Antibiotics – agents - part I

betalactams, aminoglycosides, quinolones

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Oddělení klinické mikrobiologie a antibiotická stanice

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Antibiotics - antimicrobial agents

- antibacterial agents
- antifungal agents
- antiviral agents
- antiparasitic agents

Classification of antibiotics

main groups of antibacterial agents

- betalactams
- aminoglycosides
- quinolones
- glycopeptides
- macrolides, azalides
- lincosamides
- ketolides
- streptogramines
- oxazolidinones
- chloramphenicol
- tetracyklines
- rifamycins
- sulfonamides and trimethoprim
- polypeptides
- nitroimidazoles
- nitrofurans

Classification of antibiotics

antimycobacterial agents

antibiotics active against mycobacteria

- streptomycine, rifampicin, fluoroquinolones

specific antimycobacterial agents

- PAS (para-aminosalicylic acid)
- isoniazid
- ethambutol
- etionamid, pyrazinamid
- kapreomycin, cykloserin

Classification of antibiotics

antifungal agents

polyens	amphotericin B, nystatine
azoles	fluconazole, itraconazole, voriconazole, ketoconazole
echinocandines	caspofungin
others	flucytosine, griseofulvin

Classification of antibiotics
antiviral agents

antivirotics

- nucleoside analogs: **aciclovir, valaciclovir, famciclovir, ganciclovir**
- neuraminidase inhibitors: **oseltamivir, zanamivir**
- rimantadine, ribavirin
- interferon

antiretroviral agents

- nucleoside analogs: **abacavir, zidovudine, lamivudine, zalcitabine**
- protease inhibitors: **indinavir, lopinavir, nelfinavir, ritonavir, saquinavir**

Classification of antibiotics

antiparasitic agents

antiprotozoal agents

- quinolines (chloroquine, mefloquine, primaquine, quinine)
- nitroimidazoles (metronidazole)
- sulphonamides, trimethoprim, pyrimethamin
- others (diamidines, biguanides, sesquiterpens, emetine)

antihelmintics

- benzimidazoles (mebendazole, albendazole, thiabendazole)
- others (niclosamide, piperazine, pyrantel, levamisole)

Characteristics of antimicrobial agents
key parameters

- **microbiological characteristics**
  - mechanism and character of antimicrobial action
  - antimicrobial spectrum and acquired resistance
- **pharmacological characteristics**
  - chemical structure and qualitative parameters
  - pharmacokinetics and pharmacodynamics (PK/PD parameters)
  - ways of administration, principles of dosing
  - interactions
- **clinical use**
  - indications of choice, alternative indications (dosing and duration)
  - precautions, toxicity, adverse effects

Antibiotics - antimicrobial agents

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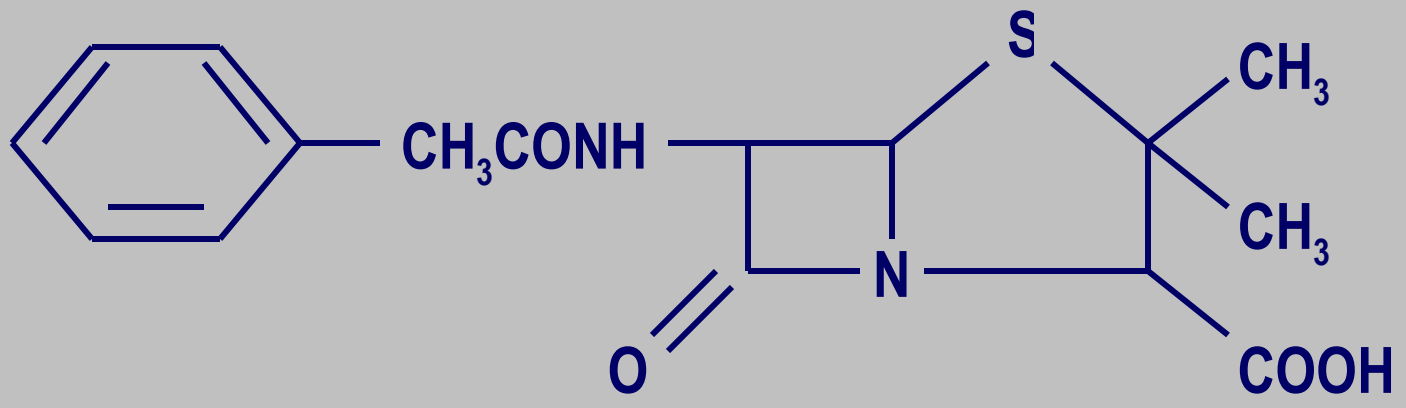
BETALACTAMS

Betalactam antibiotics
characteristics

- chemical structure - betalactam ring
- cell wall synthesis inhibitors
- bactericidal action
- time-dependent action
- low toxicity
- resistance – betalactamases, modification of target structure (abnormal PBP's), outer membrane impermeability, active efflux, …

