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ANTIBACTERIAL DRUGS
ANTITUBERCULOSIS DRUGS
ANTILEPROSY DRUGS

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Classes of ATB

1. **Beta-lactam ATB**
   - Penicillins
   - Cephalosporins
   - Monobactams
   - Carbapenems
2. **Aminoglycosides**
3. **Tetracyclines**
4. **Amphenicols**
5. **Macrolides**
6. **Lincosamides**
7. **Ansamycins**
8. **Peptides**
   - Polypeptides
   - Glycopeptides
6. **Sulfonamides**
7. **Pyrimidines**
8. **Quinolones**
9. **AntiTBC, antiLPR**

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AMINOGLYKOSIDES

- **Classic** (streptomycin, kanamycin, neomycin)
- **Modern** (gentamicin, netilmicin, tobramycin, amikacin, isepamicin)

- Impact on G-, weak on G+
- Unsuitable for anaerob. inf. (O_2 is necessary for AG uptake) or IC bacteria
- Toxicity: oto-, nephro-, neuro- (mainly in elderly patinets, increased during loop diuretics administration)
- Problem: quickly and widely generated resistance

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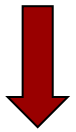
Mechanism of action

- Irreversible bond on 16S ribosomal RNA, and arrest of initiatory complex (30S-mRNA-tRNA)

- Slowdown of already initiated proteosynthesis, and induction of mRNA "*misreading*"



Bactericidal effect

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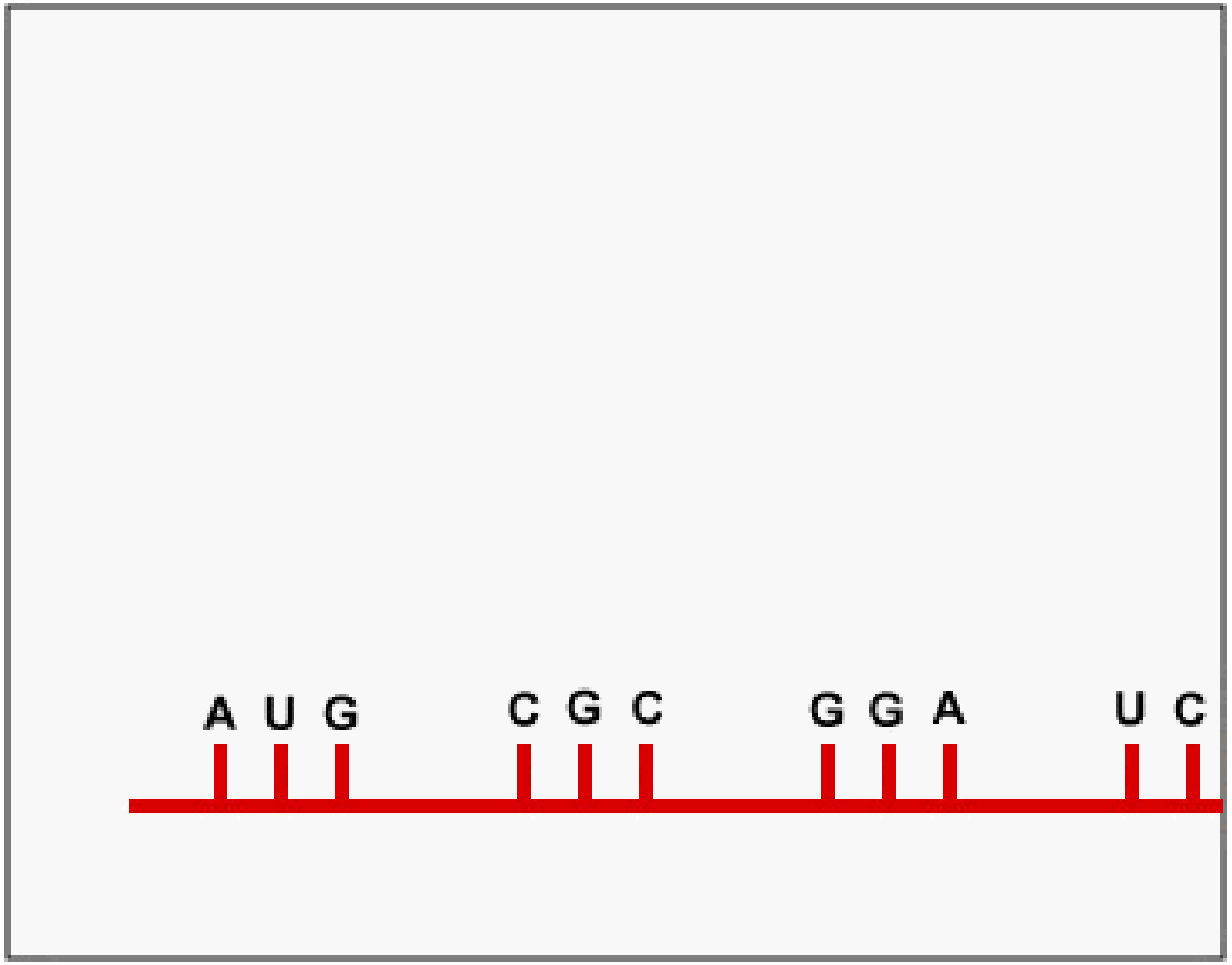

