Antimicrobials

Antibiotic - a substance of biological origin or obtained synthetically presenting bacteriostatic (inhibits the life processes of bacteria - growth, metabolism, cell division) or bactericidal properties (leads to the death of bacterial cells).

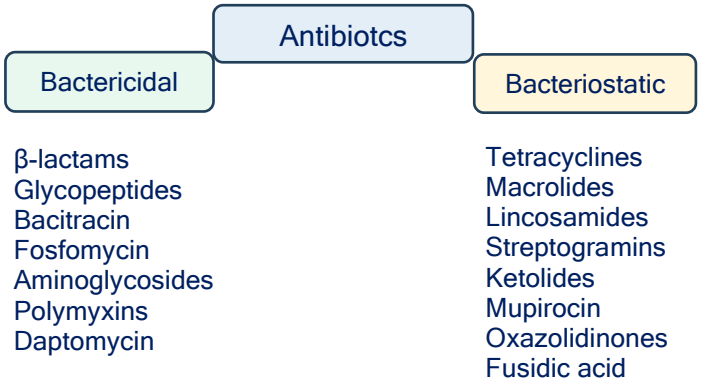
Division of antibiotics – main groups + representatives

	Group	Representatives			
1	**β-lactams**	**Penicillins**	**Cephalosporins**	**Monobactams**	**Carbapenems**
		Natural: benzyl, benzathine, procaine penicillins (parenteral) phenoxymethyl penicillin (oral)	**I generation**: cefazoline (parenteral) cefadroxil, cefalexin (oral)	aztreonam	imipenem meropenem ertapenem doripenem
		Semisynthetic: isoxazolyl penicillins (cloxacillin) ampicillin, amoxicillin, piperacillin	**II generation:** cefuroxime, cefamandole (parenteral) cefuroxime, cefaclor (oral)		**Carbapenems + BLIs:** imipenem/ relebactam meropenem/ vaborbactam
		Penicillins + BLIs ampicillin/ sulbactam amoxicillin/ clavulanic acid piperacillin/ tazobactam	**III generation:** cefotaxime, ceftriaxone, ceftazidime (parenteral) cefixime, ceftibuten (oral)		
			IV generation: cefepime (parenteral)		
			V generation: ceftaroline, ceftobiprole, ceftolozane		
			Siderophore cephalosporin: Cefiderokol		
			Cephalosporins + BLIs: ceftolozane/tazobactam ceftazidime/avibaktam ceftaroline/avibaktam		
2	**Aminoglycosides**	streptomycin, gentamycin, tobramycin, amikacin, netilmycin			
3	**Tetracyclines**	doxycycline, tetracycline			
4	**Glicylcyclines**	tigecycline			
5	**Macrolides/ Ketolides**	erythromycin, clarithromycin, azithromycin, fidaxomicin; ketolides – telithromycin, solithromycin;			
6	**Lincosamides**	clindamycin			
7	**Oxazolidynones**	linezolid, tedizolid			
8	**Glycopeptides**	vancomycin, teicoplanin			
	Lipoglycopeptides	dalbavancin			
	Cyclic lipopeptides	daptomycin			
9	**Fenicoles**	chloramphenicol			

10	**Polymyxins**	colistin (Polymyxin E)
11	**Ansamycins**	ryfampicyna, ryfabutyna, ryfapentyna, ryfaksymina
12	**Sulfonamides**	sulfamethoxazole + trimetoprim (co-trimoxazole)
13	**Nitroimidazoles**	metronidazol
14	**Nitrofurans**	furazidine, nitrofurantoin, nifuroxazide
15	**Quinolones**	nalidixic acid
	Fluoroquinolones	norfloxacin, pefloxacin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin
16	**Fusidins**	fusidic acid
17	**Fosfomycyna**	fosfomycin

Division of antibiotics:
- Natural – microbial metabolites
- Semisynthetic – natural metabolite derivatives obtained by chemical modification

Mechanisms of action of antibiotics on bacteria
Inhibition of bacterial cell wall (peptidoglycan) synthesis (e.g., β-lactam antibiotics, glycopeptides, fosfomycin, bacitracin)
Disruption of the cytoplasmic membrane (e.g., daptomycin, polymyxins)
Inhibition of protein biosynthesis (e.g., tetracyclines, aminoglycosides, macrolides, lincosamides, oxazolidinones)
Inhibition of nucleic acid synthesis (e.g., quinolones, rifamycin, TMP-SMX, fidaxomicin)