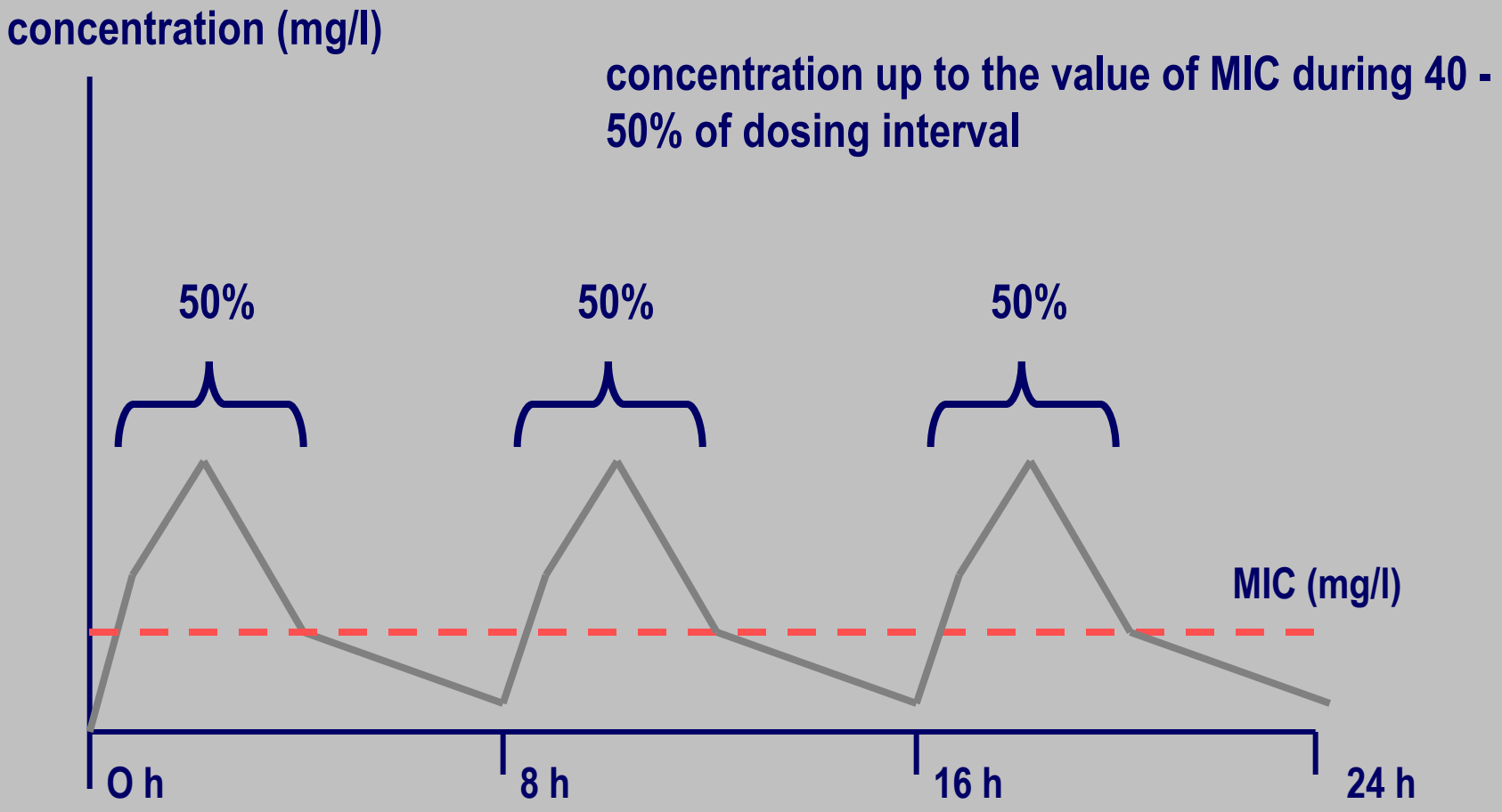
Betalactam antibiotics - betalactam ring

chemical structure of benzylpenicillin



Time-dependent action

betalactams



Betalactam antibiotics
basic classification

- penicillins
- cephalosporins
- carbapenems
- monobactams

Betalactam antibiotics

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BETALACTAMS

PENICILLINS

Betalactam antibiotics - penicillins
classification

- narrow spectrum penicillins (susceptible to betalactamase)
  - penicillin (penicillin G, penicillin V)
- penicillins resistant to betalactamase
  - oxacillin
- broad spectrum penicillins
  - aminopenicillins (ampicillin, amoxicillin)
- penicillins active against Ps. aeruginosa
  - carboxypenicillins (ticarcillin)
  - ureidopenicillins (piperacillin)

Betalactam antibiotics - penicillins
combinations with betalactamase inhibitors

- **competitive betalactamase inhibitors:**
  - clavulanic acid, sulbactam, tazobactam
- **clinically available combinations:**
  - amoxicillin + clavulanic acid
  - ampicillin + sulbactam
  - ticarcillin + clavulanic acid
  - piperacillin + tazobactam

Antimicrobial action of penicillins

	PEN	AMP	OXA	PIP	AMC	PPT
S. pyogenes	++	+	+	+	+	+
S. pneumoniae	++	++	+	+	+	+
E. faecalis+	+	-	+	+	+	
St. aureus	(++)	(+)	++	+	++	+
H. influenzae	-	++	-	+	++	+
E. coli	-	+	-	+	+	+
Kl. pneumoniae	-	-	-	-	+	+
Ent. colacae	-	-	-	+	-	+
Ps. aeruginosa	-	-	-	++	-	++
anaerobes	++	+	I	+	++	++

++ highly effective, **+** effective, **–** no or low effect, **I** irelevant, **PEN** – penicillin, **AMP** - aminopenicillins, **OXA** - oxacillin, **PIP** - piperacillin, **AMC** - amoxicillin clavulanic acid, **PPT**-piperacillin tazobactam

Betalactam antibiotics - penicillins

penicillin G and V – antimicrobial spectrum

- penicillin G – benzylpenicillin parenteral
- penicilin V – fenoxymethylpenicillin oral

- antimicrobial spectrum:
  - streptococci, pneumococci, enterococci, staphylococci
  - Listeria, Corynebakterium, Clostridium, Actinomyces, B.anthracis
  - Treponema, Borrelia, Leptospira
  - gonococci, meningococci, Pasteurella,
  - fusobacteria, oral bacteroides

Penicilliny - benzylpenicillin (penicillin G)
characteristics, pharmacokinetics and dosing

- characteristics:
  - penicillin susceptible to betalactamase (i.v. and i.m.)
- pharmacokinetics:
  - C_{max} (i.v. bolus 3g) 400 mg/l
  - biological half life 0,5 hod.
  - protein binding 60%
  - volume of distribution 0,2 - 0,7 l/kg
- dosing (adults):
  - daily dose: 2,4 - 24 MIU interval: 4 - 6 h

Penicillins - benzylpenicillin (penicillin G)
priorities of clinical use

- meningitis, sepsis due to meningococci, pneumococci, streptococci
- pneumococcal pneumonia
- endocarditis due to viridans streptococci
- alternative of ampicillin for enterococcus and listeria infections - combination with aminoglycosides (endocarditis, sepsis, meningitis)
- severe soft tissue infections due to streptococci and clostridia
- aspiration pneumonia, lung abscess due to non-sporulating anaerobes except *B.fragilis*
- actinomycosis, neuroborreliosis
- anthrax, diphteria, erysipeloid
- neurosyphilis, congenital syphilis

Penicillins - benzylpenicillin (penicillin G)
examples of dosing and duration of treatment

