Masaryk University
Faculty of Medicine

Antibiotics in Dentistry

Antibiotics for Infection Control and Prevention in Dentistry

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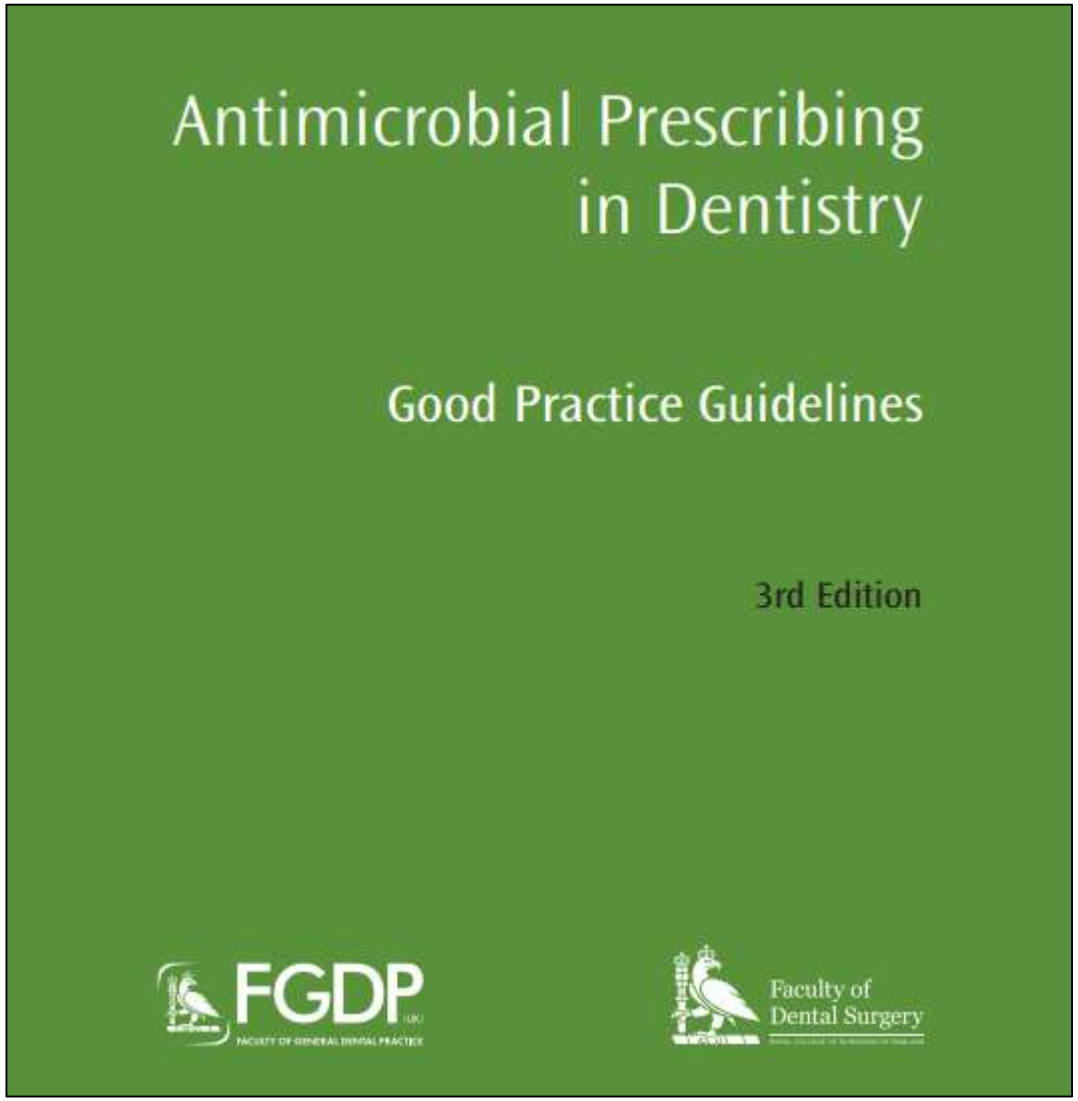
Learning Objectives

- Understand the role of antibiotics in dental infections.
- Identify antibiotic classes commonly used in dentistry.
- Discuss antibiotic resistance and its impact on dental practice.
- Implement proper antibiotic prescribing practices and dosage guidelines.

- **Agenda**:
  - Importance of Antibiotics in Dentistry
  - Classes of Antibiotics
  - Antibiotic Resistance and Stewardship
  - Activities

Before we start…



Palmer, N. (Ed). Antimicrobial Prescribing in Dentistry: Good Practice Guidelines. 3rd Edition. London, UK: Faculty of General Dental Practice (UK) and Faculty of Dental Surgery; 2020.

Why Antibiotics in Dentistry?

- Antibiotics treat bacterial infections in/around the oral cavity.

- Common indications:
  - Local infections
  - Focal infections
  - Orofacial infections: Odontogenic and nondontogenic

  - Common symptoms: Pain and Swelling

- **Prophylactic use**:
  - Preventing infections in high-risk patients (e.g., prosthetic heart valves).

- Untreated conditions lead to much severe disease states!

Correct clinical assessment (Infection)

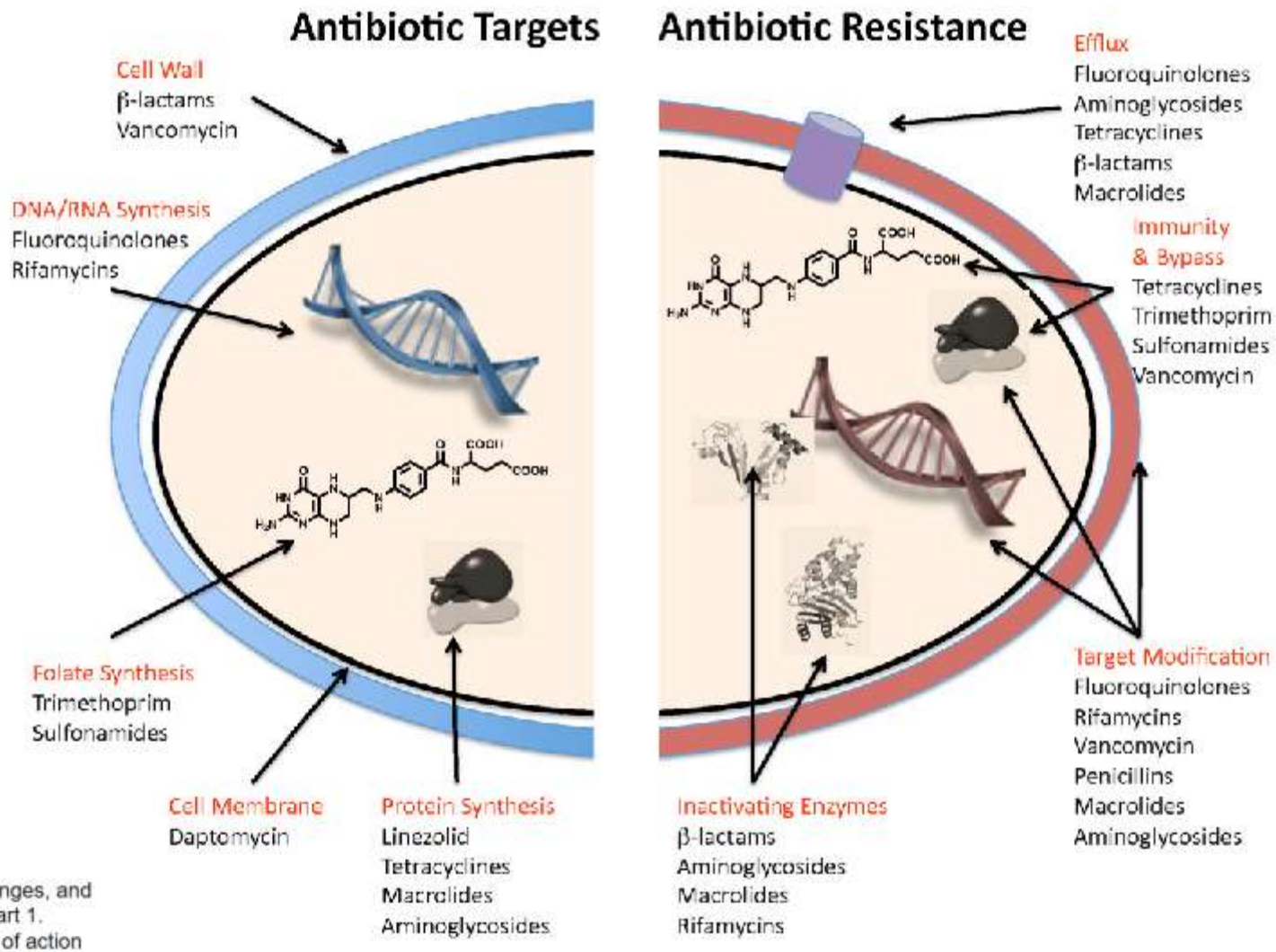
Critical !

Activity 1

- Assessment of the presence of fever (> 38°C), malaise, fatigue or dizziness
  - **Q:** In what situations fever would not be present?
  - **A:** antipyretic effect of patients taking analgesics may temporarily lower the temperature
  - **Few examples**: **paracetamol**, **NSAIDs**, **metamizole**, **celecoxib**, **Meloxicam**, **nimesulide**, **piroxicam**

Importance of Medical Records

- Measurement of the patient's pulse and temperature (normal temperature range is 36.2°C-37°C)
- Definition of the nature, location and extent of the swelling, and any lymphadenopathy
- Identification of the cause of the infection
- Assessment of presence of sepsis using a decision support tool, e.g. NICE Sepsis: Risk stratification tools

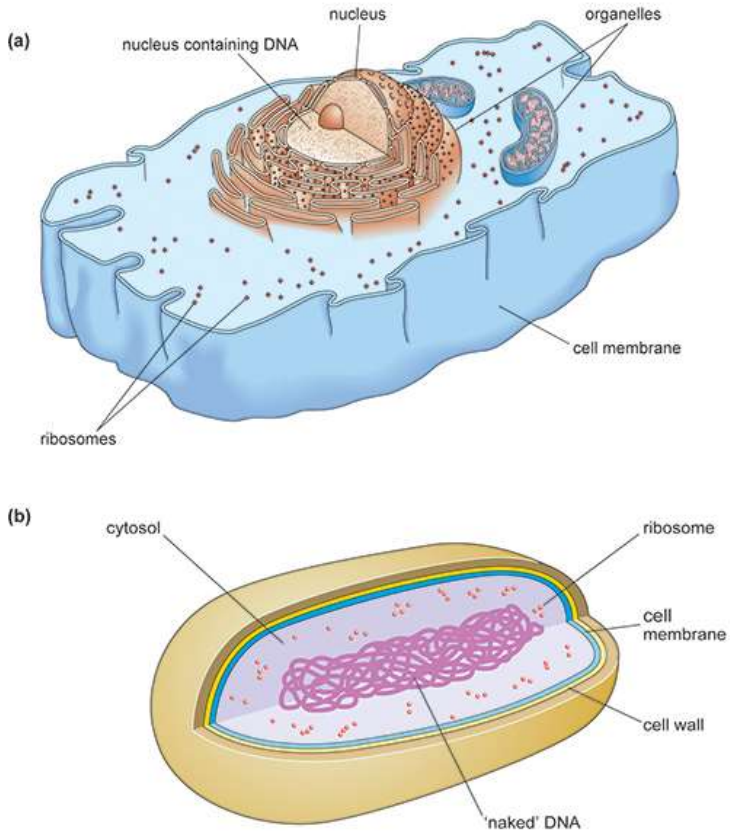


Fighting bacterial resistance: approaches, challenges, and opportunities in the search for new antibiotics. Part 1. Antibiotics used in clinical practice: mechanisms of action and the development of bacterial resistance. Full text available at: http://mir-journal.org/issues/4/3/

