# ANTIBIOTIC GROUPS AND THEIR INDICATIONS – PART 2

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# TETRACYCLINES

- **Bacteriostatic drugs**
- **Natural products: tetracycline**
- **Semisynthetic derivatives: doxycycline, minocycline…**
- **Oral and parenteral forms**
- **Broad-spectrum activity: G + and $G^-$ bacteria, mycoplasmas, chlamydia, rickettsiae, spirochetes, mycobacteria…**

# TETRACYCLINES - CLINICAL USE

- **Respiratory infections (mycoplasma chlamydia)**
- **Urogenital infections (urethritis)**
- **Lyme borreliosis,**
- **Leptospirosis,**
- **Anthrax ..**
- **Mycobacteriosis (mariunum, cheilonei, fortuitum…)**

- **High degree of resistance - streptococci, staphylococci…**

# SIDE EFFECTS, TOXICITY

- **Dysmicrobia - because of the broad spectrum of activity**
- **Indigestion, nausea, diarrhea**
- **Contraindications in pregnancy and childhood - storage in bones and teeth - chelation with $Ca^{2+}$ - disorders of bone development and tooth decay - brown spots on the enamel…**

# GLYCYLCYCLINES

- **Tigecycline**
- **Parenteral**
- **New class of antibiotics, connection to tetracyclines**
- **Broad-spectrum activity including highly resistant Gram negative bacteria (ESBL producers..) and MRSA, VRSA, VRE, … anaerobes, mycoplasmas, chlamydia**

- **Clinical use : reserve antibiotic, serious intra-abdominal infections, skin and subcutaneous infections…**

# CHLORAMPHENICOL

- **Proteosynthesis inhibitor**
- **Bacteriostatic effect**
- **Broad spectrum of activity:**
- **G + and G- bacteria**
- **Bordetella pertussis**
- **Leptospira**
- **Anaerobes…**

# CHLORAMPHENICOL – CLINICAL USE

- **Anaerobic and mixed infections**
- **Typhoid fever**
- **Abscessive infections in abdominal surgery, gynecology, pneumology..**
- **Purulent meningitis, brain abscess**

**-reliable penetration into the cerebrospinal fluid, crossing the blood-brain barrier**

# CHLORAMPHENICOL- SIDE EFFECTS, TOXICITY

- **Reversible myelosupression**
- **Aplastic anemia - fatal course (exceptionally), possibility even after local application**
- **Do not repeat the application at intervals shorter than ½ year - reducing the risk of aplastic anemia**
- **"Gray baby syndrome" - high serum levels, immaturity of the liver enzymatic systems**

- Most doctors are concerned about side effects and try to avoid the use of chloramphenicol…

# PEPTIDES

- **Disruption of cytoplasmic membrane -polymyxins or cell wall function - bacitracin**
- **Bactericidal effect**
- **Bacitracin - topical application (with aminoglycoside neomycin) – G+ spectrum of activity – staphylococci, streptococci**
- **Polymyxins A-E; colistin (polymyxin E) – parenteral forms**

# POLYMIXINS - COLISTIN

- **Spectrum of activity : enterobacteria, *Pseudomonas aeruginosa*, *Acinetobacter* spp.**
- **no activity on a Gram of positive bacteria**
- **reserve antibiotic for the treatment of serious infections of multidrug resistant ( MDR) gram negative etiology**
- **A 21st century remedy for the treatment of multidrug-resistant pseudomonas and acinobacter infections?**

**…..but in recent years a new type of plasmid transmitted resistance has emerged. It is linked to *mcr* genes.**

# COLISTIN – CLINICAL USE

- **Reserve antibiotic - especially for situations where there is no other choice**
- **Different types of pseudomonas infections**
- **Different types of enterobacterial infections**
- **Nosocomial pneumonia**
- **Sepsis**
- **Complicated UTI…**

- **topical use - inhalation in case of nosocomial pneumonia**

# COLISTIN – toxicity

- **Nephrotoxicity - the risk increases when combined with other nephrotoxic preparations (aminoglycosides, vancomycin ..)**
- **Neurotoxicity**
- **Neuromuscular blockade**