- pneumococcal pneumonia - normal phenotype
  - 2,4 MIU / day int. 4 - 6 h duration 10 - 14 days
- pneumococcal pneumonia - intermediate phenotype
  - 8-12 MIU / day int. 4 - 6 h duration 10 - 14 days
- endocarditis due to viridans streptococci
  - 18 MIU / day int. 4 - 6 h duration 4 weeks
- endocarditis due to enterococci (+ aminoglycoside)
  - 24 MIU / day int. 4 h duration 4 - 6 weeks
- actinomycosis
  - 10 - 20 MIU / day int. 4 - 6 h duration 2 - 6 weeks

Penicillins - phenoxymethylpenicillin (penicillin V)
characteristics, pharmacokinetics and dosing

- characteristics:
  - penicillin susceptible to betalactamase (p.o.)
- pharmacokinetics:
  - biological availability 40 - 70%
  - biological half life 0,5
  - protein binding 80%
  - volume of distribution 0,2 l/kg
- dosing (adults):
  - single dose: 500 - 750 mg interval: 6 - 8 h

Penicillins - phenoxymethylpenicillin (penicillin V)
priorities of clinical use, dosing, duration of treatment

- streptococcal tonsillopharyngitis:
  - 750 mg every 8 hours 10 days
  - 500 mg every 6 hours 10 days
- infections of oral cavity, stomatology infections
- streptococcal soft tissue infections
- prophylaxis of rheumatic fever (alternative for penicillin G)
- erythema migrans (lyme borreliosis) in children

Penicillin

agents corresponding to antimicrobial action of penicillin

- **oral penicillin**
  - penicillin V
  - penamecillin
- **parenteral penicillin**
  - penicillin G (crystalic penicillin) — i.v.
  - procain penicillin G — i.m.
  - benzathine penicillin — depot drug

Penicillins - oxacillin
characteristics, administration and dosing

- anti-staphylococcal antibiotic protected against action of staphylococcal betalactamase
- parenteral and oral administration
- range for dosing 4 - 18 g / day (adults)
- interval 4 - 6 h

Penicillins - oxacillin
priorities of clinical use

- staphylococcal BSI‘s, cardiovascular infections (sepsis, endocarditis, septic trombophlebitis, endarteritis)
- staphylococcal pneumonia
- staphylococcal skin and soft tissue infections (pyodermia, abscesses, empyemas, mastitis)
- staphylococcal bone and joint infections (osteomyelitis, arthritis)

Penicillins - aminopenicillins (ampicillin, amoxicillin)
characteristics, administration and dosing

- ampicillin (AMP) **parenteral**
- amoxicillin (AMO) **oral and parenteral**

- **broad spectrum penicillin antibiotics active agains some gramnegative bacteria (haemophili, enterobacteria)**

- **dosing of parenteral ampicillin**
  - **2 - 6 - 12 g / day (podle severity of infection), interval 4 - 6 h**
- **dosing of oral amoxicillin**
  - **adults** **0,75 - 1,5 g every 8 h**
  - **children** **50 - 90 mg/kg/day**

Penicillins - aminopenicillins (ampicillin, amoxicillin)
priorities of clinical use

- ampicillin
  - meningitis, sepsis, epiglotitis due to Haemophillus influenzae
  - meningitis and sepsis due to Str. agalactiae, L. monocytogenes
  - enterococcal endocarditis and sepsis (+ aminoglycosides)
- amoxicillin
  - community acquired respiratory tract infections (acute sinusitis, acute otitis media, mild pneumonia)
  - community acquired urinary tract infections (alternative to co-trimoxazole)
  - prophylaxis of infectious endocarditis

Penicillins - ureidopenicillins - piperacillin
characteristics, administration and dosing

- **piperacillin**

  penicillin antibiotic active against Ps.aeruginosa, other gramnegative rods, streptococci and enterococci

  only for parenteral administration

  dosing (adults) **4 g every 4 - 6 hours**

- **piperacillin tazobactam**

  combination with betalactamase inhibitor, extended activity (G- bacteria with acquired resistance, anaerobes)

  dosing (adults) **4,5 g every 4 - 6 hodin**

Penicillins - ureidopenicillins - piperacillin
priorities of clinical use

- **piperacillin**
  - infections due to Ps. aeruginosa (nosocomial pneumonia, sepsis)

- **piperacillin tazobactam**
  - initial therapy of serious nosocomial infections (pneumonia, intra-abdominal infections)

BETALACTAMS
CEPHALOSPORINS

Betalactam antibiotics - cephalosporins
classification

- 1st generation (cephalothin, cefazolin, cephalexin)
- 2st generation (cefuroxime, cefamandole)
- cefamycins (cefoxitin, cefotetan)
- 3st generation - basic (cefotaxime, ceftriaxone)
- 3st generation - anti-pseudomonadal (ceftazidime, cefoperazone)
- 4st generation (cefepime, cefpirome)

Antimicrobial action of cephalosporins

	CLT	CRX	CXT	CTX	CTZ	CPM
S. pyogenes	++	++	I	+	I	++
S. pneumoniae	+	+	I	++	I	++
E. faecalis-	-	-	-	-	-	
St. aureus	+	+	+	-	-	+
H. influenzae	-	++	I	++	++	++
E. coli	+	+	+	++	++	++
Kl. pneumoniae	+	+	+	++	++	++
Ent. colacae	-	-	-	+	+	++
Ps. aeruginosa	-	-	-	-	++	+
anaerobes	-	-	++	-	-	-

++ hiohly effective, **+** effective, **–** no or low effect, **I** irrelevant, **CLT** – cephalothin, **CRX** - cefuroxime, **CXT** - cefoxitin, **CTX** - cefotaxime, **CTZ** - ceftazidime, **CPM** - cefepime

1st generation cephalosporins - cefazolin - CZL
charakteristics, pharmacokinetics and dosing

- **characteristics:**
  - parenteral 1st generation cephalosporin (i.v., i.m.)
- **pharmacokinetics:**
  - C_{max} (i.v. bolus 1g) **180 - 200 mg/l end of infusion**
  - biological half life **1,5 - 2,0 h**
  - protein binding **75 - 85%**
  - volume of distribution **10 l**
- **dosing (adults):**
  - common single dose: **1 - 2 g** interval: **6 - 8 hod.**
  - high (maximum) dose (severe infections): **12 g daily**

1st generation cephalosporins - cefazolin - CZL
priorities of clinical use (indications, dosing, duration)