December 2017 · Microbiology Independent Research Journal (MIR Journal) 4(1):31-51
DOI 10.18527/2500-2236-2017-4-1-31-51

Selective toxicity

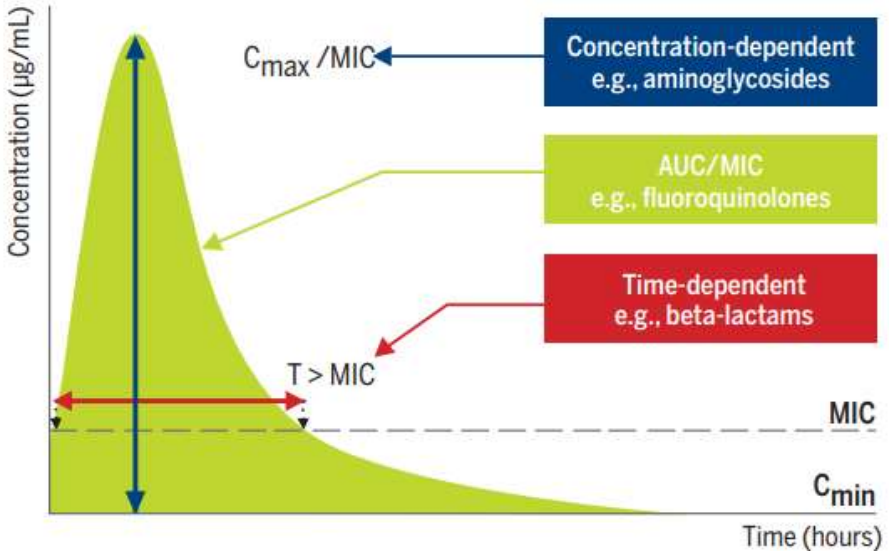
Target the disease-causing organism while causing no or minimal harm to the patient!



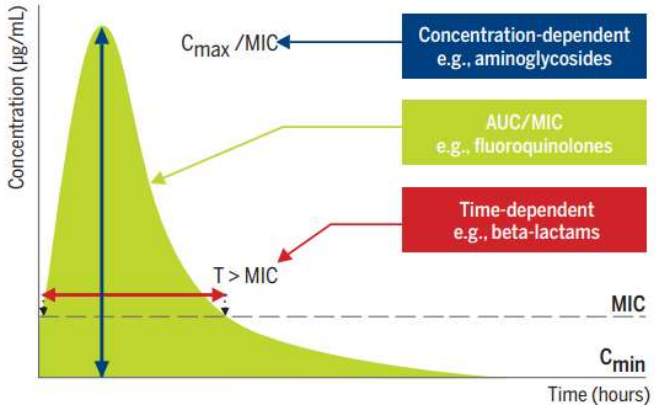
Exploit the **differences** between host cell and bacterial

Principles of antibacterial therapy

- **MIC (Minimum Inhibitory concentration)**
  - **Lowest conc. of ATB that inhibits visible growth** of a microorganism after overnight incubation
  - Effective treatment = conc. ATB higher than MIC (2-5x)
  - **Predictive** value
  - Gives an idea of susceptibility and potential resistance



Principles of antibacterial therapy



- **MBC (Minimum bactericidal concentration)**
  - Lowest concentration of antibiotic required to kill the bacteria

- **Concentration-Dependent Killing**
  - Rate and **extent of ATB killing is related to the peak concentrations achieved**
  - Aminoglycosides

- **Time-dependent killing**
  - Effect is dependent on the **time** during which ATB concentration at site of infection is **above MIC**
  - Importance is shifted to **adherence to therapy**
  - Beta-lactams

- **Concentration-dependent and time-dependent killing**
  - Dependent on the AUC
  - Related to the amount of time above the MIC and the total exposure of antibiotic to the organism
  - Importance is shifted towards **total daily dose**
  - Fluoroquinolones

When Are Antibiotics Indicated?

- Antibiotic prophylaxis
  - Immunosuppressed patients
    - With a history of cancer
    - Individuals with infective endocarditis
    - With metabolic disorders: diabetes and splenectomies
    - With prosthetic joints
    - In-dwelling catheters
    - Neurosurgical shunts
    - Valvular heart diseases
    - Surgical pulmonary shunts
    - Hypertrophic cardiomyopathy
    - Mitral valve prolapsed
    - Prosthetic heart valves

High infection risk

- Antibiotic prophylaxis
  - Healthy Patients
    - Surgery for benign tumours
    - Bone grafting
    - Implant placement
    - Periapical surgery
    - Removal of impacted teeth

When Are Antibiotics Indicated?

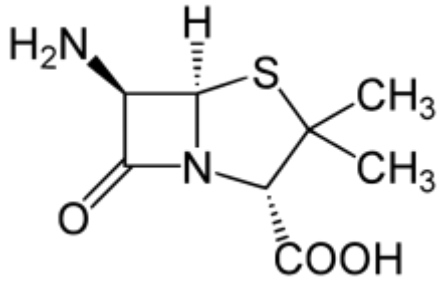
- Acute conditions
  - Necrotizing ulcerative gingivitis
  - Stage III-grade C/incisor-molar pattern periodontitis (formerly referred to as localized aggressive periodontitis)
  - Acute periapical abscess
  - Cellulitis
  - Local or systemic spreading of infection in the periodontal abscess
  - Pericoronitis
  - Periimplantitis
  - Infection of deep fascial layers of the head and neck, and in the case of fever and/or malaise

Penicillins

Bactericidal

1st to be discovered – Alexander Fleming (1928) – Inhibition of growth in culture plate with *Staphylococci* – Genus *Penicillium*

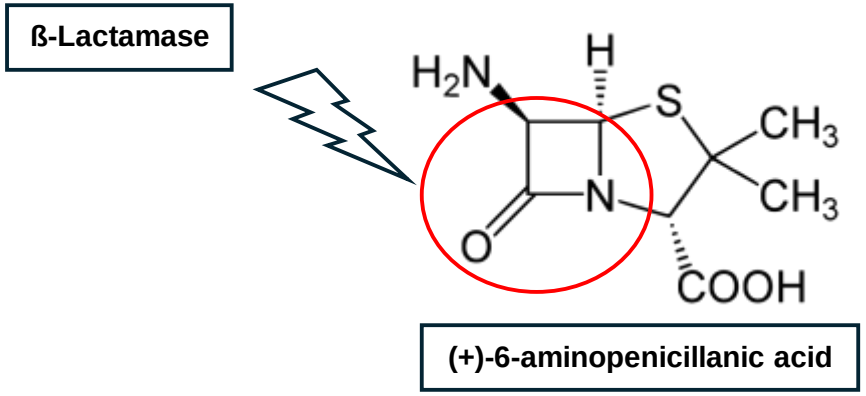
- **Non-toxic to host – least toxic drug was the first to be discovered – very safe**
  - Reason to be used as 1st choice agent
- **Part of the cell wall inhibitors**
  - **Selective toxicity** – Damage to cell wall of bacteria while lacking effect against mammalian cells
  - Interference with last step of cell wall synthesis – inhibition **transpeptidation or cross linking** – lysis
  - **Binding to PBPs** (Penicillin Binding Proteins) enzymes responsible for transpeptidation
    - **Resistance mechanisms**:
      - **Alteration of PBPs** - E.g: MRSA (Methicillin Resistant *Staphylococcus Aureus*) → ↓ Efficacy
      - **ß-Lactamase producing organisms** **(Break of ß-Lactam ring)** → ↓ Efficacy
  - **Efficacy** depends on the existence of a growing cell wall



(+)-6-aminopenicillanic acid

Resistance mechanisms

- Natural resistance
  - Innate
    - Microorganisms without a cell wall (e.g.: ***Mycoplasma pneumoniae***)
      - Intrinsically ß-Lactamase producing
    - Microorganisms with a cell wall
      - Impermeable to drugs
- Acquired resistance
  - Plasmid mediated ß-Lactamase - Antibiotic gene resistance
    - **Gram-Positive -** secretion extracellularly
    - **Gram-Negative -** Inactivation in periplasmic space
  - Efflux Pump (e.g.: ***Klebsiella pneumoniae***)
    - ↓ Intracellular concentration
  - Alteration of PBPs (e.g.: **MRSA**)
    - ↓ Lower binding affinity
  - Decrease of permeability through the cell wall
    - ↓ Amount of drug that reaches PBPs

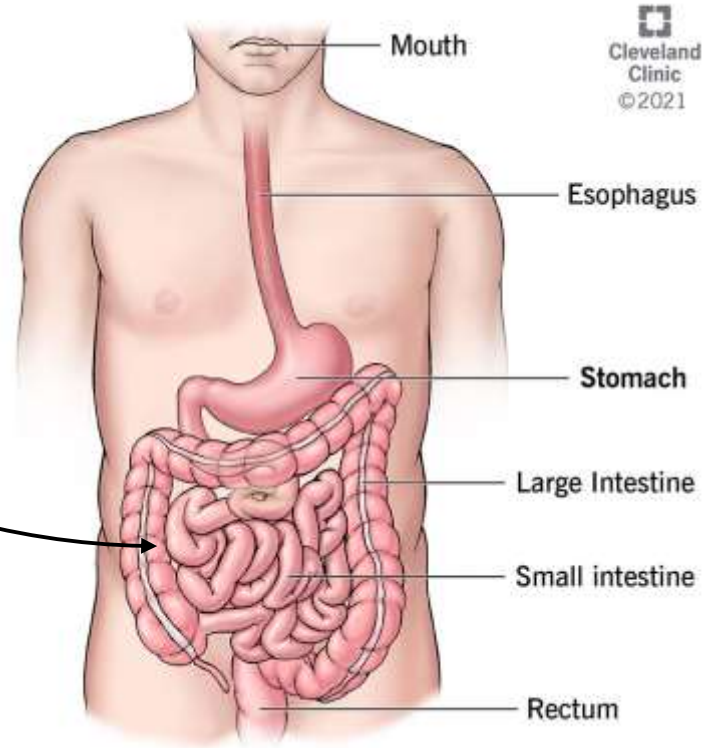


Beta-Lactam Antibiotics

- Pharmacokinetics (ADME)
  - **Absorption**

Must be taken on an empty stomach!