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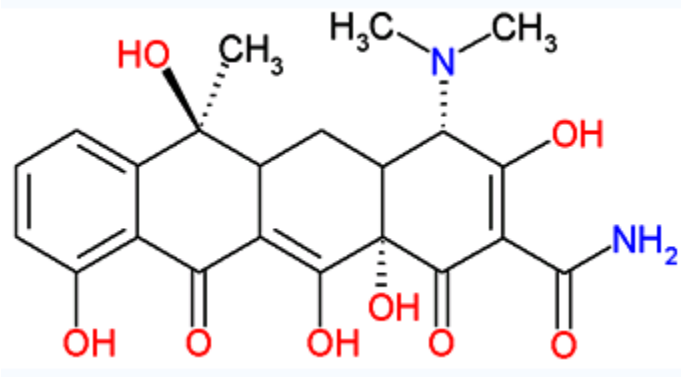
TETRACYCLINES



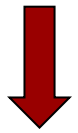
- **Basic (I. generation)** tetracycline, oxytetracykline
- **New (II. generation)** doxycycline, minocycline (1-2x a day)

- Acts on both G+ and G-, mycoplasma, chlamydia, rickettsiae
- IC penetration
- Good absorption from GIT
- Resistance is often and crossed
- Low toxicity

Mechanism of action

- Bond on 30S subunit of bacterial ribosomes

- Blocks the access of aminoacyl-tRNA to the mRNA-ribosome complex



Bacteriostatic effect

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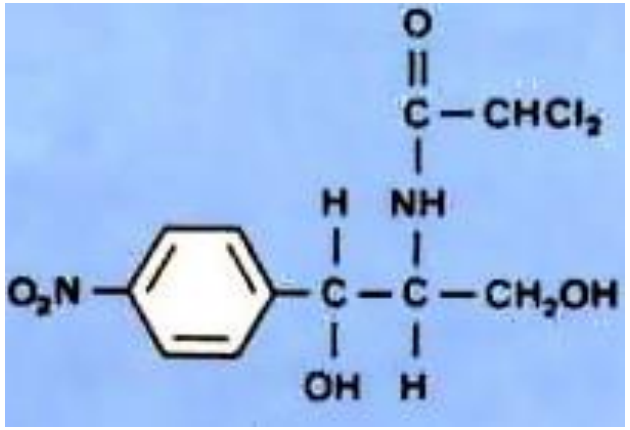
Side effects

- GIT disorders: can be decreased by concurrent use of non-milk food
- Effect on calcifying tissues: Deposits in bones and teeth
- CI in pregnancy, and in children before 8 years !!!
- Hepatotoxicity
- Photosensitivity
- Vestibular problems: (eg. vertigo, nausea, vomiting) after minocyclin
- Superinfection: candida (vagina) or resist. staphylococcus (gut)