- surgical prophylaxis
- therapeutic use is extremely rare (sometimes alternative drug for other antibiotics)

1st generation cephalosporins - cephalexin - CLX
characteristics, pharmacokinetics and dosing

- characteristics:
  - oral 1st generation cephalosporin
- pharmacokinetics:
  - availability (p.o.) up to 90%
  - C_{max} (500mg p.o.) 10 - 20 mg/l after 1 hour
  - biological half life 0,5 - 1,0 h
  - protein binding 10 - 15%
  - volume of distribution 15 l
- dosing (adults):
  - common single dose: 0,5 - 1 g interval: 8 - 12 h
  - maximum daily dose: 6 g / 24 h

1st generation cephalosporins - cefalexin - CLX
prioroties of clinical use (main indications)

- CLX is not drug of choice (only alternative for treatment mild streptococcal, pneumococcal, staphylococcal and some of common gramnegative infections - (acute cystitis due to *E.coli*)

- streptococcal tonsillopharyngitis
- community-acquired urinary tract infections (*E. coli*)
- skin and soft tissue infections (*S. pyogenes, St. aureus*)

2nd generation cephalosporins - cefuroxime - CRX
characteristics and pharmacokinetics

- characteristics:
  - 2nd generation cephalosporin (parenteral, oral)
- pharmacokinetics:
  - availability (p.o.) 40 - 50%
  - C_{max} (0,75g i.v.) 50 mg/l end of infusion
  - C_{max} (500mg p.o.) 6 - 9 mg/l after 1,8 - 2,5 h
  - biological half life 1,1 - 1,4 h
  - protein binding 30%
  - volume of distribution 11 - 15 l

2nd generation cephalosporins - cefuroxime - CRX dosing

- dosing in oral administration:
  - single dose: 250 - 500 mg interval: 12 h
- dosing in parenteral administration:
  - single dose: 0,75 - 1,5 g interval: 6 - 8 h

2nd generation cephalosporins - cefuroxime - CRX
priorities of clinical use (main indications)

- parenteral:
  - surgical prophylaxis (cardiothoracic surgery, vascular surgery, etc.)
  - therapeutic use should be rare (alternative for other antibiotics)
- oral:
  - community-acquired respiratory tract infections: alternative for penicillins in case of resistance or allergy (acute tonsillopharyngitis, sinusitis, otitis media, mild pneumonia)
  - urinary tract infections: alternative in case of resistance
  - skin and soft tissue infections: alternative for basic antibiotics

Cefamycins - cefoxitin - CXT
characteristics, pharmacokinetics and dosing

- characteristics:
  - parenteral cefamycine antibiotic
- pharmacokinetics:
  - C_{max} (1g i.v.) 150 mg/l end of infusion
  - biological half life 0,7 - 1,0 h
  - protein binding 65 - 80%
  - volume of distribution 10 l
- dosing (adults):
  - common single dose: 1 - 2g interval: 6 - 8 h
  - high dose for severe infections: 12 g / day

Cefamycins - cefoxitin - CXT
clinical use

- CXT is not used in clinical practice, now
- main indication were intra-abdominal infections with presence of mixed flora incl. anaerobes

3rd generation cephalosporins - cefotaxime - CTX
characteristics, pharmacokinetics and dosing

- characteristics:
  - parenteral 3rd generation cephalosporin
- pharmacokinetics:
  - C_{max} (1g i.v.) 90 mg/l end of infusion
  - biological half life 1,0 h
  - protein binding 40%
  - volume of distribution 32 - 37 l
- dosing (adults):
  - common single dose: 1 - 2 g interval: 8 - 12 h
  - high dose for severe infections: až 12 g / day

3rd generation cephalosporins - ceftriaxone - CTR
characteristics, pharmacokinetics and dosing

- characteristics:
  - parenteral 3rd generation cephalosporin
- pharmacokinetics:
  - C_{max} (1g i.v.) 120 - 150 mg/l end of infusion
  - biological half life 6,0 - 9,0 h
  - protein binding 95%
  - volume of distribution 0,15 l
- dosing (adults):
  - common single dose: 1 - 2 g interval: 24 h.
  - high dose for severe infections: 4 g / day

3rd gen. cephalosporins - cefotaxime, ceftriaxon
priorities of clinical use

- CNS infections (bacterial meningitis, neuroborreliosis)
- respiratory tract infections (severe community-acquired pneumonia, nosocomial pneumonia, acute epigglotitis)
- invasive infections due to S. pneumoniae, H. influenzae resistant to penicillin antibiotics, (meningitis, pneumonia, etc.)
- severe urinary tract infections (acute pyelonephritis, urosepsis)
- extraintestinal salmonelosis (infectious endarteritis, aortitis)

3rd generation cephalosporins - ceftazidime - CTZ
characteristics, pharmacokinetics and dosing

- characteristics:
  - broad spectrum parenteral 3rd generation cephalosporin active against Ps. aeruginosa
- pharmacokinetics:
  - C_{max} (2g i.v.) 185 mg/l end of infusion
  - biological half life 1,5 - 2,0 h
  - protein binding 10%
  - volume of distribution 16 l
- dosing (adults):
  - common single dose: 1 - 2 g interval: 8 h

3rd generation cephalosporins - ceftazidime - CTZ
priorities of clinical use

- severe infections due to *Pseudomonas aeruginosa* (bloodstream infections and sepsis, nosocomial pneumonia)
- severe infections due to multi-drug resistant gramnegative rods with remaining susceptibility to CTZ

4th generation cephalosporins - cefepime - CPM
characteristics, pharmacokinetics and dosing

- characteristics:
  - broad spectrum, parenteral 4th generation cepalosporin
- pharmacokinetics:
  - C_{max} (2g i.v.) 190 mg/l end of infusion
  - biological half life 2,0 h
  - protein binding 10 - 19%
  - volume of distribution 14 - 20 l
- dávkování (dospělí):
  - common single dose: 1 - 2 g interval: 8 - 12 h

4th generation cephalosporins - cefepime - CPM
priorities of clinical use

- severe infections due to enterobacteria producing chromosomal *ampC* type cephalosporinase (enterobacters, citrobacters, serratia, etc.), infections due to *Pseudomonas aeruginosa*
  (bloodstream infections and sepsis, nosocomial pneumonia)