Incomplete oral absorption



Interference with intestinal flora

GIT disturbances

Absorption

Time of Gastric Emptying

Destruction by stomach Acid

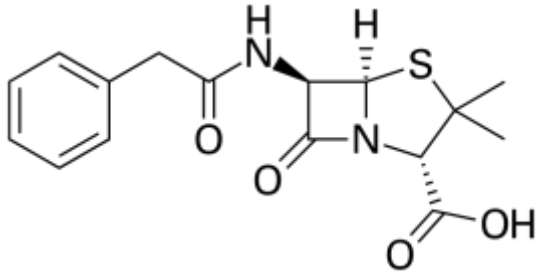
Beta-Lactam Antibiotics

- Pharmacokinetics (ADME)
  - **Distribution**
    - Generally, well distributed
    - Can cross placental barrier
    - Limited penetration to bone and CSF (unless in inflammatory states)
  - **Elimination**
    - Kidneys are the primary route of excretion (Tubular excretion + Glomerular Filtration)
    - Renal Impairment requires dose adjustment
    - Penicillins in general have a relative short T1/2
    - Excreted on the breast milk

Beta-Lactam Antibiotics

Bactericidal

- Groups of Penicillin's
  - **Natural Penicillin's – Produced from fermentation of fungus *Penicillium chrysogenum***
    - **penicillin G (benzyl penicillin)** – administered **IV, IM – poor oral absorption**
      - Effective against: **Gram-Positive Bacilli, Gram-Negative Cocci, Spirochetes**
      - Treatment of: Gas Gangrene (*Clostridium perfringens*) or Syphilis (*Treponema pallidum*)
    - **penicillin V (phenoxymethylpenicillin) -** administered **PO**
      - Same spectrum (Effective against: **Gram-Positive Bacilli, Gram-Negative Cocci, Spirochetes**)



Penicillin G

- **Anti-staphylococcal penicillin's – For ß-Lactamase Resistant**
  - **methicillin** (Not used - AIN)
  - **nafcillin** (administered **IV, IM**)
  - **oxacillin** (administered **IV, IM**)
  - **dicloxacillin (**administered **PO**)

Reserved for ß-Lactamase producing organisms

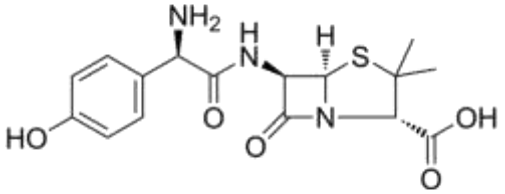
MSSA

Not to be used for Gram-Negative organisms

Penicillinase producing Staphylococci

Beta-Lactam Antibiotics

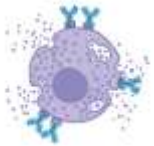
Bactericidal



amoxicillin

- Groups of Penicillin's
  - **Broad-spectrum PNC**
    - **Aminopenicillin's**
      - **ampicillin** – administered **PO**, **IV**, **IM**
        - Effective against: **Gram-Positive Bacilli, Gram-Negative Cocci, Spirochetes**
        - Treatment of: Listeriosis (*Listeria Monocytogenes*), *Enterococcal* Species
        - Commonly combined with: **sulbactam** → ↑ Extended Antimicrobial Spectrum (e.g.: Against **MRSA**)
      - **amoxicillin –** administered **PO**, **IV**
        - Effective against: **Gram-Positive Bacilli, Gram-Negative Cocci, Spirochetes**
        - Commonly used by **dentists**: **Prevention of Bacterial Endocarditis in high-risk patients**
        - Commonly combined with: **clavulanic Acid** → ↑ Extended Antimicrobial Spectrum (e.g.: Against **MRSA**)

  - **Anti-pseudomonal PNC**
    - **Carboxypenicillin's**
      - **ticarcillin - administered IV, IM**
        - Effective against: Gram-**Negative** Bacilli (Not *Klebsiella* – produces a constitutive penicillinase)
        - Treatment of: *Pseudomonas aeruginosa*
        - Commonly combined with: **clavulanic Acid** → ↑ Extended Antimicrobial Spectrum (e.g.: Against penicillinase producing organisms)
    - **Ureidopenicillin's**
      - **piperacillin - administered IV, IM**
        - Effective against: Gram-**Negative** Bacilli (Not *Klebsiella* – produces a constitutive penicillinase)
        - Treatment of: *Pseudomonas aeruginosa*
        - Commonly combined with: **tazobactam** → ↑ Extended Antimicrobial Spectrum (e.g.: Against penicillinase producing organisms)

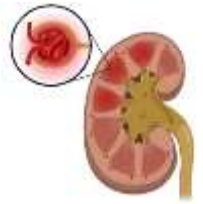


Rashes

Angioedema

Anaphylactic shock

Hypersensitivity



Methicillin – discontinued – Causes acute interstitial nephritis

Cytopenia – monitor necessary – Prolonged therapy

Piperacillin, Ticarcillin and Nafcillin - ↓ Coagulation

Haematologic complications

Nephritis

Adverse Effects

Neurotoxicity

Only with high doses or intrathecal administration

Epileptic patients at risk – GABAergic inhibition

Diarrhoea

More common from extended spectrum agents and are incompletely absorbed Disbalance of the microflora

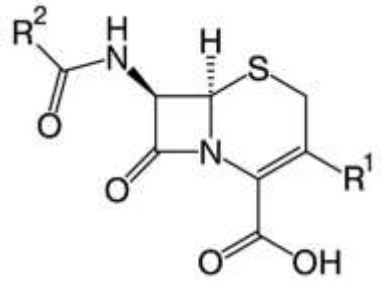
↑Risk of Pseudomembranous Colitis (caused by *Clostridium Difficile*)

Most characteristic side effect

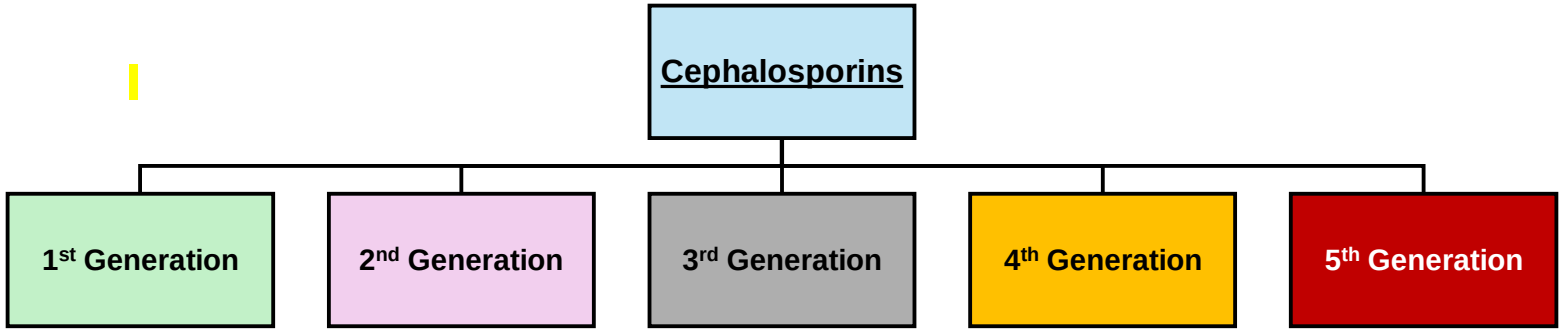
Beta-Lactam Antibiotics (Cephalosporins)

Bactericidal

- **Cephalosporins**
  - Same mechanism of action as Penicillins. Produced semi-synthetically
  - Affected by the same mechanisms of resistance
  - Tend to be more resistant to ß-Lactamase



Cephalosporin

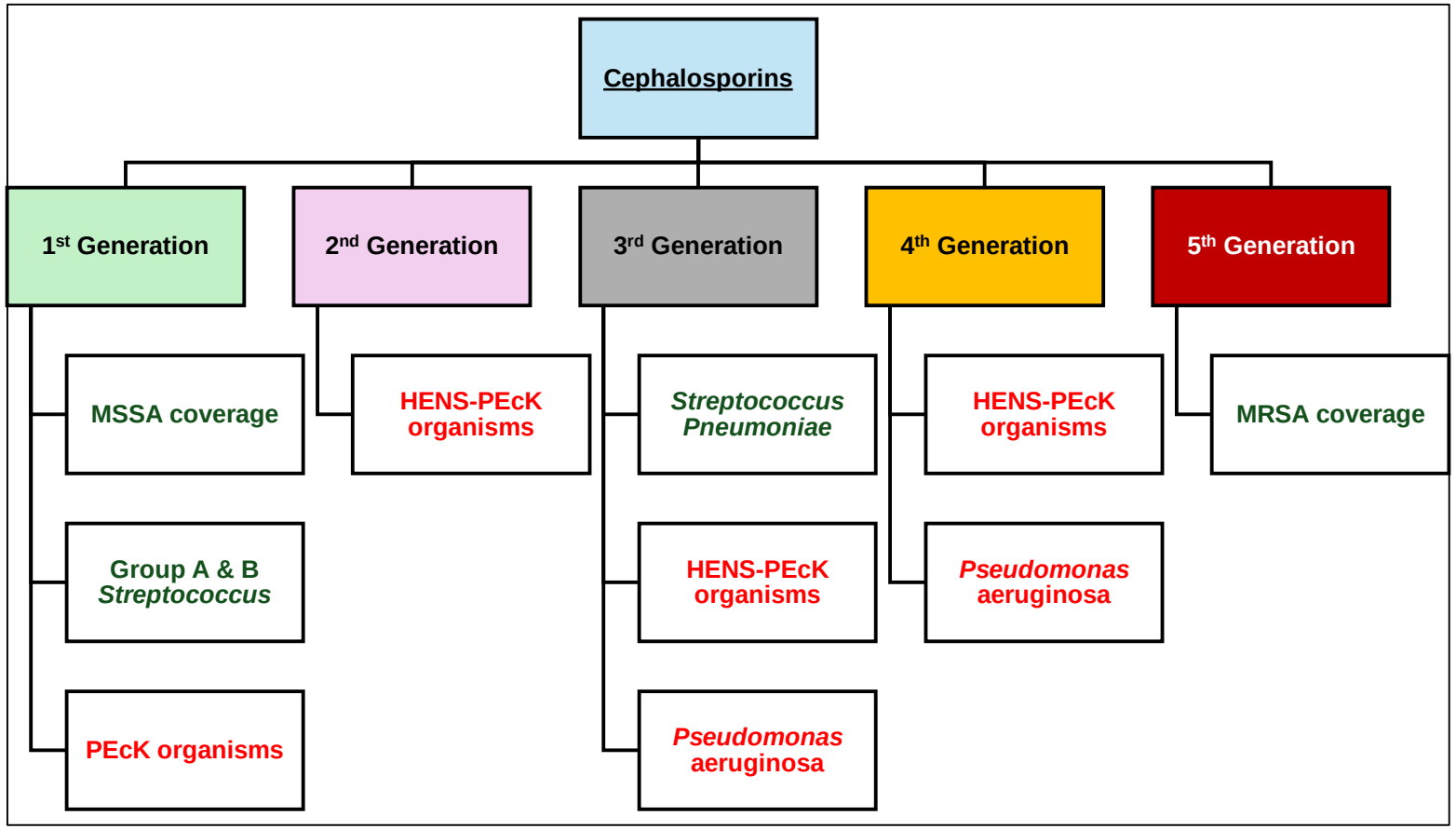


Commercially available **Cephalosporins infective against**: *MRSA, Listeria monocytogenes, Clostridium Diffcile and Enterococci*

Beta-Lactam Antibiotics (Cephalosporins)

HENS-PEcK organisms

- *Hemophilus influenzae*
- *Enterobacter*
- *Neisseria gonorrhoeae & meningitidis*
- *Serratia*
- *Proteus*
- *Escherichia coli*
- *Klebsiella*

