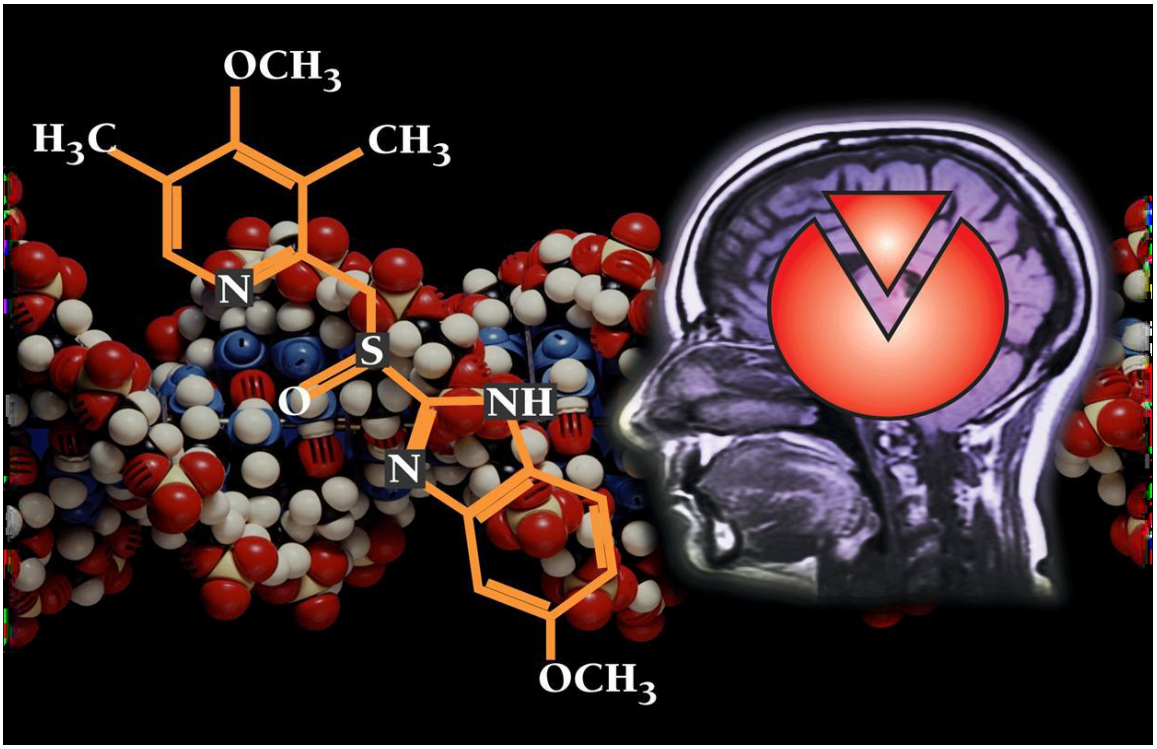
King Saud University
College Of Medicine
Pharmacology Team 430
CNS Block

Meningitis



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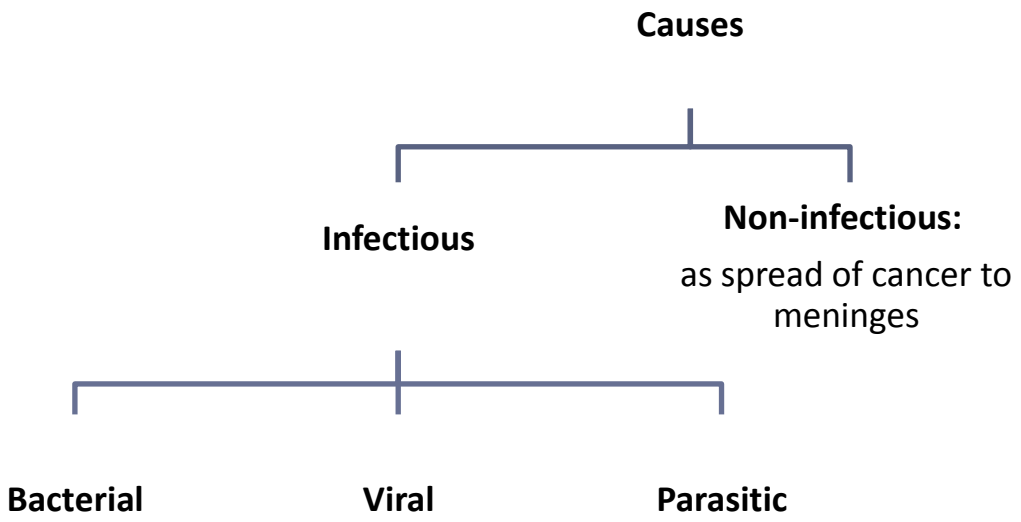
Meningitis:

Is an inflammation of the protective membranes covering the brain and the spinal cord .