# FLUOROQUINOLONES

- **Exhibit antimicrobial/bactericidal effects on DNA gyrase (bacterial topoisomerase II) and bacterial topoisomerase IV**

- **Fluoroquinolones may be classified into "generations" based on their antimicrobial targets.**
- **First generation: nonfluorinated quinolone nalidixic acid, with a narrow spectrum of susceptible organisms.**
- **Second generation ciprofloxacin and ofloxacin…**
- **Third generation levofloxacin is classified as because of its increased activity against gram-positive bacteria.**
- **Fourth generation includes only moxifloxacin**

# CIPROFLOXACIN, OFLOXACIN

- **Spectrum of antimicrobial activity: mainly Gram negative bacteria including *Pseudomonas aeruginosa*, activity on Gram of positive bacteria and anaerobes is limited**
- **Oral and parenteral forms**
- **Clinical use : urinary tract infections , prostatitis, also effective in the treatment of many systemic infections caused by gram negative bacilli, ciprofloxacin is also used as a second-line agent in the treatment of tuberculosis**

- In many countries popular antibiotics in the treatment of community and hospital infections

# MOXIFLOXACIN

- **Extended antibacterial activity on Gram of positive bacteria, atypical agents (mycoplasma, chlamydia, legionela) and partly anaerobes**
- **Clinical use : mainly respiratory tract infections ( pneumonia, sinusitis..)**
- **Sometimes referred to as "repiratory quinolone" due to the ideal spectrum for respiratory pathogens**
- **reserve antibiotic in Czech Republic, common antibiotic in countries where high levels of pneumococcal resistance to penicilline**

# FLUOROQUINOLONES – RESISTANCE

- **Cross-resistance exists among the quinolones -** it arises relatively easily and quickly
- **High levels of fluoroquinolone resistance have emerged in Gram-positive and Gram-negative bacteria, primarily due to chromosomal mutations**

- **Chromosomal mutations in bacterial genes. Both topoisomerase IV and DNA gyrase may undergo mutations**

**Decreased accumulation:**

**- decreased number of porin proteins in the outer membrane.**

**- efflux pumps**

- **Most hospital bacteria are already resistant to fluoroquinolones**

# FLUOROQUINOLONES – TOXICITY, SIDE EFFECTS

- **Inflammation or rupture of tendons,**
- **joint and muscle problems,**
- **severe skin reactions, phototoxicity**
- **damage to peripheral nerves, sensory disorders,**
- **psychiatric problems,**
- **impaired kidney or liver function,**
- **dysmicrobia**
- **Common drug interactions…**

# FLUOROQUINOLONES – CONCLUSION

- **Current recommendations :**

- **do not prescribe fluoroquinolones for non-serious infections or infections where other options are possible (especially in outpatient practice with empirical treatment),**
- **as they may rarely cause long-term / permanent disabling side effects…**

# OXAZOLIDINONES

- **Inhibition of proteosynthesis**
- **Bakteriostatic effect**
- **First representative of the group : linezolid**

**Oral and parenteral forms**

- **Spectrum: Gram positive bacteria including MRSA, VRE…**
  inactive on gram of negative bacteria
- **Clinical use : Reserve antibiotic for the treatment of infections caused by MDR bacteria (pneumonia, skin and soft tissue infections, orthopedic infections ..)**
  **Excellent tolerability, low toxicity**
- **Limit - possibility of hematopoietic attenuation - long-term administration, especially longer than 1 month**

# COTRIMOXAZOLE

- **Combination of sulfonamide (sulfamethoxazole) and trimethoprim (diaminopyrimidine)**
- **Both substances interfere with the metabolism of folic acid at different levels - synergistic action and delay of the formation of resistence**
  **Broad spectrum of antibakterial activity : Gram positive cocci (staphylococci), Gram negative bacteria - entrobacteria, *Haemophilus* spp, neisseria, *Nocardia* pp..*Pneumocystis jiroveci* *Toxoplasma gondii***

# COTRIMOXASOLE – CLINICAL USE

- **UTI**

**Respiratory infection**

**Salmonellosis**

**Brucellosis**

**Nocardiosis**

**Toxoplasmosis…**

**Long-term prophylaxis of HIV-positive, organ transplant patients and other severely immunosuppressed patients**

**The most common side effect is various forms of allergies**