Betalactam antibiotics

BETALACTAMS

CARBAPENEMS

Betalactam antibiotics - carbapenems
characteristics

- semisynthetic or synthetic betalactam antibiotics
- extremely broad spectrum (G+, G-, incl. *Ps. aeruginosa* and acinetobacters, anaerobes)
- activity against multi-drug resistant strains (G- rods)
- high probability of clinical efficacy for initial treatment of severe, especially nosocomial infections

- imipenem **IMI**
- meropenem **MER**

Carbapenems - imipenem (IMI), meropenem (MER)
pharmacokinetics and dosing

	IMI	MER
• pharmacokinetics:		
o C_{max} (500 mg i.v.)	20 mg/l	23 mg/l
o biological half life	1,0 hod.	1,0 hod.
o protein binding	20%	2%
o volume of distribution	0,2 l	0,3 l
• dosing (adults):		
o standard single dose:	1 g	1 g
o interval:	6 - 8 h	6 - 8 h
o maximum daily dose:	4 g	6 g

Carbapenems
priorities of clinical use

- initial therapy of life threatening bacterial infections
- initial therapy of nosocomial pneumonia (esp. late on-set)
- CNS infections (bacterial meningitis, ventriculitis - MER)
- inta-abdominal infections (monotherapy possible)
- acute necrotising pancreatitis (prevention and treatment of panceratic necrosis infection)

- acinetobacter infections
- infections due to multi-drug resistant enterobacteria (ESBL - extended spectrum betalactamase producers, chromosomal cephalosporinase producers)

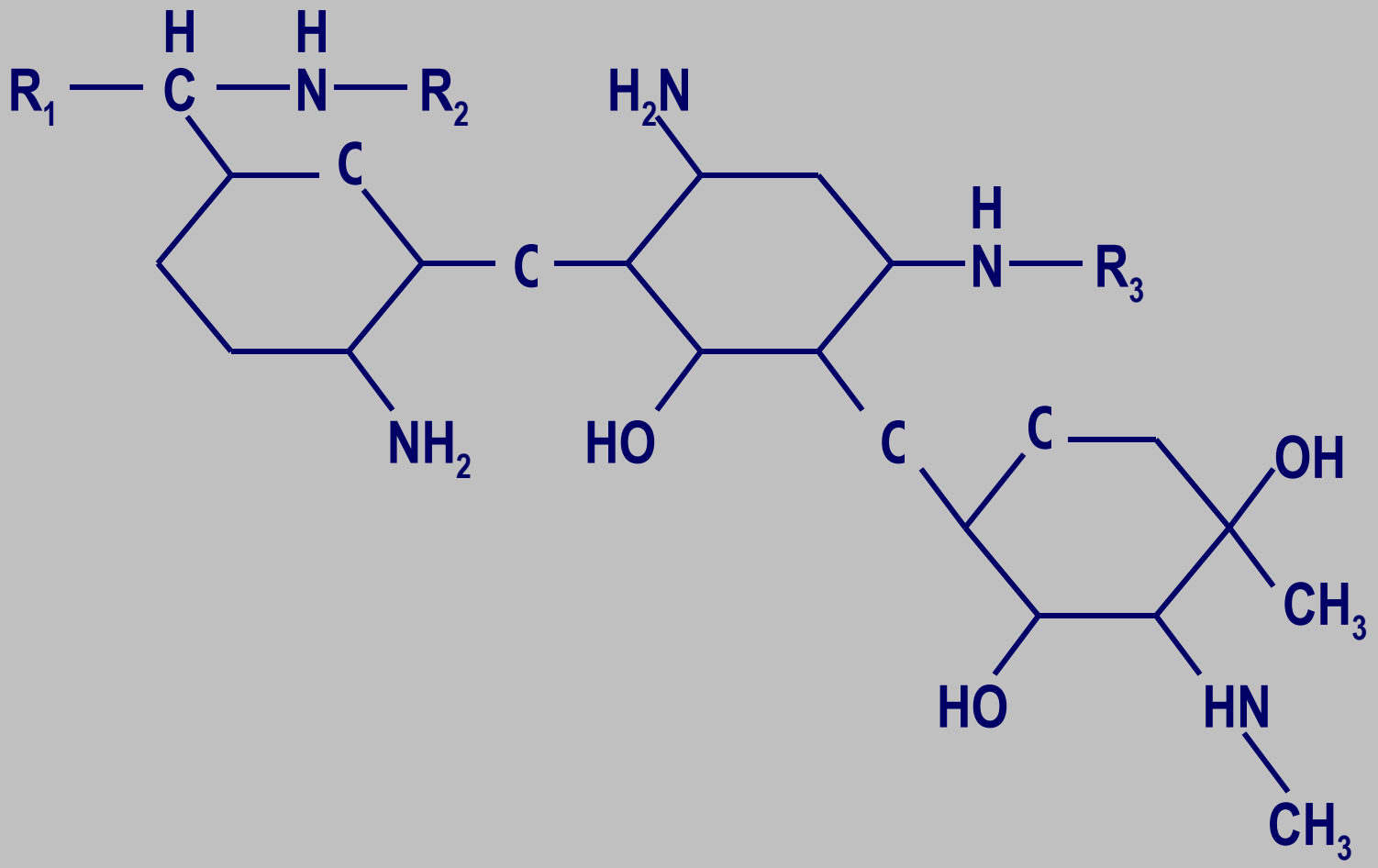
AMINOGLYCOSIDES

Aminoglycosides (aminocyclitols)
characteristics

- **glycosidic binding of amino-sugars (or amino-alcohols)**
- **proteosynthesis inhibitors**
- **mostly bactericidal action**
- **concentration-dependent action**
- **important toxicity** (nephrotoxicity, ototoxicity, neuromuscular blockade)
- **resistance: modifying enzymes** (AAC - N-acetyltransferases, APH O-phosphotransferases, ANT-O-nukleotidyltransferases), **change of target structure** (alteration in the ribosomal binding), **active efflux**