Bacterial meningitis: Is a serious, life -threatening disease that is caused by an infection of bacteria.

Microorganisms In BACTERIAL MENINGITIS :

- Neisseria meningitidis
- Haemophilus influenzae
- Streptococcus pneumoniae
- Listeria monocytogenes
- Mycobacterium tuberculosis

Route of transmission :

* The bacteria are carried by humans in the nose and throat and spread into the air by coughing and/ or sneezing. They can be picked by anyone.
* The pathogens spread from the respiratory tract to the blood stream and to the nervous system and cause bacterial meningitis.

Symptoms of bacterial meningitis :

- fever
- headache
- stiff neck
- irritability to light
- nausea & vomiting

Treatment of Meningitis

Treatment Principles:

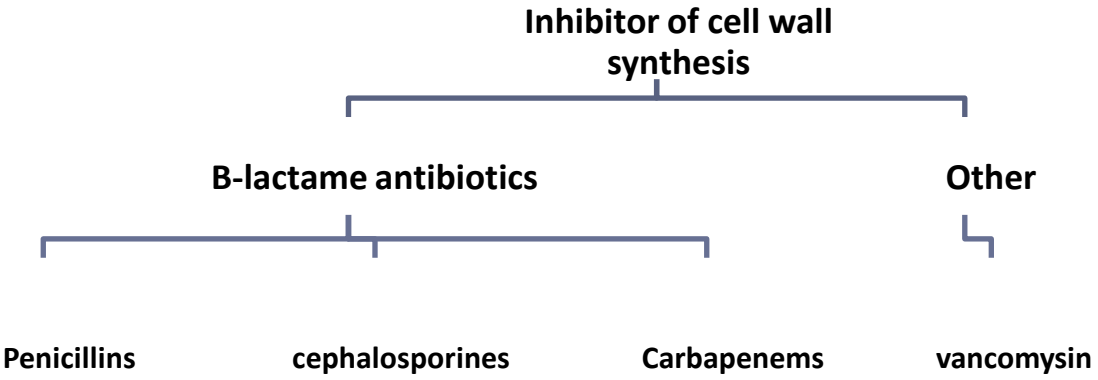
- Emergency hospitalization
- Antibiotics
- Measures for treatment of complications

Empiric antibiotics :

- Treatment without exact diagnosis (antibiotics are given to a person before the specific microorganism causing an infection is known)
- Empiric therapy may be changed after the culture sensitivity reports are available.
- Antibiotic selected must reach the meninges in adequate quantities.
- Regimen chosen must have potent activity against known or suspected pathogens in a particular geographical place.
- Also, it should be a bactericidal antibiotic and can penetrate CNS .

Antibiotics used in meningitis:

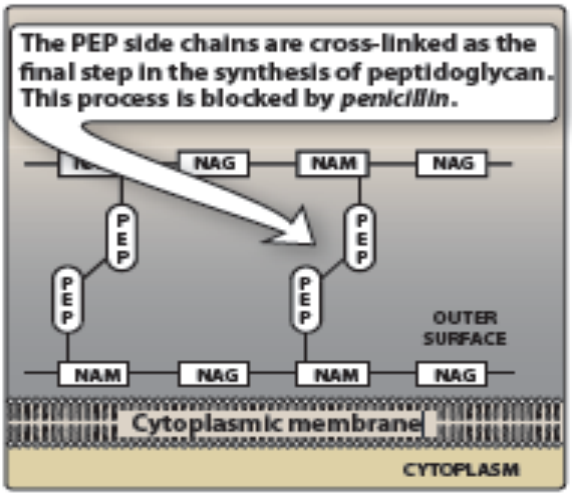
- Inhibitor of cell wall synthesis **:** as diagram bellow
- Inhibitor of DNA synthesis **: fluoroquinolones**



1-Penicillins:

- Bactericidal antibiotics

Mechanism of Action :



- Irreversibly inhibits **transpeptidase enzyme** that catalyze the final step in cell wall synthesis.
- (Inhibits the synthesis of peptidoglycan layer of bacterial cell wall)

A) Extended Spectrum Penicillins

- **Amoxicillin**
- **Ampicillin**

* Active against gram positive & gram negative microorganism.
* Inactivated by β- lactamase enzyme (nowadays they are combined with B-lactamase inhibitors are available e.g Amoxicillin + *Clavulanic acid* (augmentin)and ampicillin + *salbactum*, are more effective against B-lactamase producing pathogens) .
* Amoxicillin and ampicillin are acid stable (effective orally)
* Can also be given parenterally (I.V or I.M) as in case of meningitis
* Amoxicillin is better absorbed from the gut & not affected by food.

Note: Bacteria often develop resistance to β-lactam antibiotics by synthesizing beta-lactamase, an enzyme that attacks the β-lactam ring. To overcome this resistance, β-lactam antibiotics are often given with B-lactamase inhibitors such as Clavulanic acid.

