Treatment of Respiratory Tract Infection

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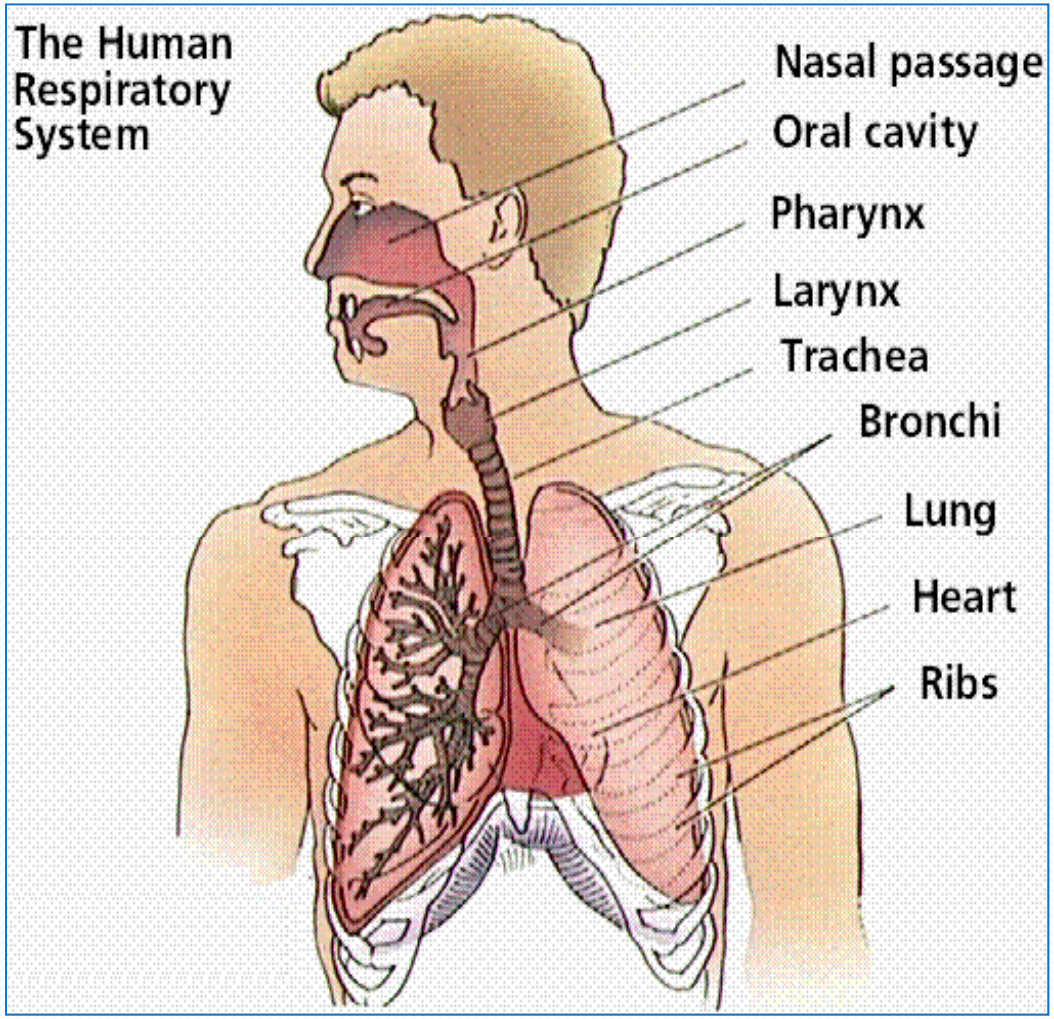
The Respiratory Tract (RT)