Mechanisms of action of antibiotics

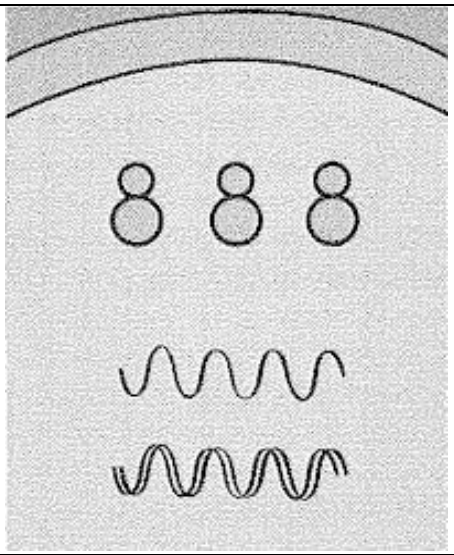
	Inhibition of bacterial cell wall (peptidoglycan) synthesis	Disruption of the cytoplasmic membrane	Inhibition of protein biosynthesis	Inhibition of nucleic acid synthesis
Grup of antibiotics	β-lactams Glycopeptides Lipoglycopeptides Fosfomycin	Polymyxins (colistin) Daptomycin	Aminoglycosides Oxazolidynones (only against streptococci)	Ansamycins Quinolones Nitroimidazoles Nitrofurans
Effect	**bactericidal**	**bactericidal**	**bactericidal**	**bactericidal**
Grup of antibiotics			Tetracyclines Glicylcyclines Macrolides Oxazolidynones (against staphylococci & enterococci) Lincosamides Chloramphenicol Fusidic acid	Sulfonamides Trimethoprim Co-trimoxazole (TMP-SMX)
Effect			**bacteriostatic**	**bacteriostatic**

Glossary:

MBC (minimal bactericidal concentration) – the lowest concentration of antibiotic needed to kill a specific population of bacteria of a given species

MIC (minimal inhibitory concentration*)* – the lowest concentration of antibiotic needed to inhibit the growth and stop the life processes of bacteria

Diagram of a bacterial cell: Action of individual groups of antibiotics on a specific region in a bacterial cell

Place of action	Bacterial cells	Antibiotics
Cell wall		β-lactams, glycopeptides, lipoglycopeptides
Cytoplasmic membrane		Polymyxins, daptomycin
Ribosome 30S unit		Aminoglycosides, tetracyclines, tigecycline
Ribosome 50S unit		Macrolides, lincosamides, streptogramins, oxazolidinones, chloramphenicol
RNA polymerase		Rifampicin (rifampin)
DNA		Quinolones (gyrase, topoisomerase), metronidazole, nitrofuran, co-trimoxazole

The scope of antibiotic action

Narrow spectrum	Natural penicillins, glycopeptides, oxazolidinones, daptomycin, dalbavancin, aztreonam, metronidazole
Broad spectrum	Semisynthetic penicillins (with or without BLIs), cephalosporins, aminoglycosides, carbapenems, fluoroquinolone, glycylcyclines, tetracyclines, chloramphenicol, trimethoprim/ sulfamethoxazole, macrolides, ketolides

The spectrum of antibacterial activity of individual groups of antibiotics

	Group	Spectrum
1	**β-lactams**	**Natural penicillins**: aerobic GP and GN cocci, spiral bacteria, anaerobic GP & GN cocci **Semisynthetic penicillins**: cloxacillin – Staphylococcus aureus MSSA; ampicillin, amoxicillin, piperacillin – as natural penicillins + aerobic GP and GN rods **Penicillins + BLIs** – aerobic GP cocci, aerobic GN rods, some anaerobic bacteria **Cephalosporins I generation** – aerobic GP cocci, aerobic GN rods **II generation** – aerobic & anaerobic GP and GN cocci; aerobic & anaerobic GN rods; **III generation** – aerobic and anaerobic GP and GN cocci; aerobic GN rods; **IV generation** – aerobic GP cocci, aerobic GN rods **V generation** – aerobic GP cocci, GN rods **Cefiderocol** – aerobic GN rods, including multi-resistant strains **Monobactams** – aerobic GN bacteria **Carbapenems** – aerobic GP and GN bacteria; anaerobic GP and GN bacteria
2	**Aminoglycosides**	aerobic GN bacteria, aerobic GP bacteria – with BLIs only
3	**Tetracyclines**	aerobic bacteria – spiral bacteria, atypical bacteria, aerobic GP cocci, and aerobic GN rods; anaerobes – high resistance
4	**Glicylcyclines**	aerobic and anaerobic GP and GN bacteria