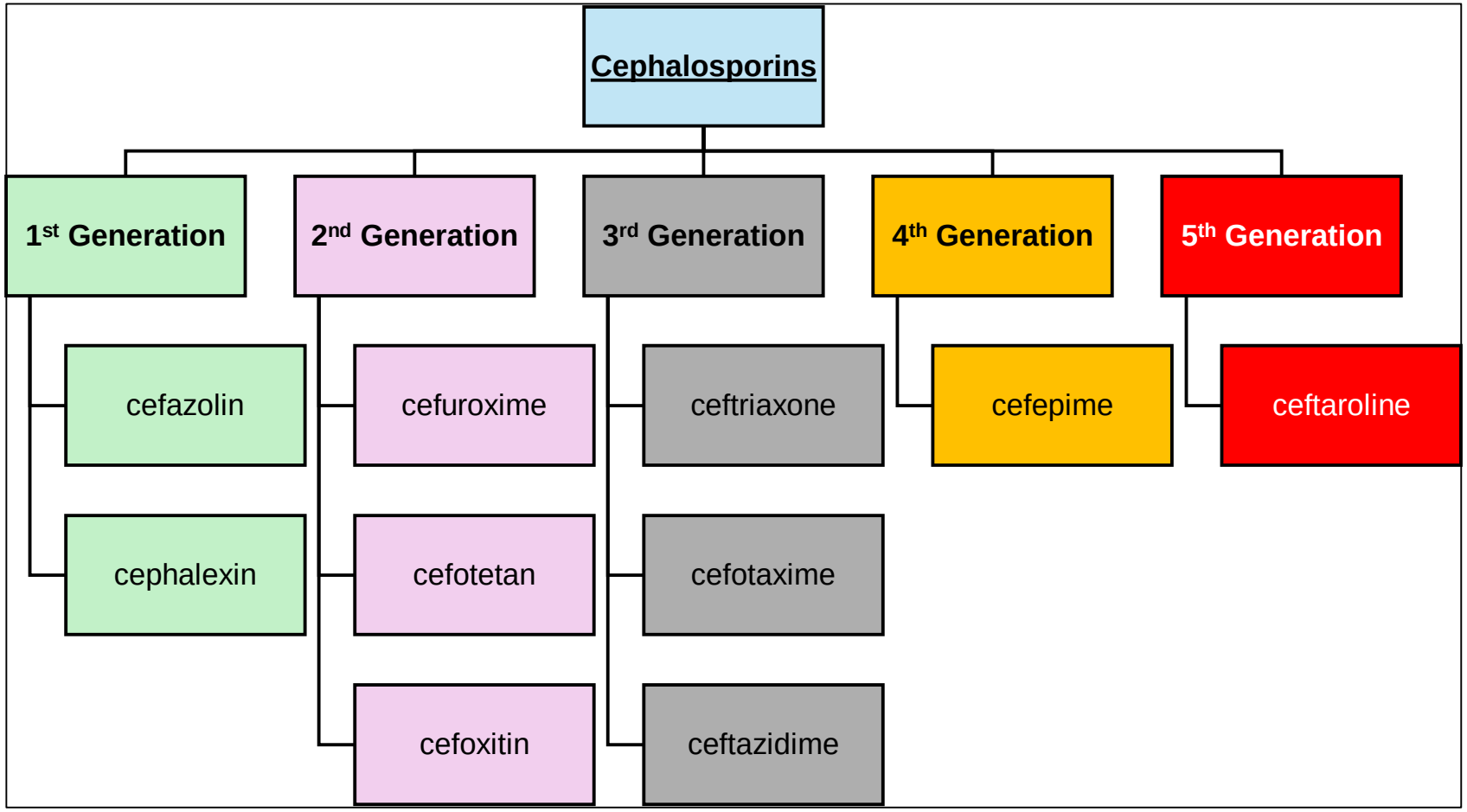


Gram (+)

Gram (-)

Extended-Spectrum Beta Lactamase Producing Bacteria (EBSL)

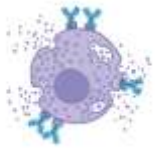
Beta-Lactam Antibiotics (Cephalosporins)



Beta-Lactam Antibiotics (Cephalosporins)

- Pharmacokinetics (ADME)
  - **Absorption**
    - Poor Oral Absorption most of Cephalosporins are administered IV, IM
  - **Distribution**
    - Well distributed to body fluids
    - All cross the placental barrier
    - **cefazolin** is used pre-surgery due to its short half-life and activity against *S.aureus (prophylaxis)*
    - Adequate therapeutic levels in CSF only achieved with a few Cephalosporins (3rd Generation: **ceftriaxone** or **cefotaxime**)
      - Treatment of Meningitis (caused by *Haemophilus Influenza*)
  - **Elimination**
    - Kidneys are the primary route of excretion (Tubular excretion + Glomerular Filtration)
    - Renal Impairment requires dose adjustment
    - **ceftriaxone** is an exception because is excreted through bile (use in renal dysfunction)

If patient showed the following with **penicillin**:
Anaphylactic shock
Stevens-Jonhson syndrome
Toxic Epidermal Necrosis
(do not use **Cephalosporins**)



Hypersensitivity

Diarrhoea
Dyspepsia
Abdominal Pain

GIT disturbances

Risk of biliary sludge

↑ Risk of Cholecystitis with **ceftriaxone**

Adverse Effects

Gastritis

Vitamin K Deficiency

Inhibition of synthesis of coagulation factors → ↓ Coagulation Factors → Risk of Bleeding

Nausea and Vomiting

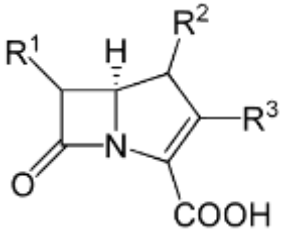
Headache

ceftriaxone – produces a **disulfiram-like reaction**: Development of symptoms like nausea, vomiting, flushing, hypotension, and tachycardia when medications are taken with alcohol

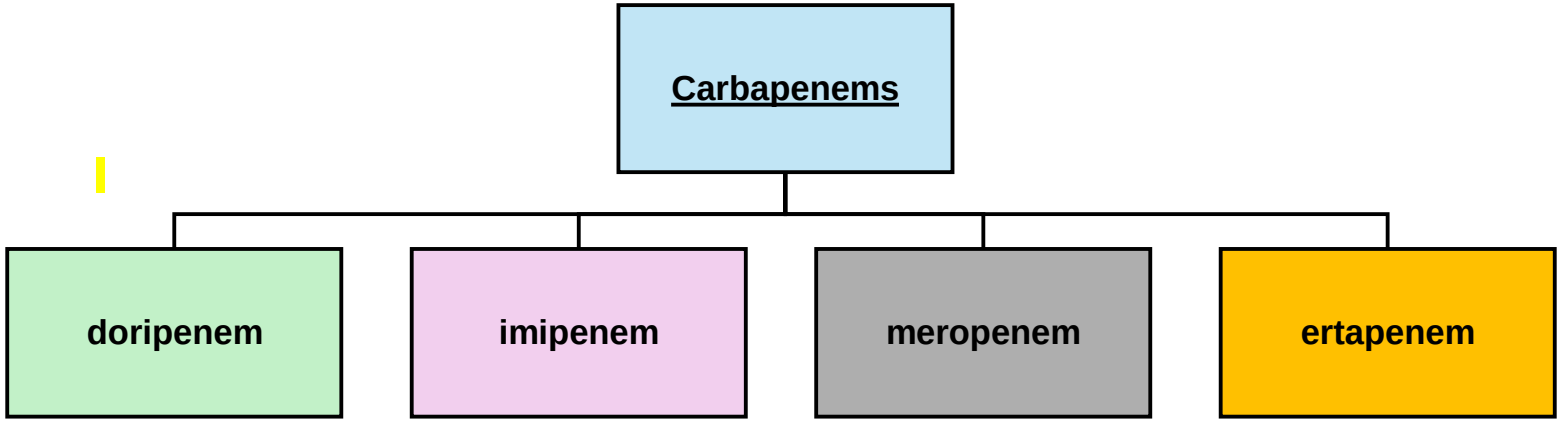
Most characteristic side effect

Beta-Lactam Antibiotics (Carbapenems)

- **Carbapenems**
  - Really broad agents
  - Same mechanism of actions as Penicillins and Cephalosporins
  - Generally unaffected by ß-lactamases
  - Affected by Metallo-ß-lactamases

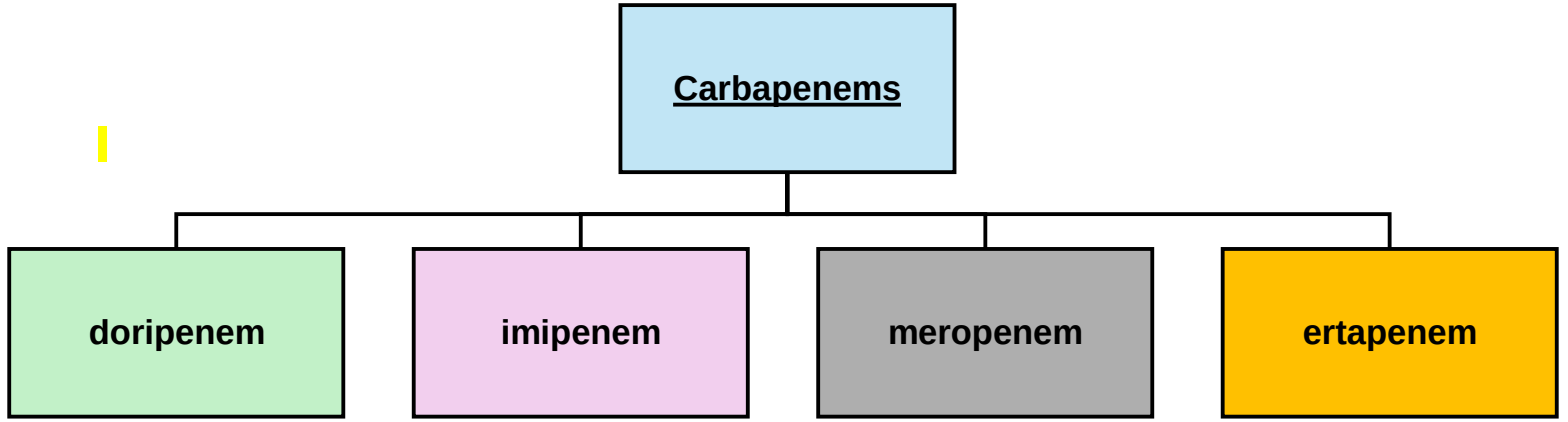


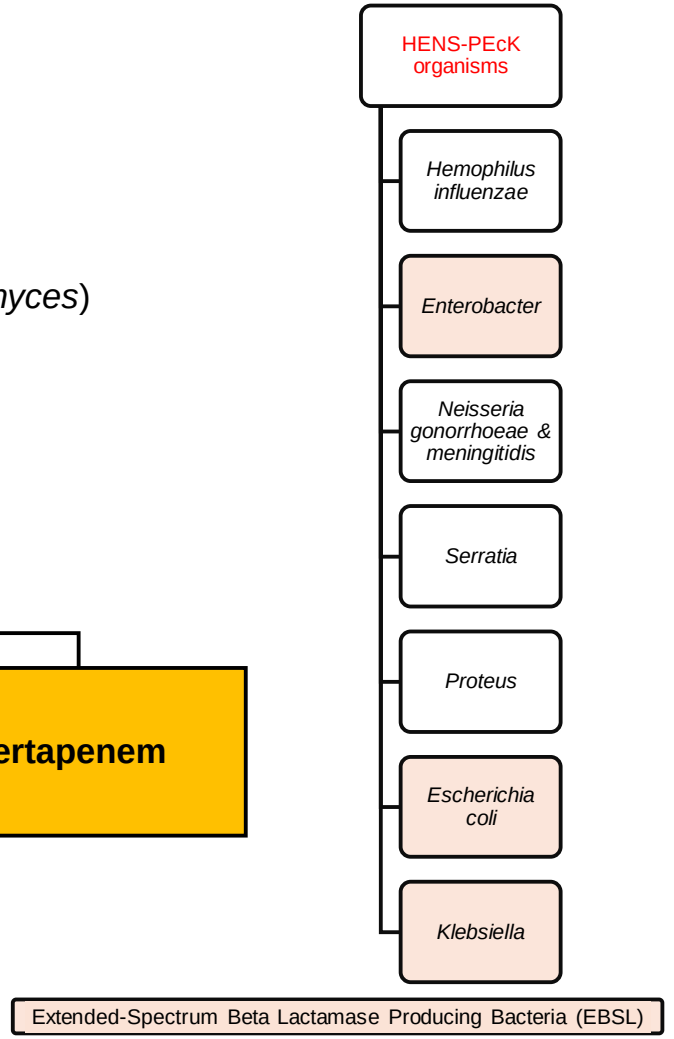
Carbapenem



Beta-Lactam Antibiotics (Carbapenems)