Components

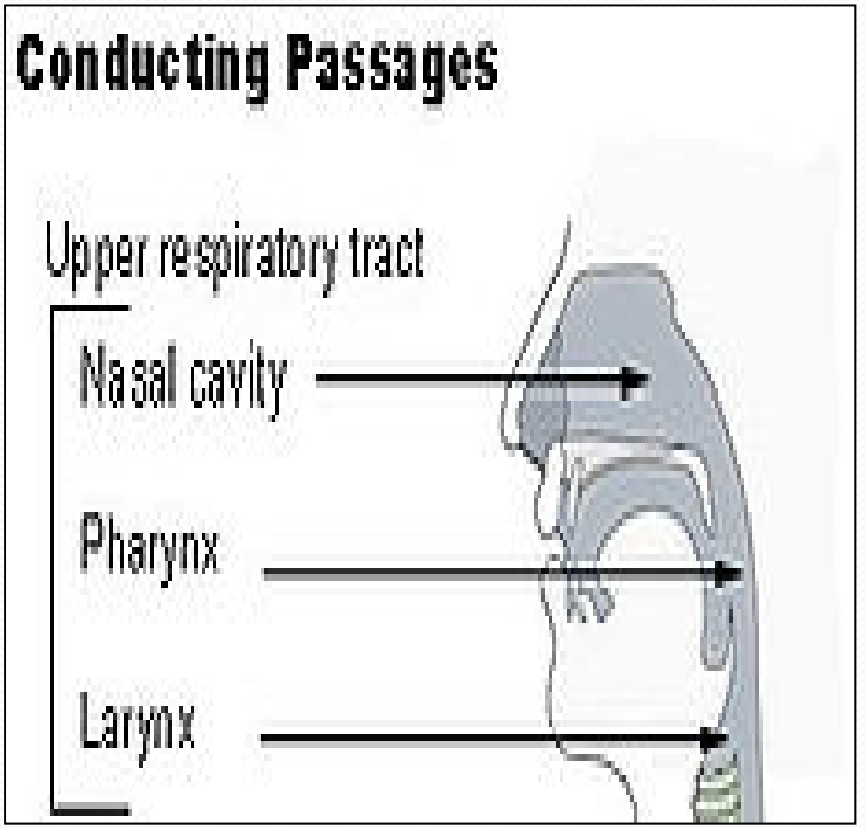
1. Nose
2. Throat
3. Larynx
4. Trachea
5. Bronchi
6. Lungs



The Respiratory Tract (RT)

The upper respiratory tract includes the:

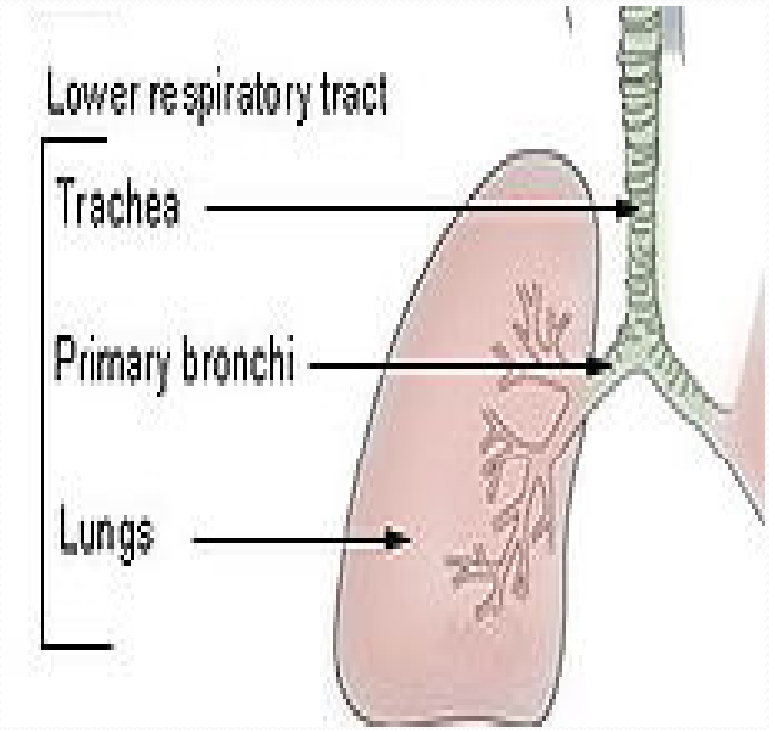
- nose
- nasal cavity
- sinuses
- larynx



