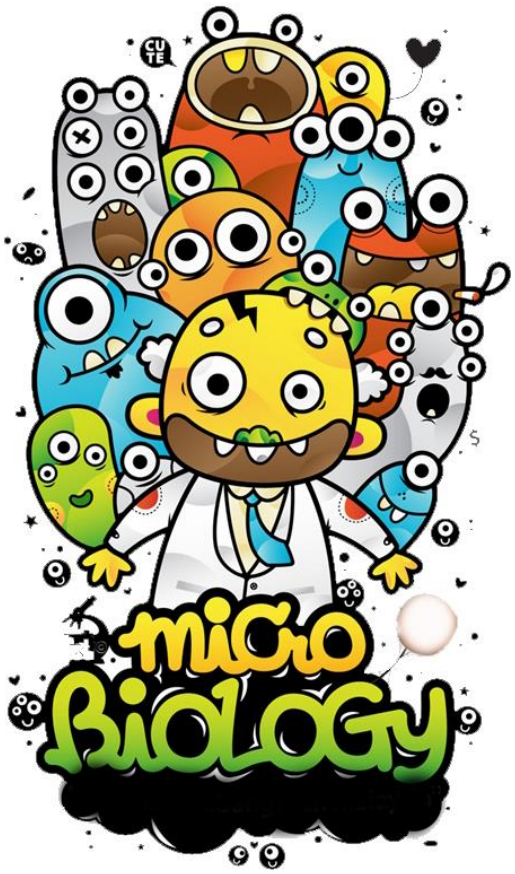


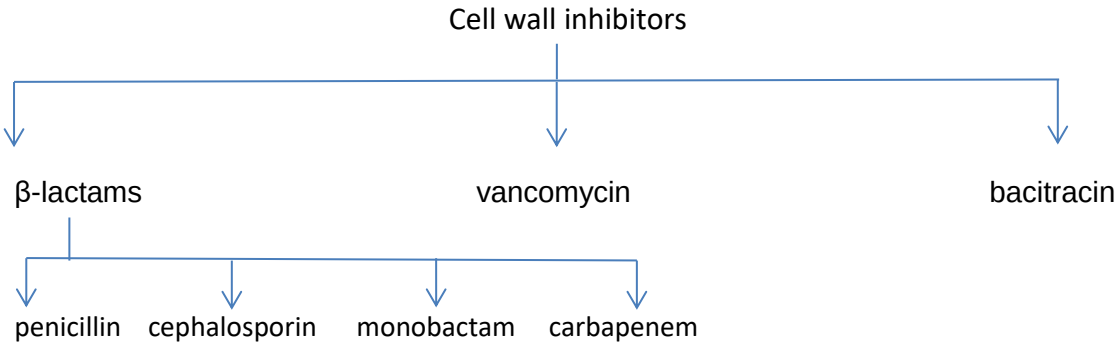
Subject: Antibiotic Summary

Done by: Farah Alhunaiti

Corrected by: Rama Toukan

1)cell wall inhibitors

-They cause disruption in cell wall synthesis which leads to cell burst due to low osmatic pressure in body fluids.



1)β-lactams : they inhibit the synthesis of peptidoglycan layer because they are analogues to D-alanyl-D-alanine residue which is the substrate for transpeptidase enzymes (PBPs) so they bind irreversibly and inhibit it from cross linking causing weakening in the cell wall.

2)vancomycin : It binds to D-alanyl-D-alanine residue forming a complex which inhibits peptidoglycan synthesis

3)bacitracin : Interfere molecules that carry peptidoglycan subunits across cell membrane to their site in cell wall

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penicillin " may be used prophylactically before surgeries"

	Name	Administration	Against	Notes
Naturally occurring	Penicillin G	IV :potassium salt IM:procaine/benzathine salt	G+ve only	Can't withstand stomach acid
	Penicillin V	Orally		Withstand stomach acid
Semi-synthetic	Ampicillin	Orally	Broader spectrum than penicillin G (both G+ve and G-ve)	
	Amoxicillin			We take it with clavulanic acid for β-lactamase
	Carbenicillin	Parenterally	Extended spectrum especially pseudomonas infections	
	Ticarcillin			
	Piperacillin			We take tazobactam for β-lactamase
	Methicillin		G+ve for bacteria resistant to penicillin	MRSA has emerged
	Oxacillin		Narrow spectrum (G+ve) for lactamase-producing staphylococcus aureus	
	Cloxacillin			
	Nafcillin			

Intrinsically resistant to β lactamase

*problems facing penicillins:

1- β-lactamase enzyme (naturally occurring) which breaks β-lactam ring and is solved in 2 ways

2- 1-5% of adults are allergic to them (anaphylactic shock⟶ death)

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cephalosporin

- **Naturally occurring**
  - -from cephalosporium
  - -not active now
- **Semisynthetic**
  - -broader spectrum than penicillin
  - -more resistant to β-lactamase but still degraded by cephalosporinase

الجدول الموجود في سلايد
١٧ صفحة ٩ مطلوب كاملا

*Problems facing cephalosporin:

1)people with penicillin allergy 4-15% are also allergic to them.

