ANTI-BACTERIAL AGENTS

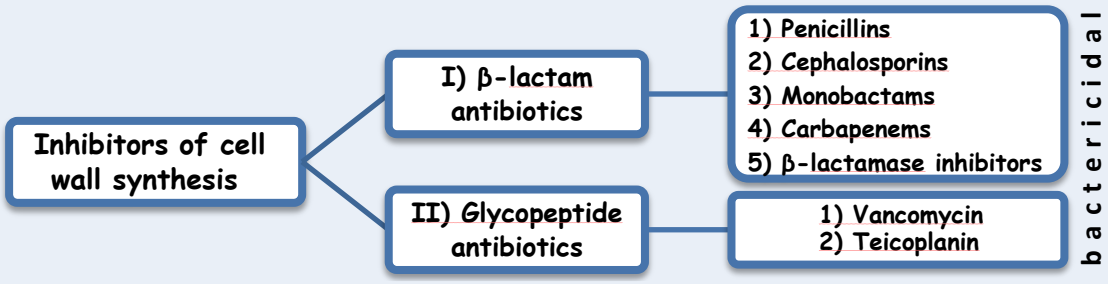
Content :

- Summarization of examples of anti-bacterial agent & their spectrum.

Classification of Anti-bacterial Agents : Inhibitor of :

1) Cell wall synthesis, **2)** Protein synthesis, **3)** Nucleic acid synthesis & function, & **4)** Metabolism.

A) Inhibitors of cell wall synthesis :



I) β-lactam antibiotics : 1) Penicillins :

CLASSIFICATION	***	EXAMPELS	SPECTEUM & EXAMPLES
Narrow spectrum	**Yes**	**1)** Benzylpenicillin (G). **2)** Phenoxymethyl-penicillin (V).	**1) Gram +ve cocci:** *streptococci*, *staphylococci* (non-penicillinase) & *pneumococci*. **2) Gram –ve cocci:** *N.meningitidis* (*meningococcal meningitis, septicemia*) & *N. gonorrhoeae*. **3) Gram +ve bacilli:** *B.anthracis*, *C.tetani* & *C.perfringens*. **4)** *Treponema pallidum* (**syphilis**), *Leptospira* (**leptospirosis**).
Antistaphylococcal	**No**	**1)** Methicillin. **2)** Flucloxacillin. **3)** Cloxacillin. **4)** Nafcillin.	**1)** Staphylocooci. **2) Streptococci.** **3) Pneumococci.**
Broad spectrum	**Yes**	**1)** Ampicillin. **2)** Amoxicillin. **3)** Co-amoxiclav.	**1) Gram +ve.** **2) Gram –ve cocci.** **3) Gram –ve bacilli:** *E.coli, H.influenzae, & Proteus mirabilis.*
Antipseudomonal	**Yes**	**1)** Ticarcillin. **2)** Piperacillin. **3)** Azlocillin. **4)** Mezlocillin.	**1)** ***Pseudomonas aeruginosa***. (Mainly) **2) Enterobacter species.**
β-lactamase inhibitors*	**No**	**1)** clavulanic acid. **2)** tazobactam.	**β-lactamase producing bacteria.**

NOTES

- The **most** widely effective antibiotics & the **least** toxic drugs known.
- **Administration:**
  - **Parenterally** : As Benzylpenicillin (penicillin G) & anti-pseudomonal penicillins.
  - **Orally** : As Phenoxymethylpenicillin (penicillin V) (resists gastric acid).
  - **Both parenterally & orally** : As ampicillin, amoxicillin & cloxacillin.
  - **Depot forms**: Procaine penicillin G & benzathine penecillin G are given IM.
- Their **plasma t1/2 = 1hr.**
- Eliminated by **renal excretion** (90 % by active tubular secretion that can be blocked by **probenecid**).

*** : β-lactamase susceptibility.

* : **Co-amoxiclav** (Augmentin) = amoxicillin + clavulanic acid (**Broad spectrum**) & **Tazosin**= tazobactam + piperacillin (**Antipseudomonal**).