The Respiratory Tract (RT)

The lower respiratory tract includes the:

- trachea
- bronchi
- alveoli
- lungs



Classification of respiratory tract infections

- **Upper respiratory tract infections (URTI's)**
- **Lower respiratory tract infections (LRTI's)**

Upper respiratory tract infections (URTIs)

- Usually very common & uncomfortable
- Not life threatening
- Illness caused by an acute infection involves upper respiratory tract (nose, sinuses, pharynx or larynx)
- Cont.....

Common types of URTIs

- **Rhinitis** – inflammation of the nasal mucosa
- **Rhinosinusitis**– inflammation of nares & paranasal sinuses
- **Pharyngitis** - Inflammation of the pharynx, uvula and tonsils
- **Laryngitis** – Inflammation of the larynx
- **Laryngotracheitis**- Inflammation of the larynx and trachea
- **Tracheitis** – Inflammation of the trachea
- **Otitis**- inflammation of middle ear

Lower respiratory tract infections (LRTIs)

- **Lower respiratory tract infections include:**

Bronchitis (acute & chronic)= inflammation of bronchi causing excessive production of mucus & swelling of bronchial walls

Pneumonia (community or hospital acquired) = filling of alveoli with pus & fluid

Lung abscess & emphysema= also included in LRTIs

- **LRTI's are more costly to treat and generally more serious than URTI's**

Causes of Respiratory tract infections

A) Viruses

E.g., Rhinoviruses, corona viruses, adenoviruses etc

B) Bacteria

Common Pathogens of Respiratory Tract Infection

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Mycoplasma pneumoniae*
- *Chlamydophyla pneumoniae*
- *Legionella pneumophila*
- *S.aureus*
- *B.pertussis*
- Gram-negatives / anaerobes

Treatment/Management of Respiratory Tract Infections

A) Non-pharmacological therapy

B) Pharmacological therapy

A) Non-pharmacological therapy

Rest, increased fluid intake, physiotherapy (assistance in respiration in pneumonia)

Cont.....

B) Pharmacological therapy

1) Symptomatic therapy

i) Pain killers or analgesics (for headaches, sore throat & muscle aches)

ii) Nasal decongestant (for common cold)

iii) Bronchodilators (for bronchiolitis & pneumonia to relieve cough)

iv) Steroids (bronchiolitis, pneumonia)

Cont.....

Special therapy for respiratory tract infections

Antibiotics (antimicrobial agents)

Drugs used for treatment & prevention of infections caused by microorganisms (bacteria, viruses, protozoa, fungi, spirochetes etc)

- Antimicrobials derived from living organisms (actinomycetes, fungi & bacteria)

E.g., **penicillin** (antibiotic) ⇒ pencillium (fungus)