- Carbapenems
  - Bacterial Coverage
    - Hens-PecK organisms
    - Anaerobic bacteria (*Clostridium, Bacteroides, Pepto streptococcus, Fusobacterium, Actinomyces*)





Beta-Lactam Antibiotics (Carbapenems)

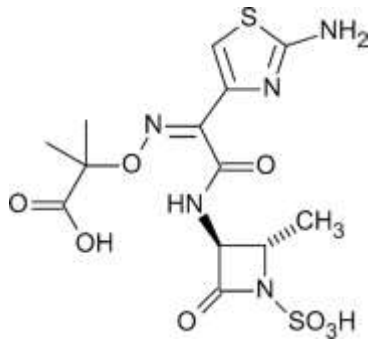
- Pharmacokinetics (ADME)
  - **Absorption**
    - Poor oral Absorption
    - Carbapenems are administered IV, IM
  - **Distribution**
    - Well distributed to body tissues and body fluids
    - **imipenem + cilastatin – Penetration to CNS**
  - **Metabolism**
    - **cilastatin** (renal dehydropeptidase inhibitor) blocks **imipenem** metabolism and prolongs its half-life
  - **Elimination**
    - Kidneys are the primary route of excretion (Tubular excretion + Glomerular Filtration)
    - Renal Impairment requires dose adjustment

High doses of **imipenem**
Less common with other carbapenems

Beta-Lactam Antibiotics (Monobactams)

Bactericidal

- **Monobactams**
  - **aztreonam** – only representative
  - Same mechanism of actions as Penicillins, Cephalosporins and Carbapenems
  - Generally unaffected by ß-lactamases
  - Affected by Extended Spectrum-ß-lactamases
  - Coverage against Hens-PEcK organisms (Gram -)
  - No coverage against Gram +
  - **IV administration**
  - Used in penicillin-allergic cases



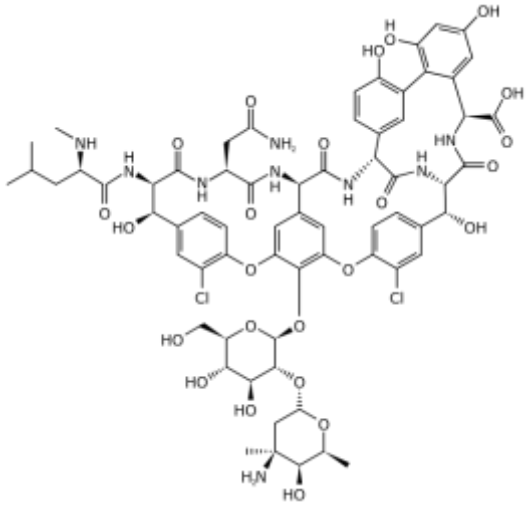
Monobactam

vancomycin and fosfomycin

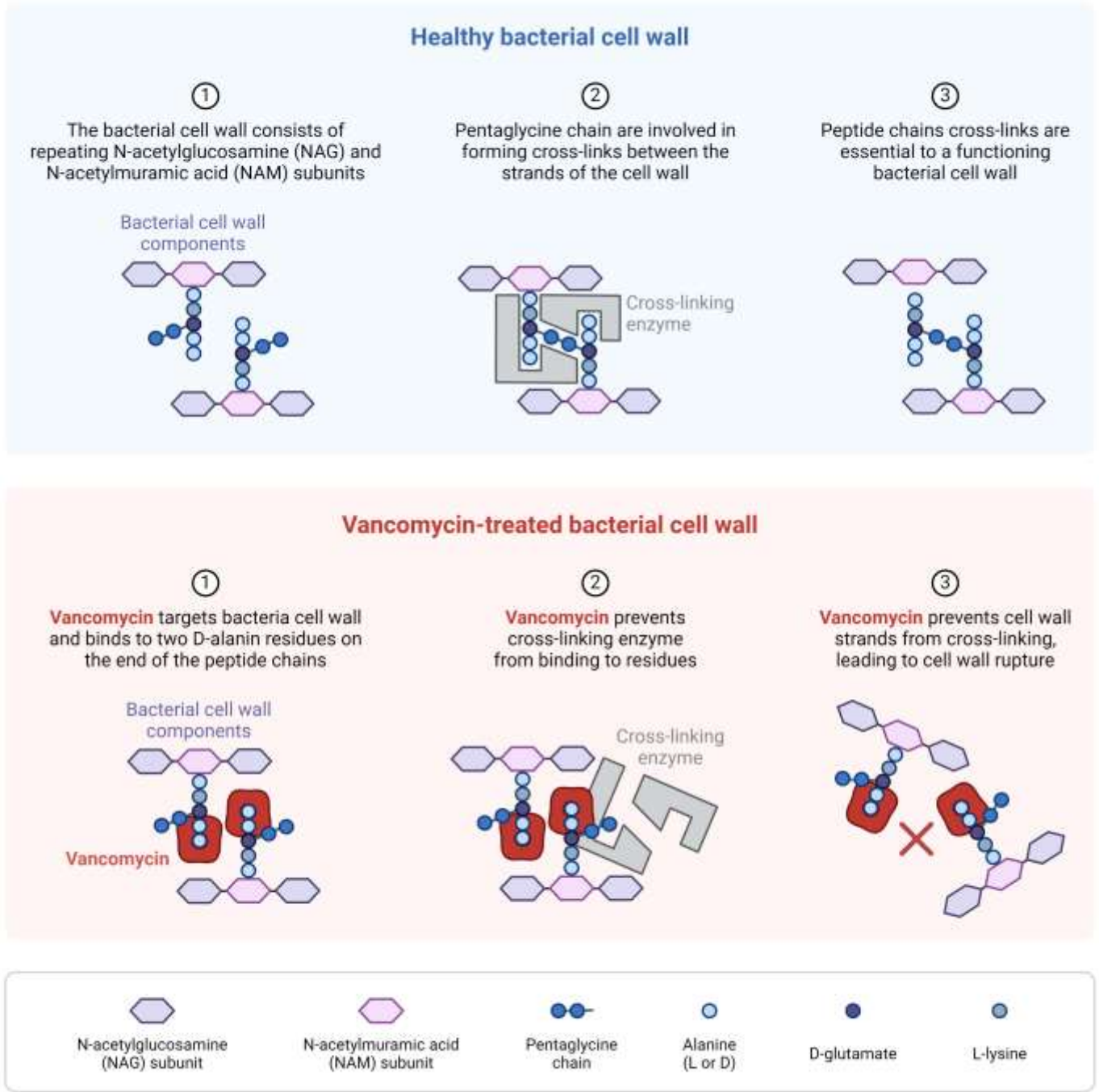
Bactericidal

- **Glycopeptide - vancomycin** - administered **IV (more common), PO**
- **Phosphonic Acid - fosfomycin –** mainly used in UTIs – administered **IV,PO**
- Mechanism of action – Inhibition of peptidoglycan synthesis
- Agents in reserve!
- Use in **severe infections**: MRSA,MRSE and Enterococcal
  - Usually, 1st option in the following situations caused by MRSA:
    - Hospital-Acquired Pneumonia
    - Skin and soft skin issues
    - Complicated UTI
    - Septic arthritis, osteomyelitis
    - Community-Acquired Meningitis (by S. pneumoniae)
    - Hospital-Acquired Meningitis
    - Sepsis

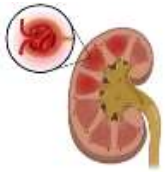
- **PO administration (not absorbed)** allows for treatment of *Cl. Difficile*



vancomycin


Healthy bacterial cell wall
1
The bacterial cell wall consists of repeating N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM) subunits
Bacterial cell wall components
2
Pentaglycine chain are involved in forming cross-links between the strands of the cell wall
Cross-linking enzyme
3
Peptide chains cross-links are essential to a functioning bacterial cell wall
Vancomycin-treated bacterial cell wall
1
Vancomycin targets bacteria cell wall and binds to two D-alanin residues on the end of the peptide chains
Bacterial cell wall components
Vancomycin
2
Vancomycin prevents cross-linking enzyme from binding to residues
Cross-linking enzyme
3
Vancomycin prevents cell wall strands from cross-linking, leading to cell wall rupture
N-acetylglucosamine (NAG) subunit
N-acetylmuramic acid (NAM) subunit
Pentaglycine chain
Alanine (L or D)
D-glutamate
L-lysine

Most characteristic side effect



Direct Nephrotoxicity

Phlebitis

Whenever **vancomycin** is pushed too quickly

Adverse Effects

Ototoxicity

Red Man syndrome

Whenever **vancomycin** is pushed too quickly
Manifest as:
Red, itchy rashes
Muscle spasms
Precipitate hypotension and a little bit of tachycardia

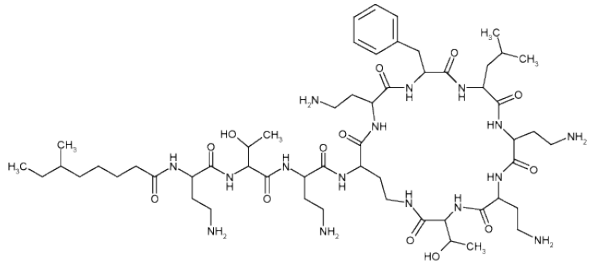
DRESS

Drug-related eosinophilia and systemic symptoms
Classic tetrad of:
Fever
Rash
↑ eosinophils
Lymphadenopathy