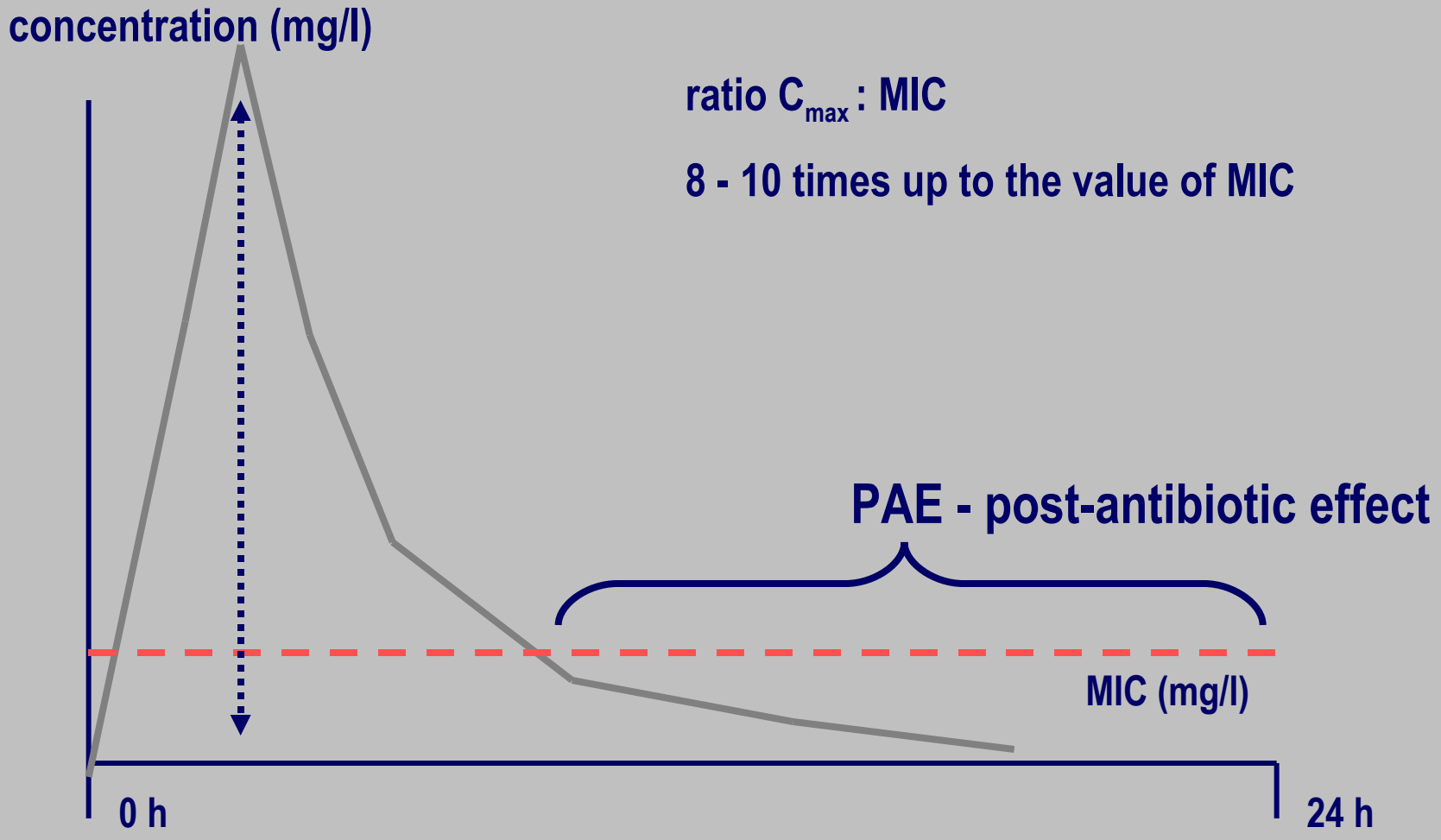
Aminoglycosides

chemical structure of gentamicin



Concentration-dependent action

aminoglycosides



Aminoglycosides (aminocyclitols)
classification

- neomycin group (NEO)
- kanamycin group (KAN)
- gentamicin group (GEN)

NEO	KAN	GEN	others
neomycin	kanamycin	gentamicin	streptomycin
	tobramycin	netilmicin	spektinomycin
	amikacin	isepamicin	

Aminoglycosides
antimicrobial spectrum (GEN, AMI)

- enterobacteria
- *Pseudomonas aeruginosa*
- acinetobacters and other non-fermenters
- staphylococci

- enterococci (susceptibility to high-level concentrations)
- streptococci (in combination with betalactams only)

- no effect against anaerobes

Aminoglycosides

pharmacokinetics and dosing

	gentamicin	amikacin
o biological half life	2 h	2,2 h
o protein binding	under 10%	3 - 11%
o volume of distribution	0,25 l/kg	0,25 - 0,3 l/kg
o dose / kg / day	3 - 5 mg	15 mg
• once daily administration:		
o dose	240 - 400 mg	1,0 - 1,5 g
• intermittent administration:		
o single dose	80 - 120 mg	500 mg
o interval	8 h	8 - 12 h