AMPHENICOLS



- **Chloramphenicol**
- **Tiamphenicol**

- Bacteriostatic
- Broad-spectrum (also on *H. influenzae*)
- Good penetration into CNS and abscesses
- Indication: meningitis, MRSA

  History: typhus and paratyphus, severe pneumonia, anaerobic or abdominal infections

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Side effects of CHF

- **Haematotoxicity**

1. Myelosuppression dependent on dose and duration of administration time
2. Aplastic anemia – irreversible, immunotoxic mechanism

- **Gray syndrom**

- **Neurotoxicity**

  Apply not longer than 14 days, and with interval longer than half a year ! (incl. local DF)

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MACROLIDES

- **Basic** (erythromycin, spiramycin)
- **Modified** (claritromycin, azitromycin, roxitromycin)

- Spectrum: mainly on G+, neisseria, leptospirosis, mycoplasma, chlamydia, helicobacter, legionella, toxoplasma
- Good tolerance (Ery-motilin!), low tox., good penetration into the tissues and cells
- Bacteriostatic effect

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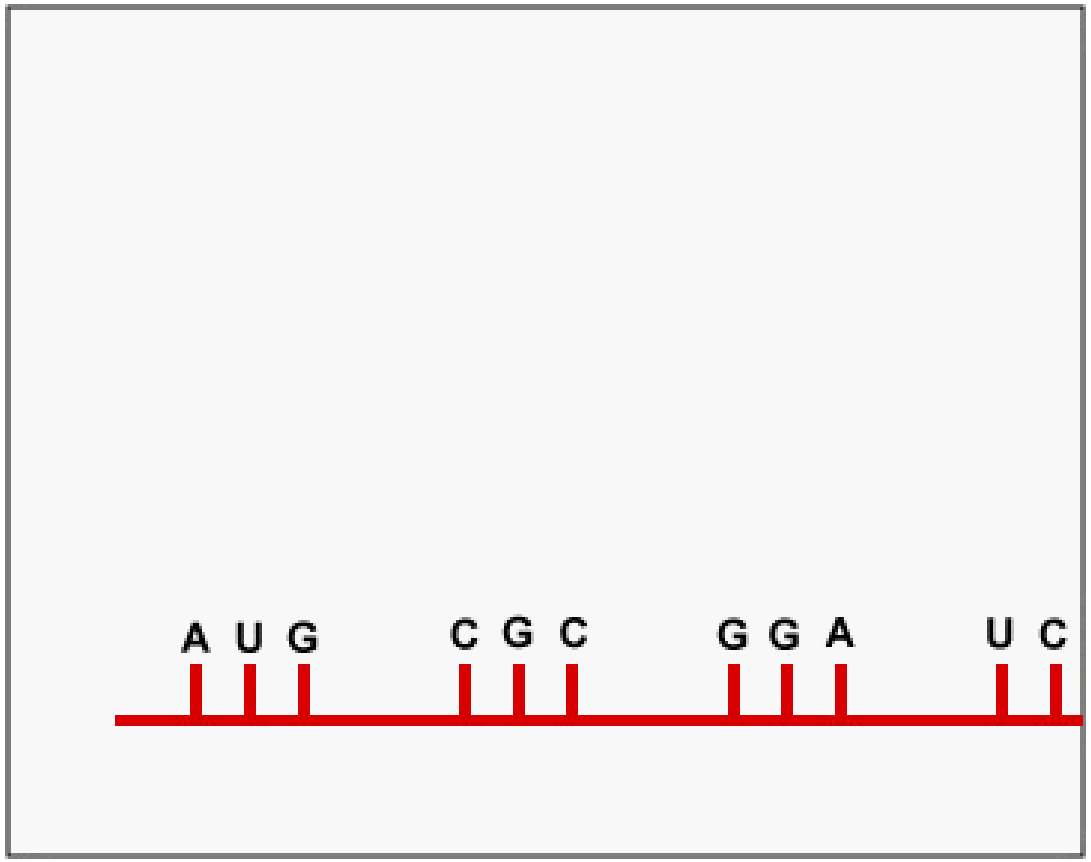
Mechanism of action

- Reversible bond on ribosome
- Affect proteosynthesis – inhibition of translocation



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Resistance in MAC class

- **Huge increase in last decade (up to 20%)**

Reasons:
- Non-rational application
- Minimal and non-significant side effects
- The increasing popularity in doctors and patients (even in vet.med.)