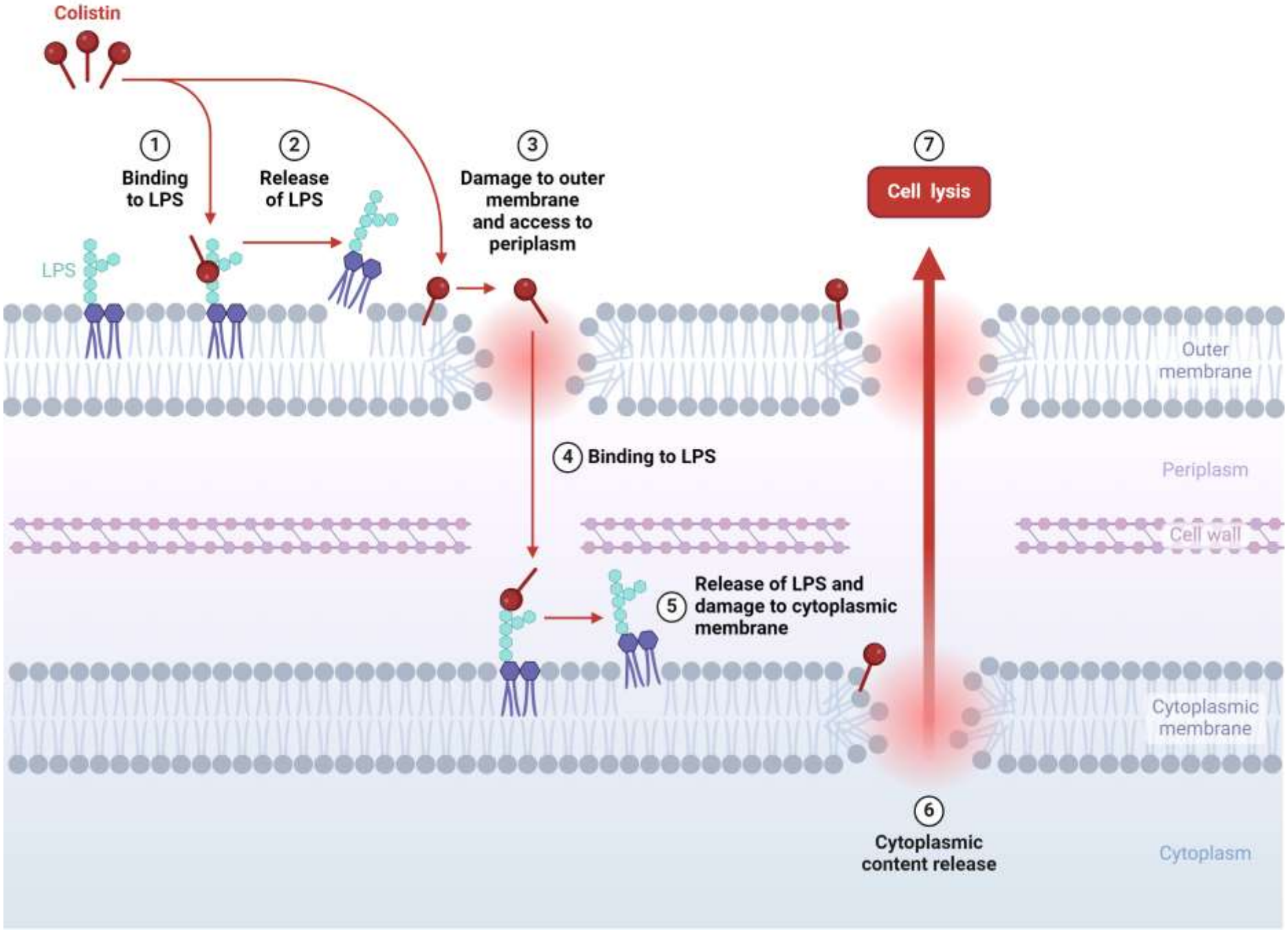
Polypeptides

Bactericidal

- **polypeptides**
  - **bacitracin –** combined with Vit. A – prevention of skin infection after cuts
    - Effective against **streptococci, pneumococci, and staphylococci**.
    - In addition, most anaerobic cocci, neisseriae, tetanus bacilli, and diphtheria bacilli are sensitive
    - Mainly **topical** use
  - **Polymyxins**: **polymyxin B and Polymyxin E (colistin)**
    - Mechanism of action – Disruption of cell membranes
    - Mainly **topical** use
    - **Gram-positive organisms**, Proteus sp, and Neisseria sp are resistant.
    - Significant Nephrotoxicity

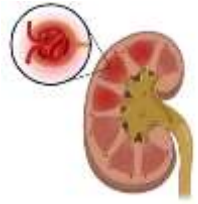


polymyxin B


Colistin
1 Binding to LPS
2 Release of LPS
3 Damage to outer membrane and access to periplasm
7 Cell lysis
LPS
Outer membrane
4 Binding to LPS
Periplasm
Cell wall
5 Release of LPS and damage to cytoplasmic membrane
Cytoplasmic membrane
6 Cytoplasmic content release
Cytoplasm

Seizures, myoclonus, encephalopathy, serotonin syndrome

Neurotoxicity



Respiratory Failure

Adverse Effects

Nephrotoxicity

With **polymyxins**

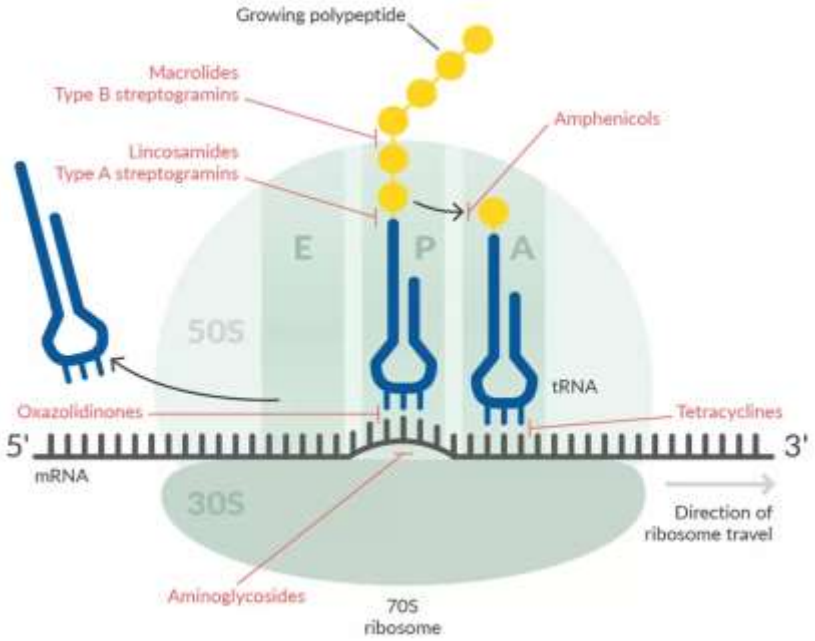
Dermatitis

With **bacitracin**

Inhibitors of Protein synthesis

Bacteriostatic

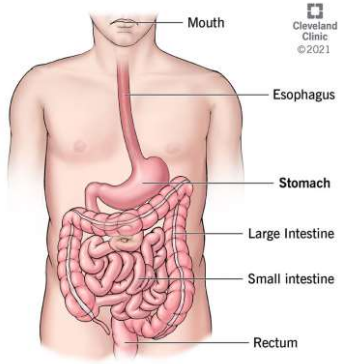
- **Characterized by their selective toxicity**
  - Bacterial protein synthesis – bacterial ribosomes contain a 50S and 30S subunit
  - Mammalian ribosomes have a 60S and a 30S subunit
  - Inhibition of translation process
    - 1st step - Inhibition of Aminoacyl-tRNA binding – **tetracyclines** and **aminoglycosides** **– bind to 30S subunit**
    - 2nd step – Inhibition of peptidyl transferase activity (transpeptidation) **– chloramphenicol – bind to 50S subunit**
    - 3rd step – Inhibition of translocation **– macrolides and streptogramins – bind to 50S subunit**



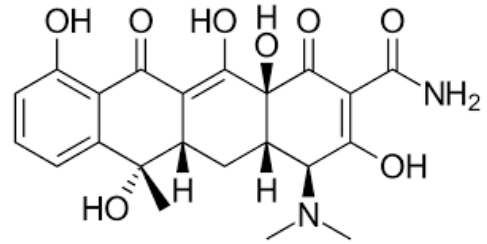
Tetracyclines

Bacteriostatic

- **Tetracyclines**
  - **tetracycline -** administered **PO,IV**
  - **doxycycline –** administered **PO,IV**
  - **Mechanism of action** – inhibition of protein synthesis – binding to 30S ribosomal subunit
  - **Broad therapeutic index** (both Gram + and Gram -, mycoplasma, **chlamydia, *rickettsiae*, *Borrelia burgdorferi***)
  - Lack of activity and resistance is common (efflux pumps – decrease intracellular concentration – reduction of therapeutic value)
  - Low toxicity
  - Cross placental barrier (contraindicated in pregnancy)



↓ **Absorption**



Tetracycline

Tetracyclines

Tetracyclines accumulate slowly in bones and teeth, because they have a **high affinity for calcium, and should not be used in children for this reason**

⇩

Weaken the tooth enamel

⇩

Contraindicated in children up to 8 years old

Most characteristic side effect

Diarrhoea

Suprainfection

Candida (vagina) or resist. staphylococcus (gut)

Adverse Effects

Vestibular problems

vertigo, nausea, vomiting

Photosensitivity

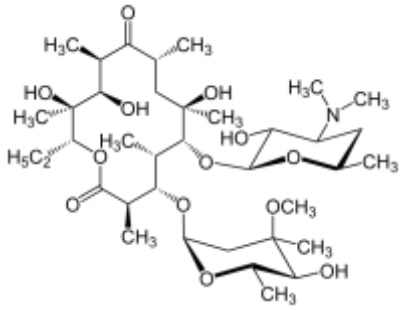
Yellow Teeth

Contraindicated in pregnancy and children before 8 years old!

Macrolides

Bacteriostatic

- **Macrolides – administration PO, IV**
  - Basic (**erythromycin**, spiramycin)
  - Modified (**clarithromycin**, **azithromycin**, roxithromycin)
  - Spectrum: mainly on **G+**, neisseria, leptospirosis, mycoplasma, chlamydia, helicobacter, legionella, toxoplasma
  - **clarithromycin, azithromycin** much more active against H.Influenzae
  - **Mechanism of action** – Inhibition of translocation – bind to 50S subunit
  - They enhance the killing of bacteria by phagocytes because they to be concentrated in the lysosomes
  - Good tolerance (Ery-motilin!), low tox., good penetration into the tissues and cells
  - CYP3A4 inhibitors (strongest erythromycin, clarithromycin) and P-gp inhibitors
    - **Prodrugs** such as **clopidogrel** have dimished therapeutic efficacy
    - Increase in blood levels of drugs such as **warfarin**



Macrolide

Lincosamides

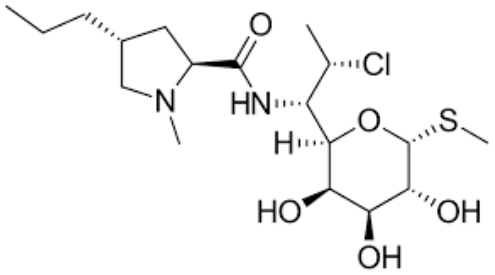
Bacteriostatic

- **clindamycin – administration PO, IM, IV or topical**
  - Spectrum: Gram +
    - MRSA, Streptococcus
    - Clostridium
    - Bacteroides
    - Pepto streptococcus
    - Fusobacterium
    - Actinomyces

Anaerobic coverage – above diaphragm

Important AB in dentistry!

  - **Mechanism of action** – Inhibition of translocation – bind to 50S subunit
  - Treatment of Staphylococcal infections of bones an joints – what's great about **clindamycin** – big penetration to bones and joints
  - Treatment of bacterial conjunctivitis as eye drops
  - Low toxicity but risk of pseudomembranous colitis and worsen Myasthenia Gravis

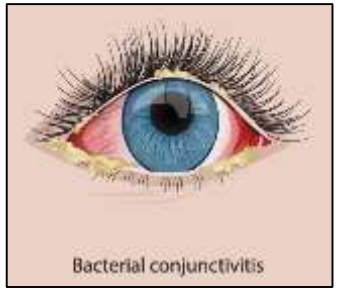


clindamycin

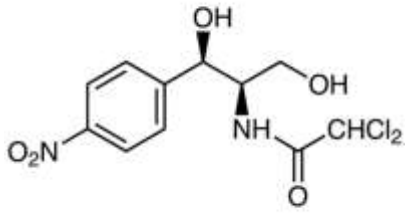
Chloramphenicol

Bacteriostatic

- **chloramphenicol – administration PO, IV, IM, topical**
  - Bacteriostatic
  - - Broad therapeutic index (both Gram + and Gram - and *rickettsiae*)
  - - Good penetration into CNS and abscesses
  - **Mechanism of action** – Inhibition of peptidyl transferase activity (transpeptidation) **– bind to 50S subunit**
  - Liver is the primary organ of inactivation
  - Indication: meningitis, MRSA
    - Reserved for serious infections: Typhoid Fever (Ciprofloxacin and amoxicillin are better options), Haemophilus Influenzae or meningitis (when penicillin cannot be used)
  - History: typhus and paratyphus, severe pneumonia, anaerobic or abdominal infections



Safe use as topical agent for bacterial conjunctivitis



chloramphenicol

Plasma monitoring to avoid grey baby syndrome in newborns!

Most characteristic side effect

Grey baby syndrome

Vomiting, diarrhoea, flaccidity, low temperature and grey colour

Systemic use is reserved for very serious infections due to haematological toxicity!