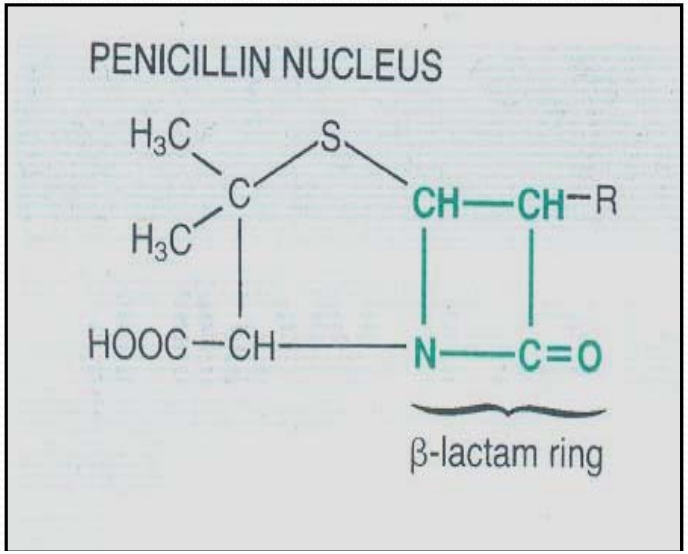
OR they could be Synthetic

Antibiotics commonly used to treat URTI & LRTI

- **Penicillins** (e.g., ampicillin, amoxycillin)
- **Cephalosporins** (e.g., cefuroxime axetil & cefprozil)
- **Fluoroquinolones** (e.g., ciprofloxacin)
- **Aminoglycosides** (e.g., gentamycin + pencillins or cephalosporins)
- **Macrolides** (e.g., azithromycin, clarithromycin)

PENICILLIN

- B-lactam antibiotic; obtained from fungi (*Penicillin notatum*)
- Acts on G+ve & G-ve bacteria (broad spectrum)
- E.g., **Penicillin G** (benzylpenicillin; prototype), Penicillin V, amoxycillin, mathicillin, amoxycillin



Penicillin notatum

Mechanism of action of Penicillin

Bactericidal in action

Interfere bacterial cell wall synthesis by preventing development of cross link in peptidoglycans+ activate autolytic enzymes ➡ death of bacteria

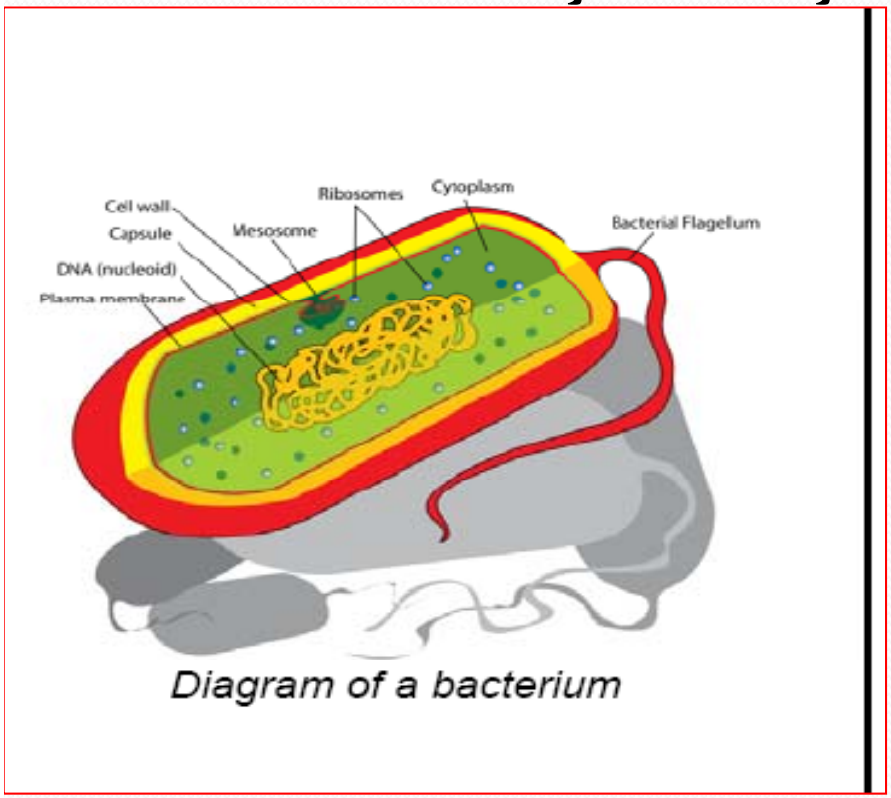
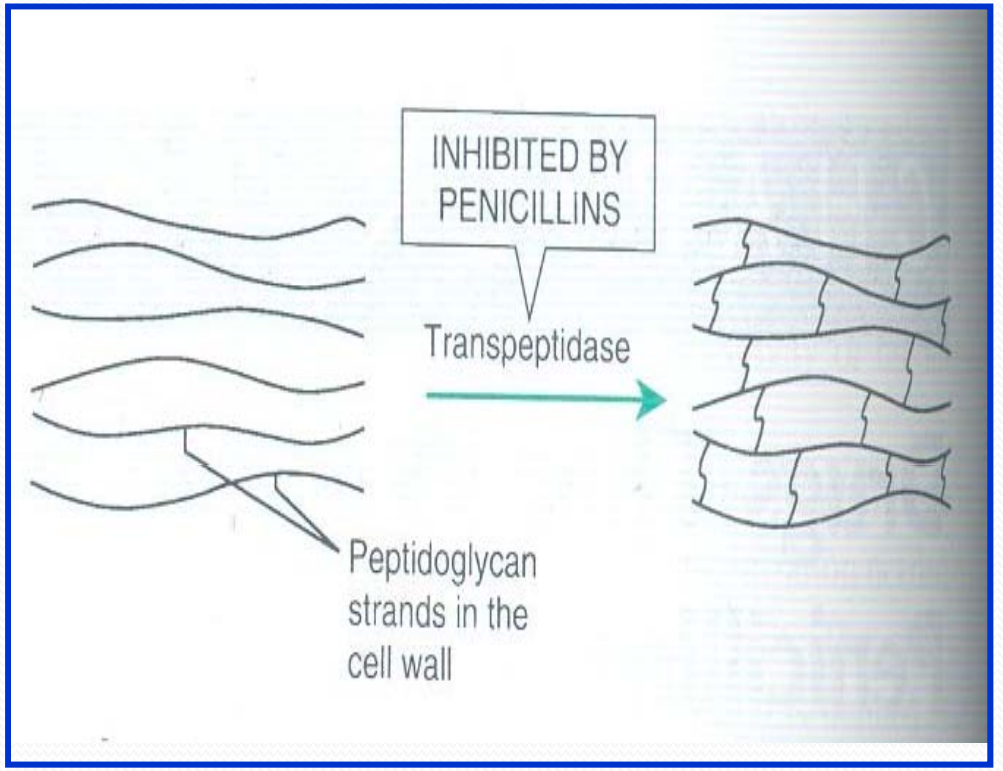