2)cephalosporin and penicillins exert their activity against metabolically active bacteria only so it can't be used with bacteriostatic agents.

Monobactam , carbapenems , vancomycin, bacitracin

Name	**against**	**disease**	**Example**	**administration**	**Resistance to β-lactamase**	**Note**
monobactam	G-ve only including pseudomonos aeruginosa	-meningitis -UTI -kidney infection	aztreonam	Parenterally	Usually yes	No cross allergy
carbapenem	G+ve and G-ve including pseudomonas aeruginosa and enterococci		Imipenem meropenem	parenterally	Highly	We take cilastatin with imipenem
vancomycin	-mainly G+ve -last resort for bacteria that are resistant to methicillin and cephalosporins (MRSA,enterococci)	Pseudomembranous -colitis		parenterally		-Used 40 years ago until VRSA emerged -toxic when combined with aminoglycosides (nephron-oto- toxic)
Bacitracin (polypeptides from bacillus)	G+ve			Topically (because it is highly toxic)		nephrotoxic

2)Disrupters of cell membrane

-Animal cells differ from fungal and bacterial cells in cell membrane so these drugs are selective in their action.

1)**polynes** " like antifungal agents ex: amphotericin, nystatin "

Action : they bind to certain sterols (ergosterol) present in the fungal membrane forming transmembrane holes which results in leakage of intracellular components .

Problem : has low therapeutic index .

2)**cyclic lipopeptides** and the include :

Name	**Include**	**Action**	**Side effect**	**Against**	**Disease**	**Administration**
Polymyxin	Compounds: A,B,C,D,E	Disrupt membrane permeability and result in: 1)leakage 2)depolarization	serious side effects when used parenterally	G-ve including pseudomonas	Skin infections Wounds Burns	Topically Parenterally(needs monitoring)
Daptomycin		Insert into the membrane forming aggregates which results in membrane disruption and depolarization		G+ve including: -VRE -MRSA		Parenterally but needs monitoring

3) inhibitors if nucleic acid synthesis

Name	**Source**	**Action**	**Include**	**Against**	**Disease**	**Side effect**
Quinolones	Synthetic	act by inhibiting DNA gyrase thus inhibiting DNA synthesis	Nalidixic acid Fluoroquinolones such as 1)ciprofloxacin 2)norfloxacin 3)enoxacin 4)ofloxacin Levofloxacin (last 3 diseases)	-G+ve & G-ve (including Pseudomonas aeruginosa) -UTI bacteria that is resistant	1)traveler's diarrhea 2)UTI 3) community acquired pneumonia 4) sinusitis 5) acute exacerbations of chronic bronchitis	
Rifamycins	Semisynthetic	binds to RNA polymerase & blocks mRNA synthesis	rifampin/rifampicin (they are the same but different accents)	Mycobacteria	TB	At high doses it turns the skin and body secretions to orange-red color, it also can result in liver damage

4)Antimetabolites

- A group of compounds that are structurally similar to normal microbial metabolites , so they interfere with microbial metabolic reaction .

-They act in 2 ways :

1) competitive inhibition of enzyme , How?

By resembling the substrate of the enzyme

2) By being incorporated into important molecules such as nucleic acids thus inhibiting their function .

-Antimetabolites

- Antifolates (sulfa drugs and trimethoprim)
- Purines analogues
- Pyrimidines analogues

Name	Source	Effect on becteria	action	Side effect	Include	Disease	Notes
Sulfonamide	synthetic	Bacteriostatic effective against most G-ve & and G+ve bacteria Staphylococci	competitive inhibition to the enzyme that acts on para amino benzoic acid (PABA) needed for folic acid synthesis	It is toxic to the bone marrow and can induce hypersensitivity reactions and Stevens–Johnson syndrome	Sulfadiazine Sulfamethoxazole	-Some kinds of meningitis -UTI -Pnemocystis pneumonia	-Folic acid is important for synthesizing nucleic acids -animal cells obtain folic acid form the diet while bacterial cells synthesize it - Sulfamethoxazole is usually given in combination with trimethoprim and This combination drug is called co-trimoxazole (TMP-SMX or TMP-SMZ)