B) Narrow Spectrum Penicillin

Penicillin G :

- Narrow spectrum
- Destroyed by gastric acidity (so it is given parentally)
- **Inactivated by β- lactamase**
- Short acting (4-6 hrs)

Adverse effects of penicillins :

- Hypersensitivity : ranging from maculopapular rash (the most common rash seen with ampicillin hypersensitivity) to angioedema and anaphylaxis ,
- Diarrhea (this gastric effect seen especially with amoxicillin)
- Nephritis
- Neurotoxicity seen with high doses or with renal faliure

2-Cephalosporins : 3rd generation : Ceftriaxone + Ceftazidime

- Bactericidal Antibiotics

- Both of them are given by intravenous infusion or injection

Mechanism of action: Inhibits bacterial cell wall synthesis

Bacterial Spectrum of 3rd Generation Cephalosporins:

- Highly effective against Gm –ve bacilli
- Anaerobic microbes
- Pseudomonas
- Highly resistant to β- lactamase

- Effective in Gm-ve meningitis

Adverse effects :

- Allergy
- Thrombophlebitis (because it is given intravenously)
- Renal toxicity
- Superinfections (infection by normal flora as diarrhea and ulcer)

3-Carbapenems : Imipenem

- Bctericidal, inhibit bacterial cell wall synthesis.
- Has a wide spectrum of activity
- Resistant to most β lactamases except metallo-β lactamase .
- *Pharmacokinetics*
- Not absorbed orally, taken by I.V.I.
- **Inactivated** by dehydropeptidases in renal tubules, so it is given with an inhibitor **cilastatin** for clinical use.
- Penetrates body tissues and fluids including C.S.F.

Note: Dehydropeptidases is an enzyme in our body in the renal tubules. This enzyme can destroy (**Imipenem),** so we give **cilastatin** to inhibit the enzyme which is Dehydropeptidases

Adverse effects:

- Nausea, vomiting, diarrhea
- Skin rash and reaction at the site of infusion
- High doses in patients with renal failure may lead to seizures (Neurotoxicity)
- ***Patients allergic to penicillins may be allergic to carbapenems .*** (cross-allergy)

Other inhibitor of cell wall synthesis

Vancomycin :

- Bactericidal
- Cell wall inhibitor
- Poorly absorbed orally
- Used orally to treat GIT infections caused by clostridium defficile e.g colitis.
- Given intravenously
- **Active only against Gm+ve bacteria**
- Used in combination with 3rd generation cephalosporins for treatment of meningitis caused by penicillin resistant pneumococci.
- Good drugs used against Methicillin resistant S. aureus (MRSA).
- May be combined with ampicillin or ceftazidime as an initial therapy of meningitis in infant, elderly and immunocompromised patients .

Adverse Effects :

(vancomycin is a toxic drug , use only when the infection is resistant to other safer drugs)

- Phlebitis
- Ototoxicity } Toxicity increase with aminoglycosides
- Nephrotoxicity
- Histamine release [red man (red neck) syndrome] (flushing and hypotension), minimized if injected slowly.
- Hypotension

Fluoroquinolones : . e.g: Ciprofloxacin

- Bactericidal drugs

Mechanism of action :

Block bacterial DNA synthesis by inhibiting:

- bacterial *topoisomerase 11(DNA gyrase*)
- *topoisomerase1V*

Bacterial Spectrum :

- Effective against : Gm-ve organisms
- Limited activity : against Gm+ve organisms
- Effective against :intracellular pathogens such as: Legionella, Chlamydia, some mycobacteriae

Pharmacokinetics

- Well absorbed orally
- Absorption is impaired by divalent cations ; iron, zinc or those in antacids as aluminium, magnesium
- Half-life 3hrs
- Widely distributed in body fluids & tissues
- Penetrates into CSF
- **Highly concentrated in bone, kidney, prostate, lung (so it is effective in case of osteomyelitis, nephritis, prostatitis, and pneumonia)**
- Excreted through kidney & **appear in breast milk**

Adverse effects

- GIT upset
- CNS : Headache , dizziness, insomnia
- Abnormal liver function tests

- Skin rash & photosensitivity
- **Cartilage damage (arthropathy)**
- Tendon damage (tendinitis)
- Enzyme inhibitor

Contraindications

- **Growing children (below 18 years)**
- Pregnancy
- Lactation
- History of epilepsy or CNS disorder

Prevention better than cure

- Haemophilus influenzae type b (**Hib)** bacterium, a leading **cause of bacterial meningitis in children**.
- **New Hib vaccines** — available as part of the routine childhood immunization schedule have greatly reduced cases of this type of meningitis.
- **Pneumococcal polysaccharide vaccine (PPSV) for older children and adults**
- **Meningococcal conjugate vaccine , also a requirement for people going to Hajj.**