Less-sensitive strains:
- Streptococcus pyogenes
- Streptococcus pneumoniae
- Staphylococcus aureus …

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LINCOSAMIDES

clindamycin, lincomycin

- MofA: bond on 50S subunit → inhibition of peptidyl transferase activity
- Bacteriostatic mainly on: G+, anaerobes
- *Drugs-of-choice* in Staphylococcus infections with PNC allergy
- Resistance often crossed with MAC
- Excellent penetration into tissues (bones)
- Low tox., but risk of pseudomembranose colitis

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ANSAMYCINS

rifampicin, rifampin, rifabutin

- MofA: bond on DNA-dependent RNA polymerase, and inhibition of initiation of mRNA synthesis
- Bactericidal effect on: G+, G-, but mainly mycobacteria, chlamydia, rickettsiae, legionella
- Low toxicity, good absorption after p.o.
- rifampicin = induction of CYP450
- rifabutin = effective even in mycobacteria resistant on rifampicin

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PEPTIDES

- *Polypeptides*
  - **bacitracin**
  - **polymyxins**:
    polymyxin B
    colistin
- *Glycopeptides*
  - **vankomycin**
  - **teikoplanin**

- Bactericidal, different spectrum of activity
- Non-absorble from GIT
- Strong toxicity
- Rezerve ATB

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Polypeptides

bacitracin

- Narrow-spectrum: G+ (*S. pyogenes*)
- Strong nephrotoxicity
- Local application in comb. with neomycin

polymyxins – polymyxin B, colistin

- Narrow-spectrum: G- (not neisseriae)
- colistin (*P. aeruginosa*) – p.o. desinfection of GIT
- Strong neuro- a nephrotoxicity

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Glycopeptides

- MofA: Inhibition of phospholipid and peptidoglycan polymers synthesis in cell wall

vancomycin

- Severe infection G+ (staphyloc., enteroc.)
- Synergy with AG – used in enteroc. endocardit
- Strong nephro- and ototoxicity

teikoplanin

- Lower toxicity
- Long $t_{½}$ - 50 h

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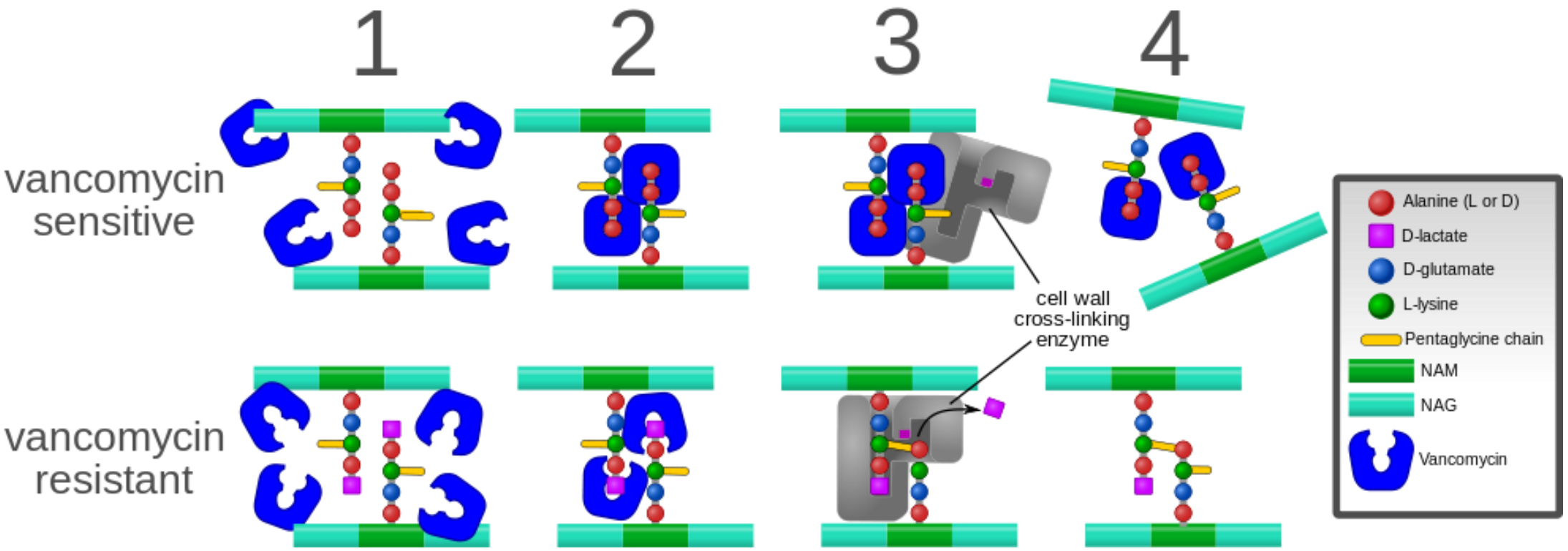
Vancomycin:
Mechanisms of action and resistance