Bone marrow suppression

Pancytopenia – decrease in all blood cell elements. Aplastic anemia and myelosuppression

Adverse Effects

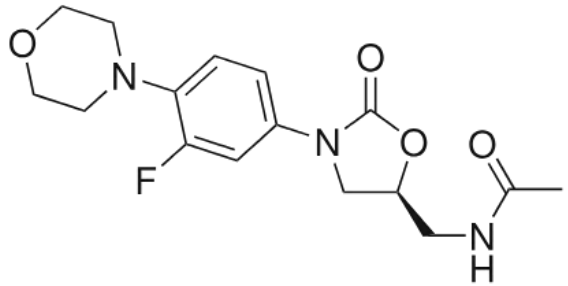
Hypersensitivity

GIT disturbances

Oxazolidinones

Bacteriostatic

- **Linezolid**
  - Spectrum:
    - Gram + (specially MRSA, Vancomycin resistant enterococci)
    - Some anaerobes (like *Clostridium difficile*)
  - **Mechanism of action** – Inhibition of tRNA binding – bind to 50S subunit
  - Last line when everything else did not work!
  - Treatment of Pneumonia, skin and soft tissue infections



linezolid

Most characteristic side effect

Serotoninergic syndrome

Linezolid act as non-selective inhibitor of monoamine oxidase

Thrombocytopenia

Adverse Effects

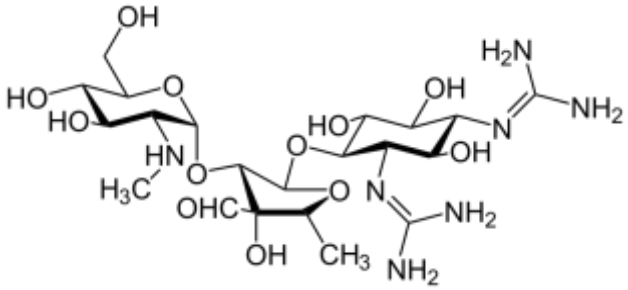
Diarrhea

Nausea

Aminoglycosides

Bactericidal

- **Aminoglycosides**
  - Classic - **streptomycin**, kanamycin, neomycin - administered **IV** **(lack of GIT absorption)**
  - New - **gentamicin**, netilmicin, tobramycin, **amikacin**, isepamicin **-** administered **IV** **(lack of GIT absorption)**
  - **Mechanism of action** – inhibition of protein synthesis – binding to 30S ribosomal subunit (and mRNA misreading)
  - Narrow therapeutic index (mainly against **Gram -,** not much activity against **Gram +**)
    - gentamycin used in *Pseudomonas aeruginosa (***Gram -** Baccili*) + combination with* ***penicillin*** or **vancomycin** – increase in activity
  - Lack of activity and resistance is common (inactivation by microbial enzymes)
  - Low toxicity
  - Cross placental barrier
  - Kidneys are the primary route of excretion (Tubular excretion + Glomerular Filtration)
    - Renal Impairment requires dose adjustment



Aminoglycosid
e

Most characteristic side effect

Neuromuscular Blockade

Rare. If given with neuromuscular-blocking agents

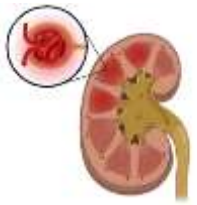
Adverse Effects

Ototoxicity

Destruction of sensory cells in the cochlea and vestibular organ of the ear

Nephrotoxicity

Plasma monitoring to avoid nephrotoxicity!



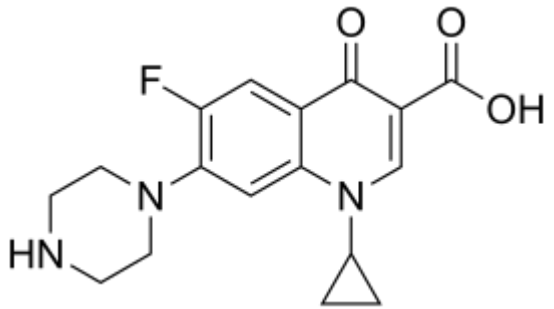
Direct damage of tubules. Specially if combined with nephrotoxic agents such as **vancomycin**

Quinolones

Bactericidal

- **Antimicrobial agents affecting topoisomerase**
- **Broad-spectrum Quinolones – administration IV or PO**
  - **ciprofloxacin**, **levofloxacin**, **ofloxacin**, **norfloxacin**
    - Effective against: less for Gram (+) and more for Gram (-) (HeNS-PEcK coverage except *Neisseria*)
    - **ciprofloxacin** and **levofloxacin** are appropriate against *Pseudomonas Aeruginosa*
    - Mechanism of Action: Inhibition of *topoisomerase II (*inhibition of the introduction of a negative coil*)*
    - Treatment of: Community Acquired Pneumonia, Git infections (with **metronidazole**), UTIs
    - **ciprofloxacin** not be used in MRSA (weak activity and high resistance)
    - **ciprofloxacin** and **norfloxacin** are **CYP450 inhibitors** **(relevant interaction with theophylline - convulsions)**

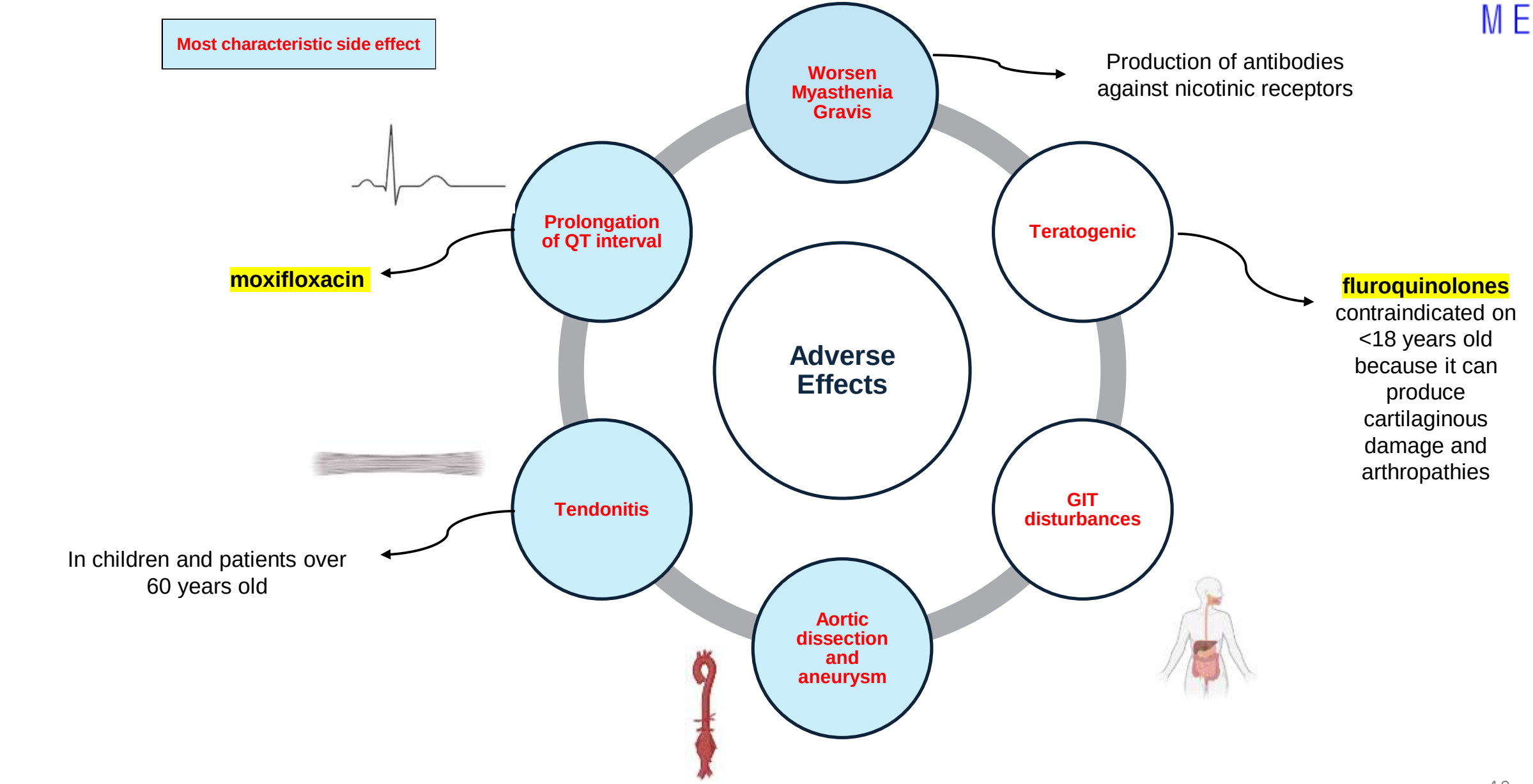
- **Narrow-spectrum Quinolones**
  - **nalidixic acid**
    - Treatment of: UTIs



Ciprofloxacin

Note: Sufix -floxacin indicates a fluroquinolone

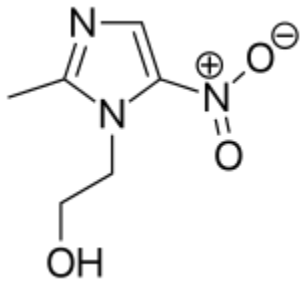
Most characteristic side effect



Metronidazole

Bactericidal

- **Miscellaneous Agent**
  - **metronidazole**
    - Effective against anaerobic bacteria (*Bacteroides*, *Clostridia spp.*)
    - Mechanism of Action: the formation of reactive oxygen species (ROS) causing damage to the DNA, RNA, and/or proteins
    - Treatment of: Infections by anaerobic bacteria **below diaphragm**
    - Typical Disulfiram-like reaction similar to **ceftriaxone**
    - Low incidence of side-effects only diarrhoea

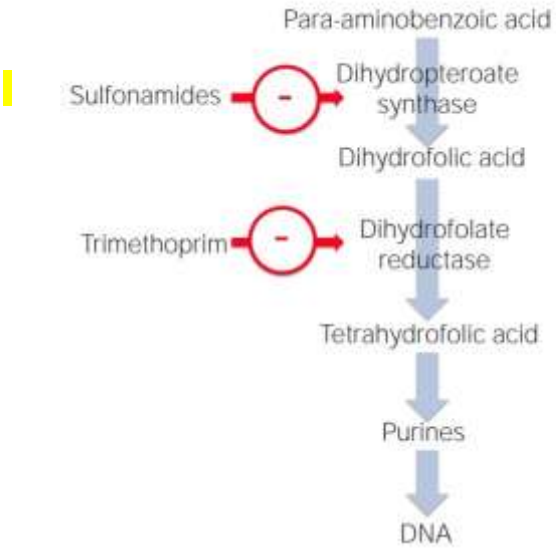


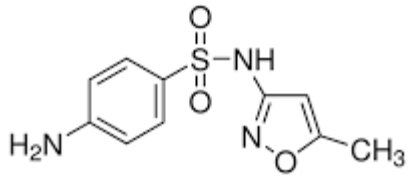
metronidazole

Sulfonamides

Bactericidal

- **sulphamethoxazole in combination with trimethoprim (as cotrimoxazole) – administered orally decreased importance (increased resistance)**
- **sulfasalazine - complex of a sulfonamide (sulfapyridine) and salicylate**
  - Mechanism of Action: Competition with PABA for the enzyme dihydropteroate synthase and inhibition of production of purines that bacteria need
  - Cross placental barrier and BBB.
  - Treatment of Ulcerative Colitis and Crohn's Disease (**sulfasalazine**)





