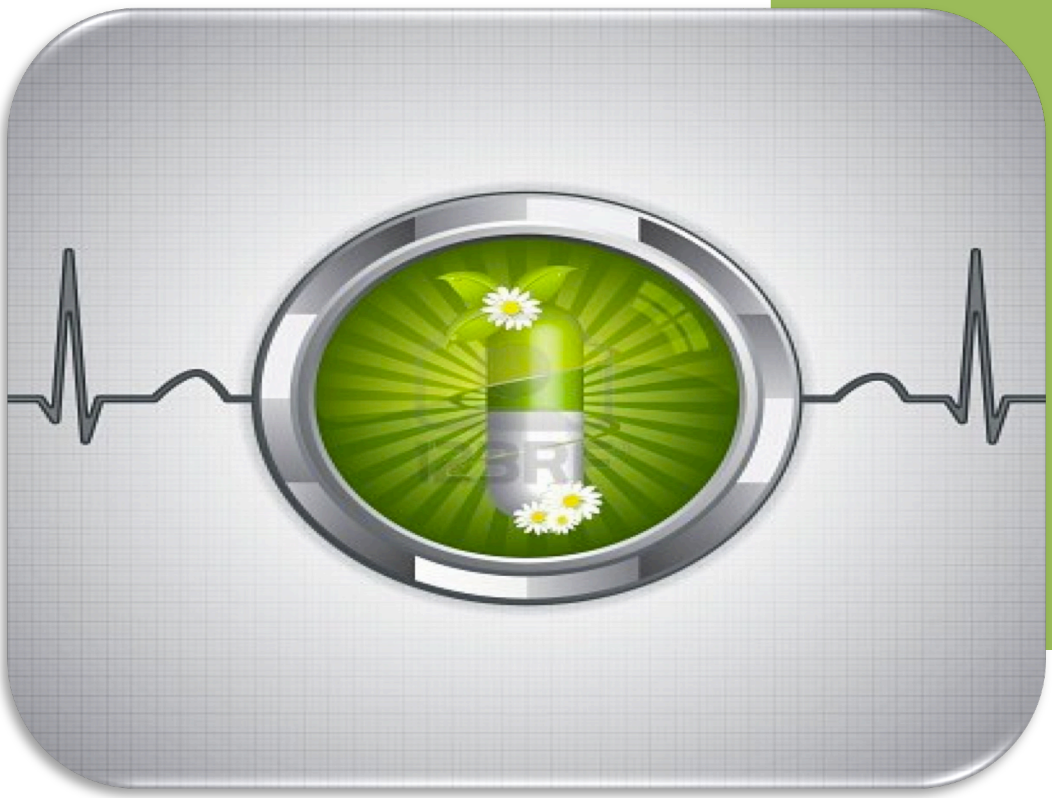
Objectives:

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

ll Types of respiratory tract infections

ll Antibiotics commonly used to treat respiratory tract infections and their side effects.

ll Understand the mechanism of action, pharmacokinetics of individual drugs.



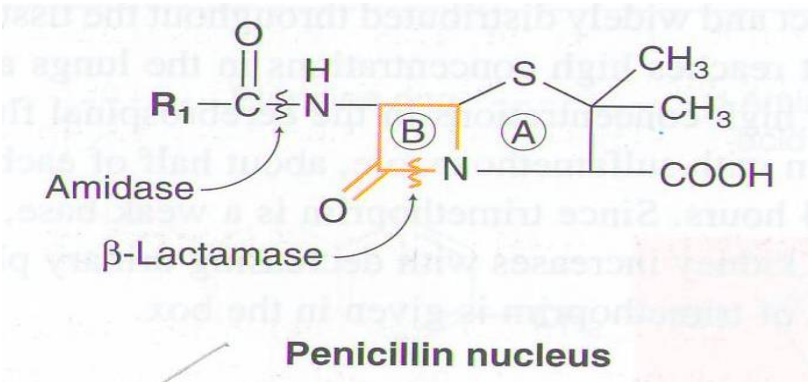
Treatment of Respiratory Tract infections

Bacteriostatic: Capable of inhibiting the growth or reproduction of bacteria

Bacteriocidal: Capable of killing bacteria

Broad Spectrum(B.S) : Act on both (+) , (-) Bacteria

Narrow spectrum(N.S) : Act on either only (+) or only (-)



Penicillin nucleus

When there is a destruction of the **B-lactan ring**, **Prenicillin** will lose its antimicrobial activity

There are some microorganism which have the ability to produce **B-lactase enzyme** to destroy the **B- lactan ring**, so they usually give them with **β-Lactamase inhibitors**.

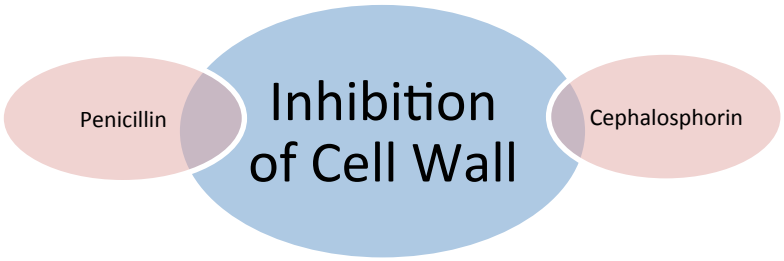
N.B. there are two tables which our team made for this lecture so you have to choose only one type of tables the next page is table which contain all the antiobiotics on one table and after that each class of the antibiotics on separate table.