Isoniazid (INH)		effective against Mycobacteria & has little effect on other bacteria	– It binds to and inhibits the enzymes that converts vitamins B3 and B6 to other metabolites – This results in inhibiting the synthesis of mycolic acid.				-Isoniazid is absorbed from GIT. - it should be transformed by bacterial enzyme to the active form (prodrug) -Resistant mycobacteria stops producing the activating enzyme so we use it in combination with rifampin & ethambutol

5) protein synthesis inhibitors

- They act on bacterial ribosomes (70s=50s+30s) so they are selective and don't act on human cells (80s=40s+60s)

- All are bacteriostatic except aminoglycosides they are bactericidal at high concentrations

*in sheet 9 in pharma they mentioned that aminoglycosides act on both cell wall and proteins (refer to it ☺)

Name	**Aminoglycosides**	**tetracycline**	**tigecycline**	**Chloramphenicol**	**macrolide**	**Lincosamide**	**Streptogramin**	**Oxazolidinone**
Source	Streptomyces micromonospora	streptomyces semisynthetic	A derivative of minocycline	-streptomyces -synthetically	Have a macrolide ring		Macromolecule from streptomyces	
Side effect	Nephrotoxicity and ototoxicity	-Teeth discoloration -abnormal bone formation (not for pregnant or children under 5) -desrtoy normal flora which lead to GIT disordars and superinfectios by : Staphylo Pseudomonas Clostridium		Aplastic anemia Bone marrow supression (fetal)		When clyndamycin is used for a long term it cause colitis		

Against	-G-ve (pseudomonas ,entero) -G+ve - -mycobacteria	-G+ve -G-ve -mycoplasma	Broad spectrum execpt pseudomonas MRSA	Broad spectrum execpt (pseudomonas and enterococcus)	Most G+ve Streptococci Pneumococci Staphylococci Corne Mycoplasma Varible against G-ve Legionella pneumophila Helicobacter pylori	Bactroid Anaerobic bacteria Antiprotozoan G+ve execpt enterococci	G+ve which is resistant to other antibiotics (vancomycin) -VRE faecium -MRSA -streptococcus pyogenes	G+ve -MRSA -VRSA -VRE
Include	Streptomycin Gentamycin Tobramycin Neomycin Kanamycin Netilmicin amikacin	Tetracycline Chlortertracycline Minocycline Doxycycline			Erythromycin Roxithromycin Azithromycin Clarithromycin	Clindamycin Lincomycin	Streptogramin A(daflopristin) 70% B(quinopristin) 30%	linezolid
administration	Parenterally Topically	orally	paremterally		orally	topically (for acne)	Parenterally	orally
Action	Bind to 30s subunit and cause misreading of mRNA resulting in altered AA composition and /or premature terminat	Bind to 30s subunit preventing the attachment of tRNA to mRNA-ribosome complex	Same as tetracycline	Acts on 50s subunit in a way to prevent elongation	Act on 50s to prevent elongatin	bind to 50S subunit & inhibit polypeptide elongation and cause early release of the polypeptide chain	A and B interact at different sites to inhibit protein synthesis A(inhibit early stage of synthesis) B(prevent elongation and cause early realese)	Inhibit the initiation of protien synthesis (prevent the formation of ribosome – mRNA-tRNA comlex
Problems	Can't be absorbed by GIT	Become inactive with Ca so don't drink it with milk and that leads to side effects						
Disease	-complicated UTI -peritonitis -joint and bone infections	Rickettsia chlamydia		Meningitis Typhoid fever	Legionnaires' disease Stomach and duodenal ulcer	Malaria toxoplasmosis acne	Life threatening infections (skin , blood , abdominal)	Complicated infections caused by multidrug – resistant G+ve bacteria
Effect on bacteria	Bactericidal	Bacteriostatic	Bacteriostatic	Bacteriostatic	Bacteriostatic	bacteriostatic	bacteriostatic	bacteriostatic
Notes	Act synergistically with cephalosporins and penicillin	Can enter the host cell effective for intracellular disease	Was approved by FDA in 2005	Due to its side effect it is used as a last choice when alternative drugs are not effective Used with patients who are allergic to penicillins and cephalosporins	Alternative to penicillin in case of allergy For penicillin resistant bacteria	Clindamycin is less toxic than lincomycin		Expensive