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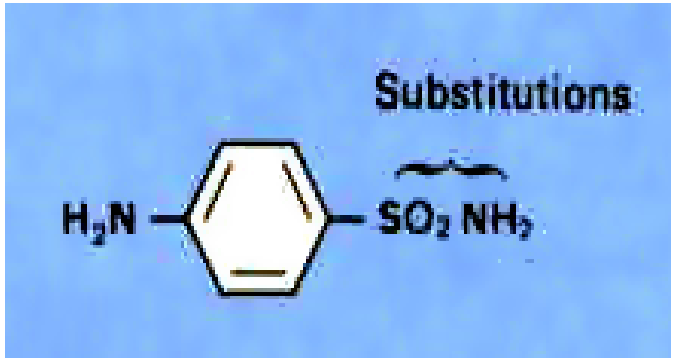
SULFONAMIDES



- PABA analogues (para-aminobenzoic acid)
- Primary bacteriostatic
- Broad-spectrum (G+, G-, toxoplasma)
- Low toxicity
- Side effects: GIT, skin allergic reactions (Stevens-Johns sy., Lyell sy.)
- Renal complication (crystaluria)
- Frequent resistance

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PYRIMIDINES

trimetoprim

- Broad-spectrum (G+, G-, *H. influenzae*, *E. coli*, *Proteus* …)
- Good absorption after p.o.
- Resistance is often and quick
- Only in combination with SA

pyrimethamin

- Antimalaric agent, toxoplasmosis, leishmaniosis
- Always in combination (+ sulfadiazin)

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Combination of sulfamethoxazol + trimetoprim

= **Cotrimoxazol** (in ratio 1 : 5)

- More effective than single compounds
- Lower doses needed decrease the SE incidency, and resistance development
- Side effects: dermatologic (often in elderly), GIT, haematologic
- Main Indication: respiratory and urologic infections