I) β-lactam antibiotics : 2) Cephalosporins :

GEN.	EX(*):	Cross BBB?	***	SPECTRUM
1st	**Cefalexin** (Oral) **Cefazolin** (Inj.)	No	Yes	**Gram +ve mainly:** pneumococci, streptococci & staphylococci (Include *S.aureus*). **Few Gram –ve:** *Klebsiella pneumonia, E. coli, Proteus mirabilis.*
2nd	**Cefaclor** (Oral) **Cefoxitin** (Inj.) **Cefuroxime** (Both)	No (except **Cefuroxime**)	Yes	**More Gram –ve than CS1:** *H.influenzae, Neisseria gonorrhea, Enterobacter.* **Gram +ve** (Less active).
3rd	**Cefixime** (Oral) **Ceftriaxone** (Inj.) **Cefotaxime** (Inj.)	Yes (except **Ceftriaxone**)	No	**Wide range of Gram –ve:** *Gonorrhoea* Meningitis, *Septicaemia & Pseudomonas* infections (**ceftazidime**).
4th	**Cefepime** (IV)	Yes	No	**Good for:** *pseudomonas, haemophillus & Neisseria.*

NOTE(S)

For mnemonic :
*Drug that have '**FA** (or **PHA**)' in their name are 1st generation except **Cefaclor** which is 2nd generation.
*Drug that have '**IME** & **ONE**' are 3rd generation except **Cefuroxime** which is 2nd generation.
*Drug that have '**PI**' in their name are 4th generation.
- They are eliminated through **kidneys** (Except **Ceftriaxone** is excreted through **bile**).
- Their **t1/2 = 1-4 hrs.** - CSs are safe during **pregnancy**.

2nd generation : Oral CS2 are used to treat upper & lower respiratory TI (***Klebsiella***, ***H. influenzae***).
- **Cefuroxime** (injectable) is effective against ***H. influenzae meningitis*** .
- **Cefoxitin** is effective against **anaerobic** organism as ***Bacteroides fragilis***, so it is useful in mixed anaerobic infections like ***peritonitis*** & ***diverticulitis***.

I) β-lactam antibiotics : 3) Monobactams & 4) Carbapenems :

NAME	***	SPECTRUM
Aztreonam (IM & IV)	No	**Only Gram –ve:** *Enterobacteriaceae, Pseudomonas aeruginosa* and *H. influenza.* **(Narrow spectrum)**
Carbapenems (IV) - **Imipenem.** - **Meropenem.** - **Ertapenem.**	No	**Broadest-spectrum B-lactam antibiotics:** penicillinase- porducing Gram +ve, Gram –ve bacilli & anaerobic B.

NOTE(S)

Carbapenems :
- **Imipenem** is inactivated by dehydropeptidase in renal tubules given as **cilastatin (Imepenem + cilastatin = Tienam).**

II) Glycopeptide antibiotics : 1) Vancomycin 2) Teicoplanin :

NAME	***	SPECTRUM
Vancomycin (Orally & IV)	No	**Aerobic & anaerobic Gram +ve bacteria including (MRSA), enterococci.**
Teicoplanin (IV & IM)	-	**Is very similar to vancomycin** (but longer duration =50hrs).

NOTE(S)

Vancomycin:
- Serious infections caused by **Gram +ve cocci.**
- Prophylaxis & treatment of **endocarditis.**
- Eliminating ***Clostridium difficile*** of **antibiotic-associated colitis** (Given orally).

** **For systemic effect** → **IV infusion 12 hourly.**
** **For local effect** → **orally.**
- **Half-life (t1/2) 6-10 hrs.**

(*)= Route of admintration. ***= β-lactamase susceptibility.
S.Es & therapeutic uses for all above → from slides.