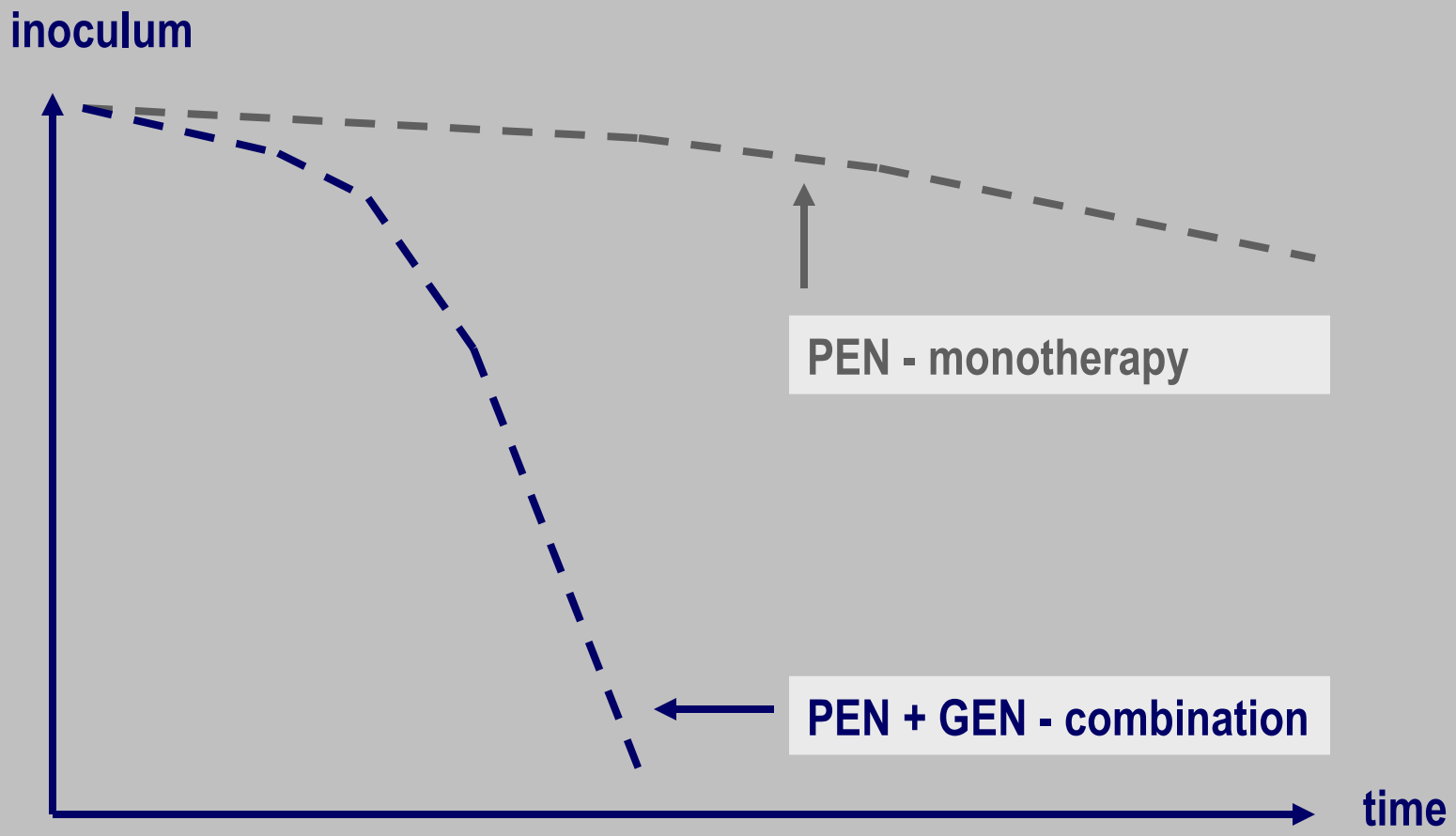
Aminoglycosides
pharmacodynamics

- **gram-negative infection** — once daily administration
  - important PAE
  - short duration of treatment
  - lower toxicity

- **gram-positive infection** — intermittent administration
  - no (or very short) PAE
  - synergy with betalactams and glycopeptides
  - higher toxicity

Aminoglycosides - bacterial killing curve

enterococcal endocarditis - effect of combination therapy



Aminoglycosides
priorities of clinical use

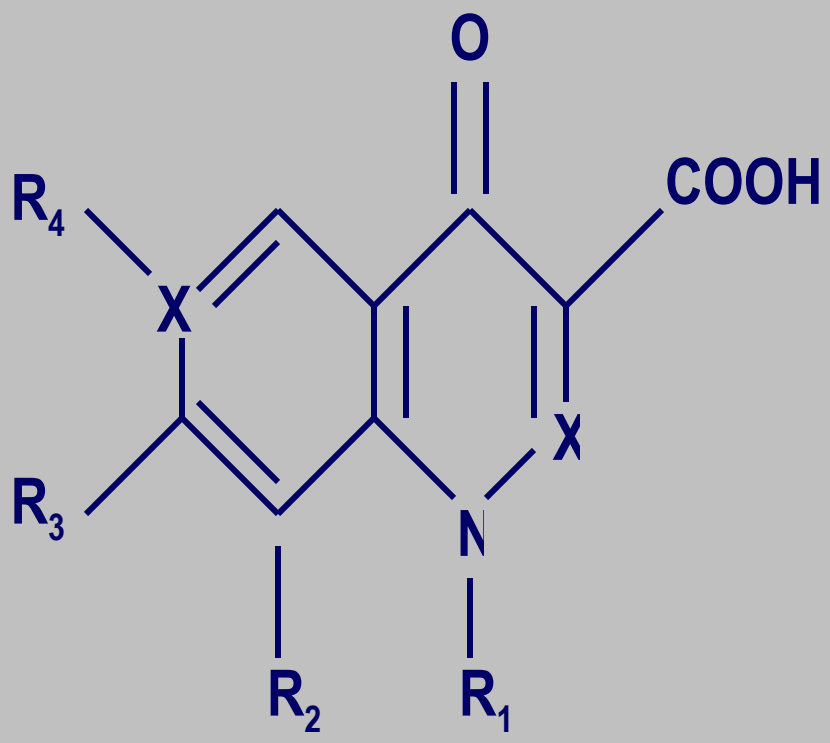
- combination therapy of gram-negative systemic infections
- combination therapy of serious *Ps. aeruginosa* infections (BSI, sepsis, pneumonia)
- combination therapy of streptococcal, enterococcal and staphylococcal systemic infections (endocarditis, sepsis)
- combin. therapy of intra-abdominal infections (peritonitis)
- combination therapy of bone and soft tissue infections
- urinary tract infections (monotherapy is possible)
- local treatment of bacterial CNS infections (intrathecal administration in nosocomial gram-negative infections)