	Penicillins	Cephalosporins		Macrolides		Fluoroquinolone
Mechanism of action	-Inhibits bacterial cell wall synthesis -Bactericidal (kill)			-Inhibit protein synthesis by binding to 50 S subunit of the bacterial ribosomes -Bacteriostatic -Bacteriocidal at high concentration		-Inhibit DNA synthesis by inhibiting DNA Gyrase enzyme
examples	-Amoxicillin -Ampicillin	2ed generation: -Cefuroxime axetil -Cefaclor	3ed generation: -Ceftriaxone -Cefotaxime	-Erythromycin		-Moxifloxacin -Gatifloxacin
				Clarithromycin	Azithromycin	-Ciprofloxacin
Acts on	both G +ve & G -ve microorganisms	Effect **mainly** on G -ve bacteria. It means that they affect on both	Effect **mainly** on G -ve bacilli. It means that they affect on both	More effective on G+ve bacteria	More effective on G ve bacteria	**Antibacterial spectrum.** **Mainly effective against G-ve bacteria**
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)**.	**-Well absorbed orally** **-Active against β-lactamase – producing bacteria**	**-Given by IV route** **-Effective treatment in pneumonia produced by β-lactamase producing bacteria**	-Stable at gastric acidity -Inhibits cytochrome P450 system -Metabolized to active metabolite -Excreted in urine20,40% unchanged or metabolite Bile approx.60% -Half-life 4-5 hours	-Stable at gastric acidity -Undergo some hepatic metabolism (inactive metabolite) -Biliary route is the major route of Elimination -Only 10-15% excreted unchanged in the urine -Half- life (3 days) -Once daily dosing No effect on cytochrome P-450	**Well absorbed orally (available 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** **Half-life 3.3 hrs**
		In general: **-Given parenterally or orally** **-Relatively lipid insoluble** **-Excreted Mostly unchanged in the urine.** **-Half-life 30-90 min (increased in renal failure)**				
Adverse effects	-Hypersensitivity reactions -**Convulsions** (after high dose by IV or in renal failure) -Diarrhea (Superinfections) -**Nephritis**(not common)	-Hypersensitivity reaction. **-Thrombophilibitis** -Superinfections -Diarrhea		-Affect the live. - jaundice -GI disturbances.		-Nausea -vomiting -diarrhea -CNS effects (confusion, insomnia, headache, dizziness & anxiety). -Damage growing cartilage. (**arthropathy)** Phototoxicity
Uses	**Lower** and **upper** respiratory tract infections					-Acute exacerbation of chronic obstructive pulmonary disease -Community acquired pneumonia -Legionella pneumonia
combinations	**With β-Lactamase inhibitors** **Ex- Clavulanic acid** **Sulbactam** **Themselves have no antibacterial activity.** **They inactivate β-lactamase enzyme.** **e.g. Amoxicillin/clavulanic acid (augmentin)** **Ampicillin/ sulbactam**					

Contraindications :

Is preferably avoided in adolescents (under 18 years because of arthropathy)

Pregnancy/lactation



Antibiotic Class	Examples	MOA	S/E	Clinical Uses
Penicillin	Amoxicillin Ampicilin	Bactericidal **Inhibit cell wall synthesis of bacteria** **B.S : Act on (+) & (-)**	**Hypersensitivity** Convulsion (high dose) **Diarrhea** Nephritis	1-URTI **especially Group A Streptococci** (β-Hemolytic) 2-LRTI

N.B.

Amoxicillin & Ampicilin are **sensitive to β-lactamase enzyme** ,so we mix them with **β-lactamase inhibitors** to be more strong ,here are examples about them :

Amoxicillin + **Calvulanic Acid** (Agumientin)

Ampicilin + **Sulbactam**

Antibiotic class	MOA	Examples		S/E
Cephalosphorins Has generations	**Inhibit bacteria cell wall synthesis** Bactericidal	2nd generation: **Cefuroxime axetil, Cefaclor** **N.S: (-)**	Absorbed orally **Active against β-lactamase inhibitors**	**Hypersensitivity** **Thrombophilibitis** **Super infection** **Diarrhea**
		3rd generation: **Ceftriaxone** **Cefotaxime** **Spectrum:** Have enhanced activity against gram-negative bacilli	Given I.V. **Effective against pneumonia** produced by β-lactamase producing bacteria	

Antibiotic class	MOA	Examples	S/E
Macrolides Erythromycin: 1- Clarithromycin 2- Azithromycin	Inhibit protein synthesis 50-S subunit of ribosome Bacterostatic Bactericidal (high dose)	***Clarithromycin** **N.S: (+)** Inhibit cytochrome P-450	**GI Disturbances** **Jaundice**
		***Azithromycin** **N.S: (-)** Once daily dose No effect on cytochrome P-450	

Antibiotic class	MOA	S/E	Clinical Uses
Flouroquinolones e.x Ciprofloxacin	Inhibit DNA synthesis by inhibiting DNA-gyrase **N.S: (-)** Interfere with Di& Tri cations such as milk and its derivatives Doesn't cross BBB	Nausea, vomiting& diarrhea CNS affect (headache, confusion…) ***Cartilage damage ,so we don't give it to <18 years old or pregnant patient** Phototoxicity	**Community aquaria pneumonia** **Acute exacerbation of COPD** **Legionella Pneumonia**