B) Inhibition of bacterial proteins synthesis:

I) Drug that affect the 30S ribosomal subunit:

NAME	FEATURES (PK)	CLINICAL USES & SPECTRUM	RESISTANCE?
Aminoglycosides - **Gentamicin** - **Neomycin** - **Streptomycin** -**Spectinomycin**	- Highly polar. - Given: IM & IV. - Limited tissue penterated. - Can't cross BBB & eyes. - Excreted by renal.	- Aerobic gram -ve bacteria (**serious** infections). - **Streptomycin**→tuberculosis. - **Spectinomycin**→gonorrhea (IM).	Plasmid-mediated fromation of inactivating enzymes.
Tetracyclines - **Doxycycline** - **Minocycline** - **Tetracycline**	- Oral absorption is impaired by (calcium, iron, aluminum). - Wide distribution. - Can cross plasental barrier. - GO entero-hepatic cycling. - Eliminated by kidneys except **doxycycline** (feces).	**1ry use:** *Mycoplasma pneumonia, Chlamydia, Rickettsia, Vibrio.* **2ry use**: alternative to **syphilis**, prophylaxis against infections in bronchitis & treatment of acne. **Selective uses: Tetracycline** → H.pylori infection in the ulcer. **Doxycycline** → inhibits the renal action of ADH.	Plasmid-mediated fromation of inactivating enzymes. Development of efflux pump.

II) Drug that affect the 50S ribosomal subunit:

NAME	FEATURES (PK)	CLINICAL USES & SPECTRUM	RESIS.
Chloramphenicol - **Clindamycin (cleocin)** - **Quinupristin-dalfopristin (synercid)**	- Very lipophilic (well absorbed). - Highly accumulated in the CNS (treatment of menengitis). Metabolized partly glucuronate conjugation. - Kidney excretion, has a short half life.	- Meningococal and pneumococal infections (*H. İnfluenzae).* - Treatment of **serious** infections caused by *Ricettsia.* - Topical use for eye infection	
Linezolid	- Binds to the 23S ribosomal RNA of the 50S subunit.	- Effective against gram +ve & *M. Tuberculosis.*	
Macrolides (Prevent translocation step)	- **Wide distribution** (clarithro and azithro → extensive penetration). Minimal CSF penetration. - **Eliminated** by **liver** (Clarithro is partially eliminated by the **kidney**). - Typically bacteriostatic. (Bactericidal at high conc.)	**1) Gram +ve aerobes : (Cla > Ery > Azi)** Methicillin-susceptible *S.aureus, S.pneumoniae* (only PSSP), Group and viridans streptococci, *Bacillus sp & Corynebacterium sp.* **2) Gram -ve aerobes : (Azi > Cla > Ery)** H. influenzae (not erythro), M. catarrhalis & Neisseria sp. **3) Atypical Bacteria. 4) Anaerobes.** **5) Other Bacteria** – Mycobacterium avium complex (MAC – only A and C), Treponema pallidum, Campylobacter, Borrelia, Bordetella, Brucella & Pasteurella. **(therapeutic uses/ drug interactions – from slides)**	Active efflux. Alterd target site. Cross - resistance occure between all macrolides.
- **Erythromycin**	- **t1/2=1.4 hrs.** - Variable absorption.	**"Drug of Choice" for :** Mycoplasma pneumonia, Legionella pneumophila, C.pneumoniae, C. trachomatis B.pertussis (whooping cough) & C. diphtheriae .	
- **Clarithromycin**	- **t1/2= 3 to 7 hrs.** - Low toxicity. - Well-absorbed (regardless of presence of food).	- Strongest activity on Gram +ve, Legionella pneumophila, Chlamydia pneumoniae & H.pylori. **USES:** Atypical mycobacterial infections (MAC), Resistant leprosy, Toxoplasmosis & H.Pylori induced peptic ulcers.	
- **Azithromycin**	- **t1/2= 68 hrs.** - Excellent tissue concentration. - Food decreases absorption.	- Strongest activity against mycoplasma pneumoniae. - More effective on Gram-ve, H.influenzae, Legionella. - Mainly used in respitory tract infection.	
- **Roxithromycin**	- Reaches highest blood conc. - Bioavailability up to 72~85%.	Respiratory tract and soft tissue infection.	