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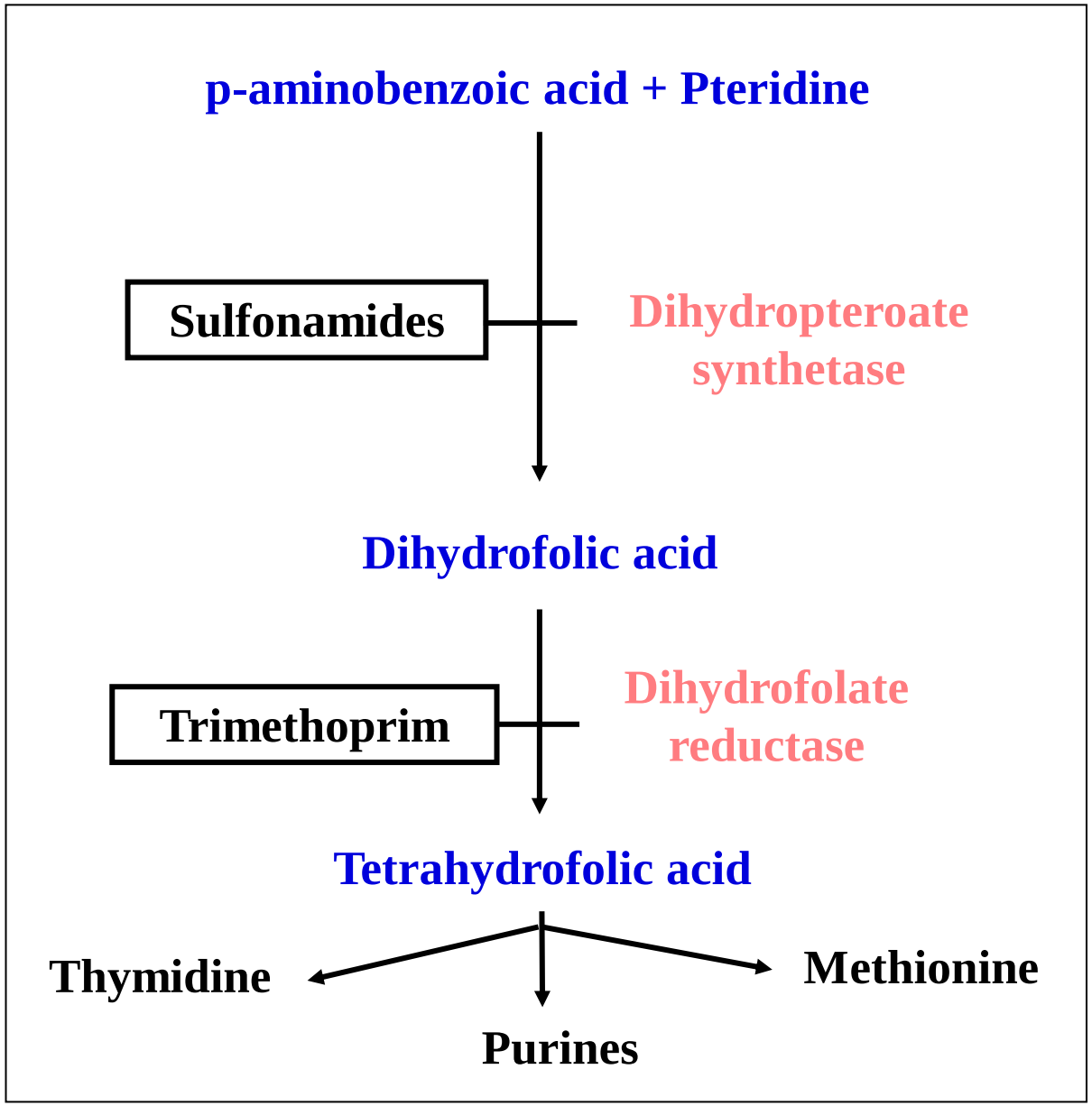
Mechanism of action



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QUINOLONES

- **I. generation:**

nalidixic acid, oxolinic acid (nonF QUIN)

norfloxacin (F QUIN)

- **II. generation:**

ofloxacin, ciprofloxacin, levofloxacin, pefloxacin, fleroxacin, lomefloxacin, nadifloxacin, rufloxacin, delafloxacin, prulifloxacin

- **III. generation:**

prulifloxacin, moxifloxacin, gemifloxacin, sparfloxacin, pazufloxacin

- **IV. generation:**

trovafloxacin, alatrofloxacin

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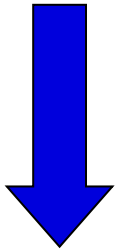
Mechanism of action

Inhibition of DNA synthesis by the bond on A subunit of DNA gyrase (topoisomerase II), and interfere with topoisomerase IV



Intensive bactericidal effect, mainly on G-

(G+ and anaerobes are less sensitive)