Diagram of a bacterium



Pharmacokinetics of Penicillins

Oral & parenteral (i.m or i.v)

- Absorption varies, affected (↓) by food
- Widely distributed in body fluids
- Not metabolized in human
- Relatively lipid insoluble
- Half-life 30-60 min (increased in renal failure)
- Excreted mainly in urine

Combination of penicillins

Amoxicillin+calvulanic acid (β lactamase inhibitor)= Augmentin

Ticarcillin+calvulanic acid= Timentin

Clinical Uses of Penicillins

- Bacterial meningitis; skin & soft tissue infections
- Bone & joint infections
- Pharyngitis (phenoxylmethylpenicillin)
- Otitis media, bronchitis, UTI, sinusitis, gonorrhea (amoxicillin)
- Syphilis

Adverse Reactions of penicillin

- **Hypersensitivity reactions**: (most common)
  - skin rashes (maculopapular rashes, urticarial rash), fever, bronchospasm, vasculitis, serum sickness, exfoliative dermatitis, Steven Johnson syndrome, and anaphylactic shock.
- **Other adverse reactions**:
  - Bone marrow depression, granulocytopenia, and hepatitis (oxacillin and nafcillin), nausea, with or without vomiting, mild to severe diarrhea (oral)
  - Mild mental confusion, headache, seizures (high dose), superinfections

Cephalosporins

- Broad spectrum; Beta-lactam antibiotics
- Similar to Penicillins (structure & mechanism of actions)
- Prevent synthesis of cell wall + activate autolytic enzymes ⟶ death of bacteria
- Bactericidal
- **Classified into Four generations** =1st, 2nd, 3rd & 4th
  - E.g., Cefuroxime axetil, Ceftazidime, Cefipime