NOTE(S)

Aminoglycosides : Antibacterial synergy may occur with the combination of wall synthesis inhibitors.

	Erythromycin	vs	Clarithromycin & Azithroomycin	
	Narrow spectrum, Acid labile, Poor GI tolerance & Short elimination half-life.		Broader spectrum, Acid stable, Better bioavailability, Better tissue penetration, Prolonged half-lives & Improved tolerability.	

C) Antifolate drugs:

DRUGS	FEATURES (PK)	CLINICAL USES	SPECTEUM (Activity)
Sulfonamides - Inhibition of dihydropetroate synthase.	1) Oral absorbable. 2) Oral, nonabsorbable. 3) Topical. 4) Serum protein bind. (20 ~ 90%) 5) Excreted into urine.	**Oral absorbable agents:** **Sulfisoxazole, sulfamethoxazole** :To treat urinary tract infection. **Sulfadiazine**: Toxoplasmosis. **Sulfadoxine**: long acting (7-9 Days), in a combination for treatment of malaria. **Oral nonabsorbable agents:** Ulcerative colitis, enteritis, other inflammatory bowel disease. **Topical agents:** **Sulfacetamide**: Ophthalemic. **Mafenide & silver sulfadiazine**: Topically.	1) Gram +ve & Gram -ve. 2) Nocardia, chlamydia trachomatis. 3) Some protozoa. 4) Some enteric bacteria. 5) Rickettisiae.
Trimethoprim	1) given **orally** (Combine w/ **sulfamethoxazole**). 2) Excreted into urine. 3) More antibacterial activity in prostatic & vaginal fluids.	**Oral Trimethoprim:** - Acute urinary infection. **Oral trimethoprim-sulfamethoxazole:** - P jiroveci pneumonia, shigellosis, systemic salmonella infection, complicated urinary tract infection. - Active against many respiratory pathogen. **Intravenous trimethoprimsulfamethoxazole:** - Gram -ve sepsis, pneumocystis pneumonia. - Shigllosis, typhoid fever. **Oral pyrimethamine with sulfanamide** - With **sulfadiazine** in Leishmaniasis, toxoplasmosis. - With **sulfadoxine** in malaria.	

NOTES

Sulfonamides :
Resistance :1) Overproduction of PABA, 2) Low affinity dihydropetroate synthase, & Loss of permeability to sulfonamides.

Trimethoprim :
Resistance : 1) Reduced cell permeability, 2)Overproduction of DHF reductase, & 3) Altered affinity of reductase.

CO-trimoxazole : Combination of **sulfamethoxazole** & **Trimethoprim**.

D) DNA gyrase inhibitors:

NAME	FEATURES (PK)	CLINICAL USES	SPECTRUM (Activity)
Fluoroquinolones - Block of bacterial DNA synthesis by inhibiting **topoiso-merase** II, IV.	1) Well absorbed **orally**. 2) Good distribution. 3) Divalent cations impair absorption.	**1) Urinary tract infection.** Even with multi-drug resistant organisms. **2) Bacterial diarrhea.** Shigella, salmonella, toxigenic E. coli. **3) Infections of soft tissues, bones and joints.** **4) Intra-abdominal and respiratory tract infections.** **5) Gonococcal infection,** **6) Chlamydial urethritis and cervicitis.** **7) Legionellosis.** **8) TB & atypical mycobacterial infections.**	1) Gram +ve & Gram -ve. 2) Mycoplasma & clamydia, legionella. 3) Some mycobacteria. 4) Anaerobic bacteria.
Nalidixic acid & cinoxacin	Excreted too rapidly.	**Useful for urinary tract infections.**	

NOTE(S)

Fluoroquinolones: Resistance : 1) Change in permeability & 2) Loss of affinity.

(PK)= Pharmacokinetics.

وفقكم الله جميعـا
لا تنسونا من صالح دعائكم