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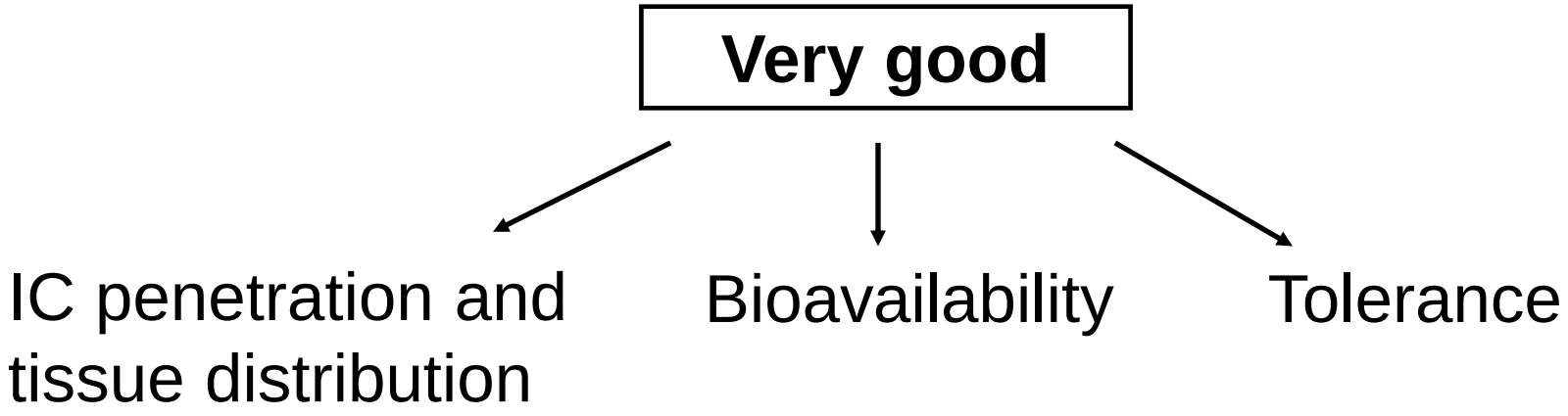
Basic characteristics

- Post-antibiotic effect: lasts 1 - 2 h, elongates with higher concentration
- Low toxicity, but broad-spectrum of SE
- Administration by i.v. or p.o. route



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Generation	Drug Names	Spectrum
I.	nalidixic acid oxolinic acid, norfloxacin	G- but no effect on Pseudomonades
II.	levofloxacin ciprofloxacin prulifloxacin ofloxacin	G- (incl. Pseudomonades), some G+ (*S. aureus*) and some atypical bacteria
III.	sparfloxacin prulifloxacin moxifloxacin gemifloxacin	Same as II. gen., moreover wider G+ and atypical bacteria
IV.	trovafloxacin alatrofloxacin	Same as III. gen., moreover broad coverage of anaerobes

Negatives of Fluoro QUIN use

- Interactions:
  - ↓ absorption: Al^{3+}, Mg^{2+} and Ca^{2+} antacids
  - CYP450 inhibitory → potential interaction
    = may increase levels of warfarin (INR real changes are rare, but better monitor)

- Side effects:
  - GIT: nausea, vomiting
  - CNS: headache, dizziness, confusion, insomnia, delirium, hallucinations, seizures (rare)
  - CVS: arrhytmias (rare)
  - Musculosceletal systém: myalgia, paraesthesia, joint swelling, weakness
  - Phototoxicity
  - Hypoglycemia

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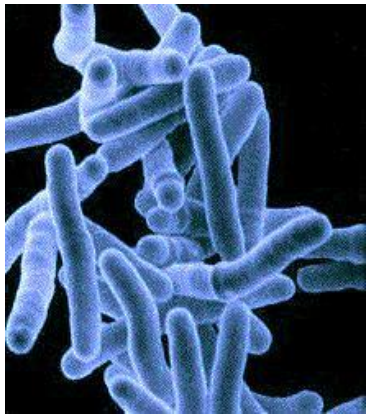
ANTITUBERCULOTICS, ANTILEPROTICS

- Causative agent: *Mycobacterium tuberculosis*
- antiTBC:
  1. line = rifampicin, isoniazid, ethambutol, streptomycin, pyrazinamide
  2. line = PAS, capreomycin, cycloserin, ethionamid, F QUIN, MAC