Pharmacokinetics

- Given orally & parenterally (IM & IV)
- Widely distributed
- Relatively lipid insoluble (like penicillins)
- Excreted Mostly unchanged in the urine.
- Half-life 30-90 min (increased in renal failure)

Clinical uses

- Septicaemia
- Pneumonia, meningitis (ceftriaxone)
- Biliary tract infection, gonorrhea
- Urinary tract infection (in pregnancy)
- Sinusitis & otitis media (cefuroxime axetil & cefprozil)

Adverse effects of Cephalosporins

1. **Hypersensitivity reactions- most common**

   Anaphylaxis, bronchspasm, urticaria

   Maculopapular rash- more common

2. **Thrombophlebitis (i.v admin.)**
4. **Superinfections**
5. **Diarrhea-oral cephalosporins**
6. **Nephrotoxicity**

Fluoroquinolones

- Quinolones antibiotics (synthetic & active against G-ve only) with one or more fluorine substitution

E.g., Ciprofloxacin (prototype) & ofloxacin

Antibacterial spectrum

Active = mainly effective against G-ve aerobic bacteria (some G+ve)

Highly active=Salmonella, Shigella, Campylobacter jejuni, E.coli (causing enteritis)

Cont.....

- **Other sensitive** = Pseudomonas aeroginosa. H.influenza, gonococci, meningococci, streptococci

Poor activity = anaerobs

Pharmacokinetics

Well absorbed = i.v., p.o.

Antacids (Ca^{2+}, Mg^{2+}, AL^{3+}; di or trivalent)= inhibit absorption

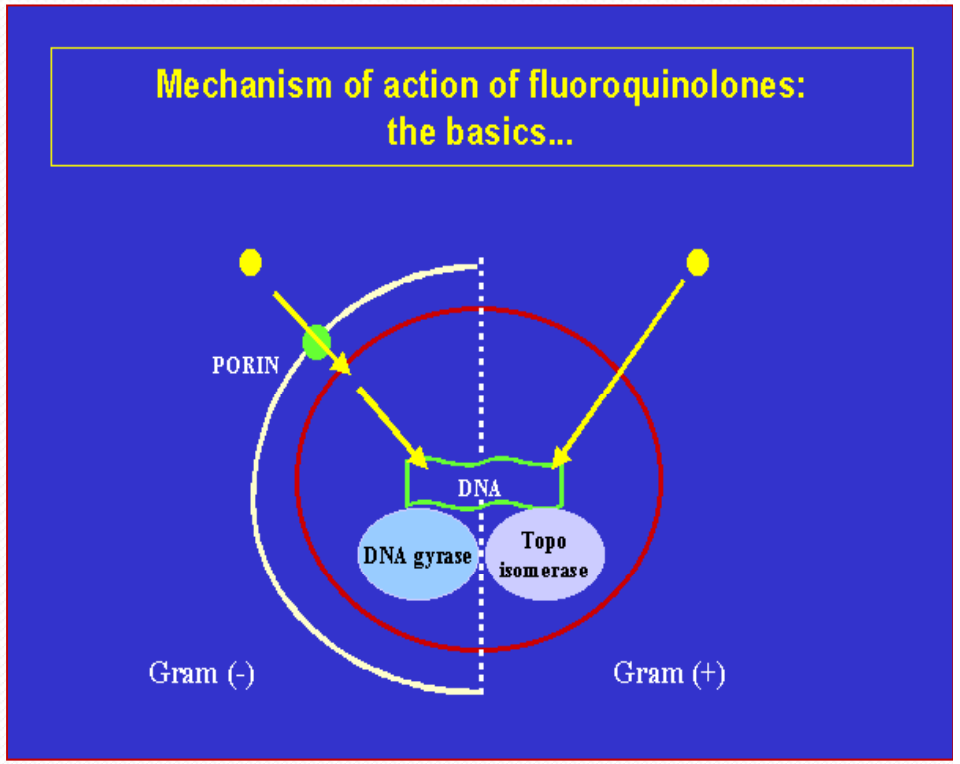
Wide distribution; concentrated in kidney, prostate, neutrophils & macrophages