Sulfamethoxazole

Most characteristic side effect

Hypersensivity

Rashes, fever, erythema multiforme

Cyanosis

Caused by methemoglobinemia

Adverse Effects

Renal Crystalluria

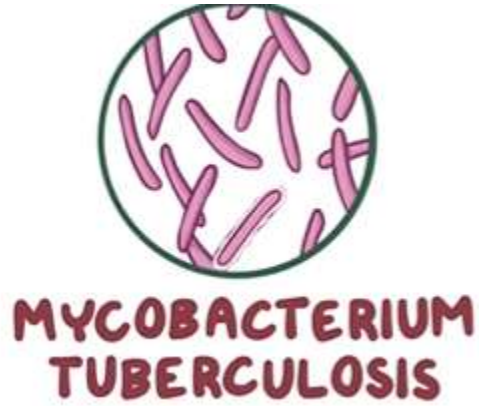
Precipitation of acetylated metabolites in urine

GIT disturbances

Steven-Johnson Syndrome

Antimycobacterial agents

- **Treatment of Tuberculosis and Leprosy**
  - Caused by *M. Tuberculosis* and *M. Leprae*
    - Mycobacteria survive inside macrophages after phagocytosis
    - 1st line drugs: **isoniazid**, **rifampicin**, **rifabutin**, **ethambutol** and **pyrazinamide**
    - 2nd line drugs: **capreomycin**, **cycloserine,** **streptomycin,** **clarithromycin and** **ciprofloxacin**
    - Combination therapy needed → ↓Resistance
      - Initial Treatment phase – 2 months – **isoniazid** + **rifampicin** + **pyrazinamide** and **ethambutol** (if resistance)
      - Continuation phase – 4 months – **isoniazid** + **rifampicin**

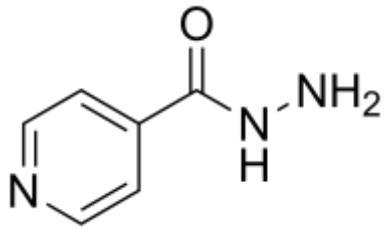


Mycolic Acid makes Mycobacterium hard to kill

Antimycobacterial agents

Bacteriostatic and Bactericidal

- **isoniazid**
  - Limited to treatment of infections by *Mycobacterium*
    - **Administered orally and parenterally**
    - Inhibits growth and replication of Bacteria
    - Passes freely to mammalian cells and is effective against intracellular organisms
    - **Pro-drug**
    - **Mechanism of action: Inhibition of production of Mycolic Acid**
    - **Well absorbed from GIT**
    - Metabolism by acetylation and excretion in urine
    - Short Half-life (T1/2 ≈ 3 hours)



isoniazid

Most characteristic side effect

CNS disturbances

As consequence of Vitamin B6 deficiency. Supplementation is necessary undergoing treatment

Hepatoxicity

Symptoms of hepatitis and jaundice

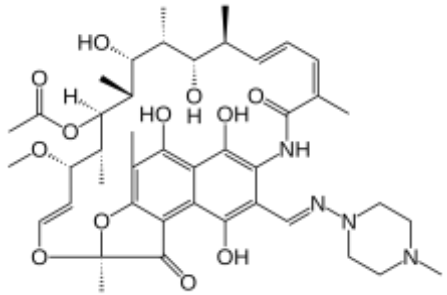
Adverse Effects

Fever

Systemic lupus erythematosus

Antimycobacterial agents

- **rifampicin**
  - Active against procaryotic agents but not eukaryotic. Effective against Leprosy and Tuberculosis
    - **Administered orally**
    - Inhibits growth and replication of Bacteria
    - Passes freely to mammalian cells and is effective against intracellular organisms
    - **Pro-drug**
    - **Mechanism of action: Inhibition of DNA dependent-RNA polymerase**
    - Resistance develops quickly (hence combination with other agents is necessary)
    - Widely distributed to various tissues, body fluids and CSF
    - Excreted in urine and bile
    - Short Half-life (T1/2 ≈ 1-5 hours)
    - Low toxicity



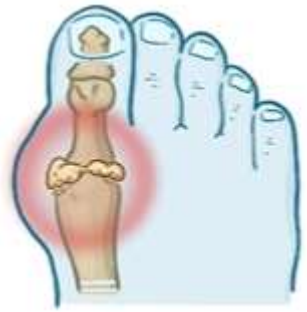
rifampicin

Orange urine characteristic of Rifampicin administration

Inducer of CYP450 - DDI with warfarin, HIV antiretroviral drugs, glucocorticoids, narcotic analgesics

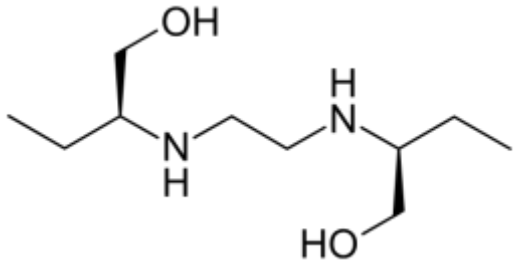
Antimycobacterial agents

- **Ethambutol**
  - Active against Mycobacteria
    - **Administered orally**
    - **Mechanism of action: Inhibition of bacterial cell wall synthesis (blocking arabinosyltransferase, which synthesizes the arabinogalactan)**
    - Passes freely to mammalian cells and is effective against intracellular organisms
    - Resistance develops quickly (hence combination with other agents is necessary)
    - Widely distributed to various tissues, body fluids and CSF
    - Causes **gout** and **optic neuritis** as side effects



Gout

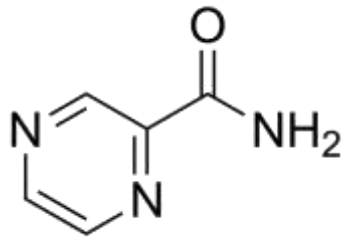
Optic Neuritis



ethambutol

Antimycobacterial agents

- **pyrazinamide**
  - Active at tuberculostatic acid pH
    - **Administered orally**
    - **Mechanism of action: Inhibition of production of Mycolic Acid**
    - Passes freely to mammalian cells and is effective against intracellular organisms
    - Widely distributed to various tissues, body fluids and CSF
    - Pyrazinamide can cause **gout**
    - Other side effects are arthralgias, anorexia, nausea, and vomiting. But the most important is liver damage.



pyrazinamide

Commonly used antibiotics in

Key insights

Increased use of **Aminopenicillins with Beta-Lactamase Inhibitors** and **Lincosamides (clindamycin)**

Decline in **Narrow-Spectrum Penicillins**, **Tetracyclines**, and **Macrolides**

Empirical Use Based on Clinique and Bacteriological Factors

Commonly Used Antibiotics in Pediatric Dentistry: β-lactam antibiotics, macrolides, tetracyclines, clindamycin, and metronidazole

When Are Antibiotics Indicated?

Activity 2

- Acute conditions – Specific situation – Acute periapical abscess
  - Local or systemic spreading of infection in the periodontal abscess

Q: How do we deal with this specific situation? Does it make sense to make use of antibiotics?

A: Depends on the signs!

- If there is **elevated temperature**, evidence of **systemic spread and local lymph node involvement**.
  - **Strong recommendation + moderate quality evidence**

Use of ABs

- Uncomplicated dental acute infections - removal of the cause by **drainage of the associated abscess**, **removal of infected pulp** contents or by **extraction of the tooth**
  - **Strong recommendation + low quality evidence**

Avoiding the use of ABs

Complementary Clinical Advice:

Analgesics – Control of pain and fever + Maintenance of fluid balance + Assessment after 3 days

When Are Antibiotics Indicated?

Activity 2

- Acute conditions – Specific situation – Acute periapical abscess
  - Local or systemic spreading of infection in the periodontal abscess

Q: What antibiotic would I use for this specific situation? What would be the dose and duration of treatment?

A:

1st choice:

- A penicillin (**phenoxymethylpenicillin** or **amoxicillin**)
  - Coverage against most **Gram +** organisms
  - Penicillin V is narrow spectrum while amoxicillin is broader spectrum
  - 500mg orally four times a day for up to 5 days (**Penicillin V**)
  - 500mg orally three times a day for up to 5 days (**Amoxicillin**)

Most infections are resolved in 2-3 days!

ASSESS

2nd choice:

- **Metronidazole**
  - Coverage against anaerobic bacteria (Clostridium, Bacteroides, Pepto streptococcus, Fusobacterium, Actinomyces)
  - When patients are allergic to penicillin
  - If a **predominantly anaerobic infection** is suspected or **microbiologically proven**
  - 400mg orally three times a day for up to 5 days

clarithromycin is a valid 2nd option too

Extra considerations

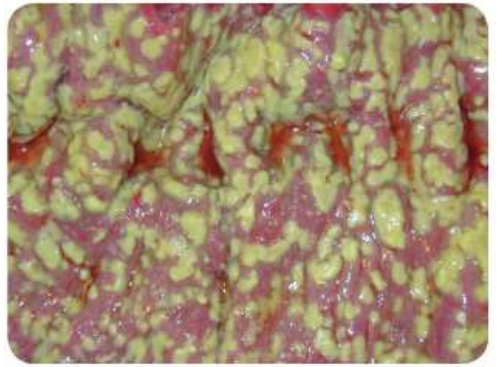
- Acute conditions – Specific situation – Acute periapical abscess
  - **clindamycin** could also be considered for this patient
    - Good option for infections with anaerobes that occur above the diaphragm - Very common seen the prescription of this drug
  - Why should the use be **reconsidered**?

Same efficacy as penicillins but ↑↑ adverse effects

- ↑ Risk of Infection by *Clostridium difficile* - significant morbidity/mortality associated with *Clostridium difficile*

- GIT problems – Diarrhoea ,Vomiting

Pseudomembranous Colitis



When Are Antibiotics Indicated?

Activity 3

- Specific situation – Pericoronitis
  - Without evidence of systemic spread

Q: What antibiotic would I use for this specific situation? What would be the dose and duration of treatment?

A: It is not necessary!

Managed with local measures, such as removal of the cause (extraction or operculectomy), incision and drainage where necessary.

When Are Antibiotics Indicated?

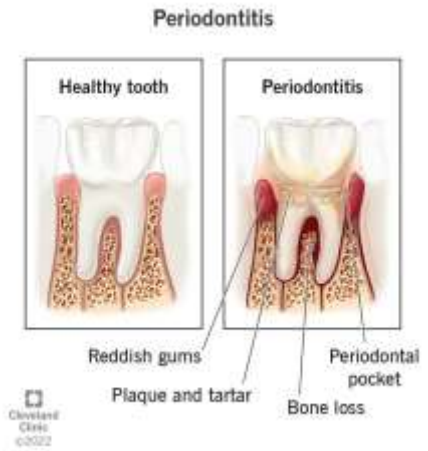
Activity 4

- Acute conditions – Periodontitis - Stage I, II, III; Grade A, B periodontitis
  - The recent reclassification of periodontitis is based on staging (initial [I], moderate [II], severe [III], very severe [IV]) in terms of interproximal bone loss and grading (slow [A], moderate [B], rapid [C]) progression in terms of percentage bone loss compared to patient age

Q: What antibiotic would I use for this specific situation? What would be the dose and duration of treatment?

A: There is no recommendation. Root surface debridement (RSD) combined with good patient oral hygiene. **doxycycline** might be considered for a host modulating agent inhibiting collagenase activity present in periodontitis, however…

The adverse effects outweigh the benefits!



When Are Antibiotics Indicated?

Activity 5

- Prophylaxis – Healthy Patients – Dental implant

Q: What antibiotic would I use for this specific situation? What would be the dose and duration of treatment?

A: Depends if there is bone augmentation or not.

Without: No antimicrobial regimen is recommended.

With: ↑↑↑ risk of having an infectious complication

- 1st choice: **Amoxicillin**
  3000 mg orally 1 hour before surgery
- 2nd choice: **Clindamycin – consider the side effects**
  600mg orally (4x150mg) one hour before surgery

Nausea, Vomiting

The End

Thank you for your attention!