- Causative agent: *Mycobacterium leprae*
- antiLEP:
  - rifampicin
  - dapson

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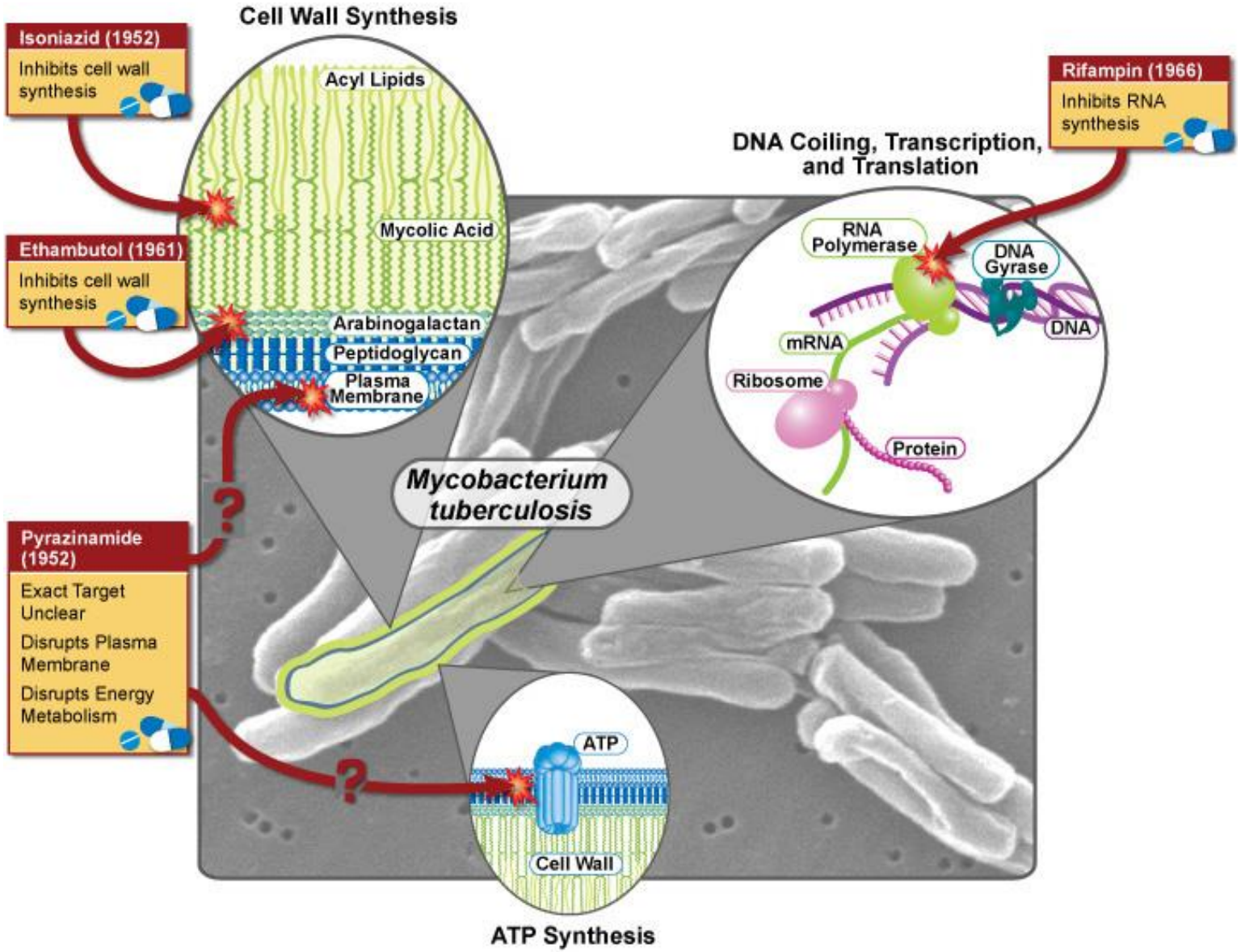
Mechanism of action



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Characteristics of the treatment

- Treatment before sensitivity detection
- Slow growth of microbes → long-term application (6 – 12 months)
- antiTBC drugs of 2. line:
  - either not effective than 1 series
  - or are more toxic
  - or effective against atypical strains

Often resistance → treatment always in combination, synergy, affects both IC and EC forms of bacteria

- No of multiresistant strains is increasing

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Thank you
for your attention

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