Plasma ½ life= 3 h (norfloxacin & ciprofloxacin) to 20 h (sparfloxacin)

Elimination=Kidney ; dose adjustment in renal failure (accumulates in renal insufficiency)

MOA of Fluoroquinolones

- Block DNA synthesis by inhibiting bacterial ***topoisomerase II or DNA gyrase*** (G-ve) & ***topoisomerase IV*** (G+ve)
- Prevent division or multiplication of microorgansim



Clinical uses

- Complicated & multidrug resistant UTI (norfloxacin, ofloxacin)
- Genital infections
- Respiratory tract infections (pharyngitis & others), Malignant otitis, prostatitis , gastrointestinal and abdominal infections

Adverse Effects

- Nausea, vomiting & diarrhea, headache, insomnia, dizziness, abnormal liver function & skin rashes; Photosensitivity, prolongation of QT interval + arrhythmias
- Reversible arthropathy in children < 18 y (damage to growing joint cartilage); Tendinitis in adults

Contraindications

- Pregnancy (not safe), children/adolescents (<18), and lactation
- Convulsions with NSAIDs

Aminoglycosides

- Bactericidal; broad spectrum antibiotics
- Mostly used for G-ve aerobic bacteria
- Not effective against G+ & anaerobes
- Carry +ve charges = can not cross memb., not absorbed from GIT
- Inhibit protein synthesis (30 s subunit)

E.g., **Streptomycin** (prototype) ⇒ **oldest**

- *Gentamycin & tobramycin*⇒ **mostly use**

Pharmacokinetics

- Not absorbed from intestine (polycations; carry +ve charges); do not pass into CSF
- IM & IV injections; Plasma ½ life= 2-3 h
- Always used with β-lactam antibiotics = ⇑coverage for G+ve + synergism in b/w aminoglycosides & β -lactam antibiotics
- Excreted unchanged (not metabolized) from kidney by GF; Renal failure= adjust dose

Clinical uses

Endocarditis, infected burns, wounds or skin lesions, meningitis, second line drug in TB, Plague

Adverse Effects

Nephrotoxicity & ototoxicity (common & serious)

Neuromuscular blockade, allergic reaction (rare)

Special problems with AGS use:

Narrow toxic- therapeutic ratio

Monitoring of serum levels

Macrolides

Antibiotics with macrocyclic lactone ring

- Drug of choice & alternative to penicillin (allergic to penicillin)
- Broad spectrum antibiotic
- Bacteriostatic (usually) but Bactericidal at ⇑ conc.
- **Erythromycin** = prototype
- Semi-synthetic=***Clarithromycin*** (methylated) & ***Azithromycin***

MOA=Inhibit protein synthesis by binding to the 50s subunit

Pharmacokinetics

- Orally & parenterally
- Erythromycin destroyed by acid, azithromycin & clarithromycin are more stable
- All three readily diffuse into most tissues but do not cross BBB
- Undergo some hepatic metabolism (inactive)
- Biliary route is the major route of elimination
- Half- life of erythromycin=90 min; clarithromycin=4.5 h
- Azitrhomycin=approx. 3 days

Advantage of azithromycin over erythromycin & clarithromycin

Once daily dosing; No inhibition of cytochrome P- 450

Clinical uses

- Diptheria, corynbacterial sepsis, whooping cough, respiratory tract infection, neonatal, ocular or genital chlamydial infections, (as prophylaxis for endocarditis (dental procedures) with valvular heat disease patients

Adverse Effects

A) GIT = Anorexia, nausea, vomiting & diarrhea

B) Liver toxicity= Main effect (acute cholestatic jaundice)

C) Allergic Reactions= Fever, eosinophilia & skin rash

Drug-Interactions

Erythromycin = inhibit Cyt P450 = ⇑serum conc. = theophylline, carbamazepine, oral anticoagulants, methylprednisolone