		atypical bacteria, mycobacteria
5	**Macrolides/Ketolides**	atypical bacteria, aerobic GP and GN bacteria, spiral, mycobacteria, atypical bacteria, anaerobic GP and GN bacteria
6	**Lincosamides**	anaerobic GP and GN bacteria, aerobic GP bacteria
7	**Oxazolidynones**	aerobic GP bacteria, including multi-resistant strains, mycobacteria
8	**Glycopeptides**	aerobic and anaerobic GP bacteria
	Lipoglycopeptides	aerobic GP bacteria
	Cyclic lipopeptides	aerobic and anaerobic GP bacteria
9	**Chloramphenicol**	aerobic GP and GN bacteria, spiral bacteria; anaerobic GP bacteria, atypical bacteria
10	**Polymyxins**	aerobic GN bacteria, including multi-resistant
11	**Ansamycins**	Rifampin – aerobic GP and GN, atypical bacteria, anaerobic GP, mycobacteria Rifaxmin – aerobic GP and GN bacteria, anaerobic GP and GN bacteria
12	**TMP-SMX**	aerobic GP and GN bacteria, atypical bacteria
13	**Metronidazole**	anaerobic GP and GN bacteria
14	**Nitrofurans**	aerobic GP cocci and GN rods
15	**Quinolones**	aerobic GN
	Fluoroquinolones	aerobic GP and GN cocci, GN rods, atypical bacteria; mycobacteria
16	**Fusidins**	aerobic GP and GN bacteria, mycobacteria, anaerobic GP bacteria
17	**Fosfomycyna**	aerobic GP cocci and GN rods, including multi-resistant

Antibiotic activity against bacterial groups

Anaerobes	Atypical bacteria	Spiral bacteria	GP bacteria ONLY	GN bacteria ONLY
β-lactams (penicillins, cephalosporins, carbapenems) Tetracyclines Glicylcyclines Macrolides/Ketolides Lincosamides Glikopeptydy Cyclic lipopeptides Chloramphenicol Ansamycins Metronidazole Fusidins	Tetracyclines Glicylcykliny Macrolides/Ketolides Chloramphenicol Ansamycins Co-trimoxazole Fluoroquinolones	β-lactams (penicillins) Tetracyclines Macrolides/Ketolides Chloramphenicol	Oxazolidynones Glycopeptides Lipoglikopeptydy Cyclic lipopeptides	Polymyxins Quinolones Monobactams

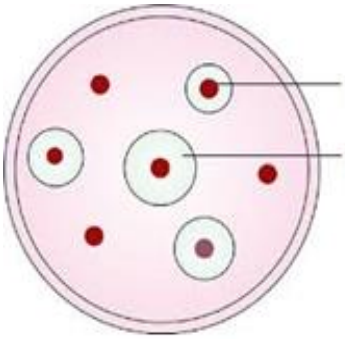
Part II - Practical

Determination of bacterial sensitivity to antibiotics – Phenotypic methods (qualitative and quantitative)

1. Qualitative methods – allow you to categorize the sensitivity of a microorganism to an antibiotic.
Sensitive (S-susceptible)
Resistant (R-resistant)
Sensitive increased exposure (I-intermediate)

Disk diffusion method, according to Kirby-Bauer
It uses the phenomenon of the formation of a concentration gradient as a result of the diffusion of an antibiotic from a disk in an agar medium (usually Mueller-Hinton, MH medium) with an evenly applied suspension of a microorganism with a specific number of cells (inoculum - 0.5 according to the McFarland scale corresponds to the density of the bacterial suspension of 1 - 2 x 108 CFU/ml). After 16-24 hours of incubation, the diameter of the zone of inhibition of the microorganism's growth (in mm) around the antibiotic disk is measured. The size of the growth inhibition zone is

proportional to the degree of sensitivity of the microorganism to a specific antibiotic. The measurement result is related to the limit values (breakpoint) applicable in European (EUCAST - European Committee on Antimicrobial Susceptibility Testing) or American (CLSI - Clinical Laboratory Standards Institute) recommendations.



Disc impregnated with antibiotic

The zone of bacteria growth inhibition

2. Quantitative methods - allow you to determine the MIC value at a specific density of bacterial inoculum (bacterial suspension) and at a specific time. The result is expressed in mg/L – plus interpretation of S, R, or I

a. Method using antibiotic concentration gradient strips
b. Serial broth dilution method (macro- and micro-scale)
c. Serial agar dilution method
d. Automatic methods

Task: completed by the student

Read the antibiogram – determine the microorganism's sensitivity to antibiotics. Assign individual preparations to a specific group of antibiotics

Bacterial strain name…….

Antibiotic name	Group	Diameter of growth inhibition (in mm)	S, R, I

Part III

Questions to help organize your knowledge about antibiotics

- Which groups of antibiotics have a broad and which have a narrow antimicrobial spectrum?
- Do glycopeptides and β-lactams act the same way on the cell wall?
- What differences and similarities can you point out between individual groups of antibiotics within β-lactams?
- Why do some antibiotics only work against GP bacteria?
- What role do β-lactamase inhibitors play?

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Teacher's sign