QUINOLONES

Quinolones
characteristics

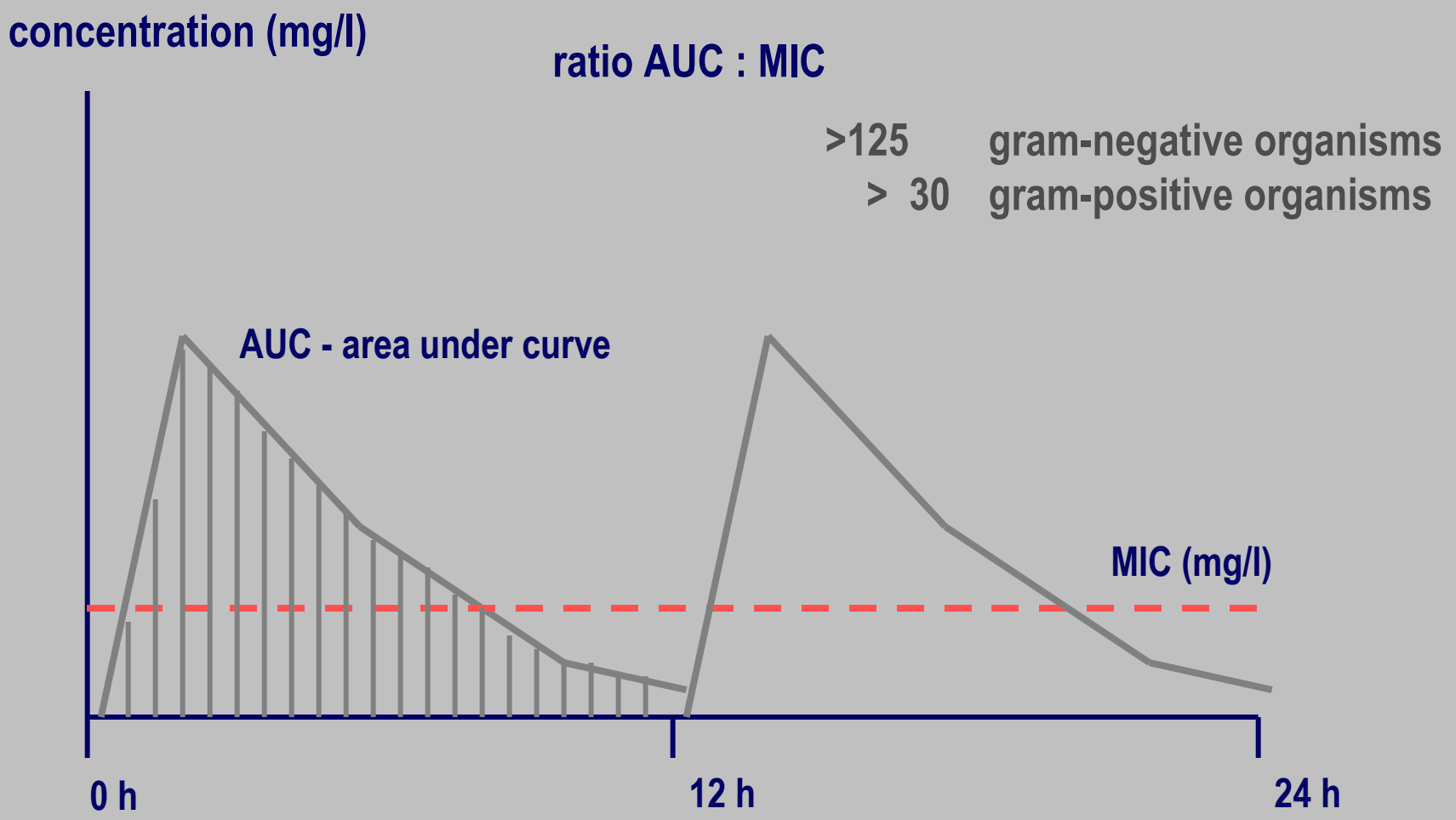
- 4-quinolone nucleus
- inhibition of bacterial nucleic acids synthesis (inhibition of DNA-gyrase, DNA-topoisomerase)
- mostly bactericidal action
- concentration-dependent action (AUC : MIC ratio)
- toxicity (hepatotoxicity, phototoxicity, neurotoxicity)
- resistance: change of target structure (chromosomal mutation of topoisomerase II a IV), active efflux

Quinolones
chemical structure



Concentration-dependent action

quinolones



Quinolones
classification

- group 1 - **“urinary“ chemotherapeutics**
- group 2 - **systemic fluoroquinolones**
- group 3 - **“respiratory“ fluoroquinolones**
- group 4 - **broad spectrum fluoroquinolones**

Quinolones
classification

group 1	group 2	group 3	group 4
pipemidic acid	norfloxacin	gatifloxacin	trovafloxacin
nalidixic acid	pefloxacin	sparfloxacin	moxifloxacin
oxolinic acid	ofloxacin		
	ciprofloxacin		
	levofloxacin		

Antimicrobial action of guinolones

	group 1	group 2	group 3	group 4
S. pyogenes	-	-	+	+
S. pneumoniae	-	-	+	++
E. faecalis -	-	-	+	
St. aureus	-	+	+	++
H. influenzae	-	++	+	++
E. coli	+	++	+	++
Kl. pneumoniae	+	++	+	++
Ent. colacae	+	++	+	+
Ps. aeruginosa	-	++	+	+
anaerobes -	-	-	+	

++ highly effective, **+** effective, **–** ineffective or moderately effective

Quinolones

priorities of clinical use - systemic quinolones

- **systemic quinolones are alternatives for basic antibiotics (drugs of choice) in the most clinical situations**

- urinary tract infections
- sexually transmitted diseases
- respiratory tract infections
- skin and soft-tissue infections
- bone and joint infections
- enteric infections (enteric fever)
- meningitis

Quinolones - ciprofloxacin - CIP
characteristics, pharmacokinetics and dosing

- characteristics:
  - group 2 quinolone with systemic action - parenteral and oral
- pharmacokinetics:
  - C_{max} (200mg i.v.) 3,5 mg/l (end of infusion)
  - C_{max} (500mg p.o.) 1,5 - 2,0 mg/l (after 1 - 2 h)
  - biological half life 3,0 - 4,0 h
  - protein binding 20 - 40%
  - volume of distribution 3 - 4 l/kg
- dosing (adults):
  - per os: single dose: 500 - 750 mg interval: 12 h.
  - i.v.: single dose: 200 - 600 mg interval: 12 h.

Quinolones - ciprofloxacin - CIP
distribution

- excellent penetration to the body fluids and tissues
  - equal tissue and plasma concentrations
  - penetration to CSF - 50% of plasma concentration
  - cummulation in lung and prostatic tissue
- excellent intracellular penetration
  - concentration in phagocytic cells equal to plasma

Quinolony - ciprofloxacin - CIP
priorities of clinical use

- urinary tract infections, prostatitis
- uncomplicated gonorrhoea (single dose therapy)
- respiratory tract infections (purulent bronchitis, AECB, pneumonia except pneumococcal, infectious complications of cystic fibrosis)
- legionellosis
- gram-negative osteomyelitis
- enteric fever (salmonelosis, shigelosis, campylobacteriosis, cholera)
- mycobacterial infections (combination therapy)
- mycoplasma and chlamydia infections