DRUGS USED IN MENINGITIS

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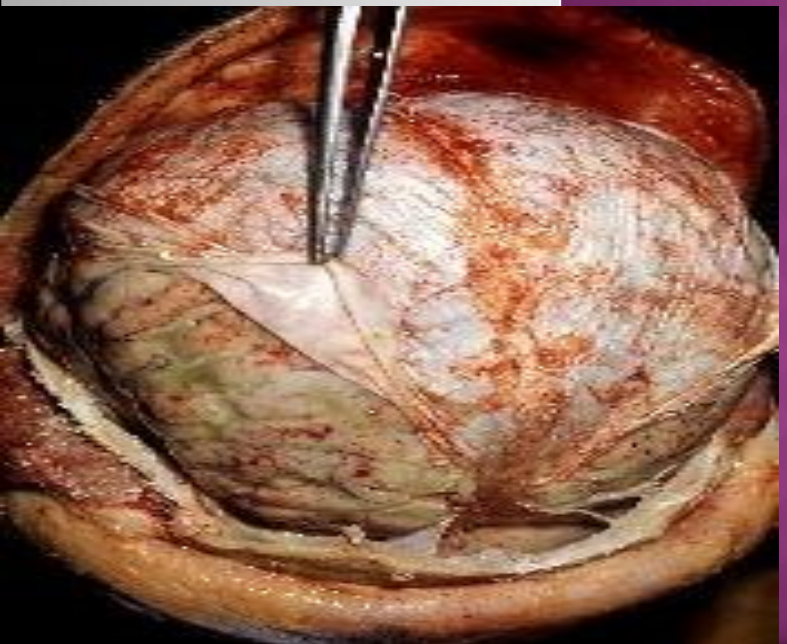


OBJECTIVES

At the end of the lecture, students should be able to:

- Describe briefly common types of meningitis
- Describe the principles of treatment
- List the name of antibiotics used for treatment of meningitis
- Describe the mechanism of action & adverse effects of the individual drugs

DEFINITION

Meningitis is an inflammation of the protective membranes covering the **brain** and the **spinal cord** (meninges).

CAUSES

Infectious

- **Viruses**
- **Bacteria**
- **Fungi**

Non-infectious

e.g. spread of cancer to meninges (malignant meningitis),etc.

BACTERIAL MENINGITIS

- Is a serious, life threatening disease.
- May lead to serious long-term consequences, e.g.:
  - Deafness
  - Epilepsy
  - Hydrocephalus
  - Cognitive deficits.

CAUSES OF BACTERIAL MENINGITIS

- ***Neisseria meningitidis*****
- ***Streptococcus pneumoniae*****
- ***Haemophilus influenzae***
- ***Staphylococcus aureus***
- ***Pseudomonas aeruginosae***
- ***Listeria monocytogenes***
- ***Mycobacterium tuberculosis*** **(tuberculous meningitis)**

ROUTE OF TRANSMISSION

- The bacteria are carried by humans in the nose and throat and spread by coughing and/or sneezing, kissing, sharing eating utensils.

- The pathogens spread from the respiratory tract to the blood stream**(septicemia)** and to the nervous system and cause **bacterial meningitis** .

SYMPTOMS OF BACTRIAL MENINGITIS

- **High fever**
- **Severe headache**
- **Stiff neck**
- **Irritability**
- **Seizures**
- **Vomiting**

TREATMENT PRINCIPLES

- **Emergency hospitalization**
- **Antibiotics**
- **Measures for treatment of complications**

ANTIBIOTICS

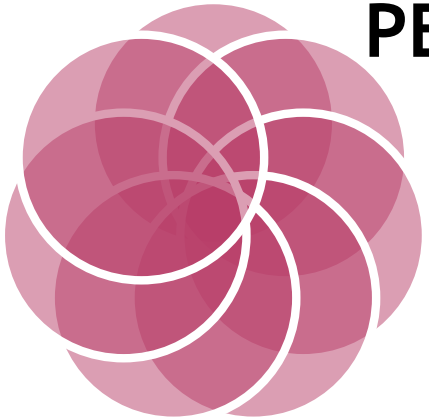
- **Antibiotic selected must penetrate adequately into the CSF.**

- **Regimen chosen must have potent activity against known or suspected pathogens & exert a bactericidal effect.(Empiric?)**

ANTIBIOTICS FOR TREATMENT OF BACTERIAL MENINGITIS

INHIBITORS OF CELL WALL SYNTHESIS (B-LACTAMS)

PENICILLINS



Carbapenems

CEPHALOSPORINS

PENICILLINS

Mechanism of action:

Inhibit bacterial cell wall synthesis by inhibiting the peptidoglycan layer of bacterial cell wall **(bactericidal)**.

NARROW SPECTRUM PENICILLIN

Penicillin G (benzyl penicillin)

- **Narrow spectrum of activity**
- **Destroyed by gastric acidity**
- **Has poor oral absorption.**
- **Given by intravenous infusion**
- **β- lactamase sensitive (penicillinase sensitive)**
- **Short acting (4-6 hrs)**
- **Half- life 30-60 min.**

EXTENDED SPECTRUM PENICILLINS AMINOPENICILLINS

- Amoxicillin
- Ampicillin

EXTENDED SPECTRUM PENICILLINS AMINOPENICILLINS

- **Broad spectrum of activity than penicillin G**
- **Active against gram positive & gram negative microorganism.**
- **Not active against pseudomonas aeruginosa.**
- **Amoxicillin and ampicillin are acid stable (effective orally).**
- **Can also be given parenterally (I.V or I.M)**
- **Amoxicillin is better absorbed from the gut & not affected by food.**

EXTENDED SPECTRUM PENICILLINS AMINOPENICILLINS

- **Inactivated by β-lactamase enzyme**
- **combination with β-lactamase inhibitors are available**
  - **e.g. Amoxicillin + Clavulanic acid (orally)**
  - **e.g. Ampicillin + sulbactum (injection)**
- **This combination is intended to:**
  - Prevent enzymatic hydrolysis by β-lactamase
  - Extend antimicrobial activity.

ADVERSE EFFECTS

- Hypersensitivity reactions (Anaphylactic reactions)
- Antibiotic-associated diarrhea.
- Super-infections or secondary infections (candidiasis, oral thrush).
- Nephritis
- High dose in renal failure (seizure).

CEPHALOSPORINS

- **3rd generation Cephalosporins**
  - **Ceftazidime**
  - **Ceftriaxone**

- **Both of them are given by intravenous infusion**

MECHANISM OF ACTION

- **Inhibit bacterial cell wall synthesis**
- **Bactericidal**

BACTERIAL SPECTRUM OF 3RD GENERATION CEPHALOSPORINS

- **Highly effective against Gm –ve bacilli**
- **Against Pseudomonas (ceftazidime)**
- **Highly resistant to *β- lactamases.***

ADVERSE EFFECTS

- Allergy
- Thrombophlebitis at site of injection
- Renal toxicity
- Super-infection
- GIT Upset & diarrhea

CARBAPENEMS

Imipenem

- Inhibits bacterial cell wall synthesis **(bactericidal).**
- Has a wide spectrum of activity (aerobic & anaerobic gram negative and gram positive bacteria, including pseudomonads)
- Resistant to most **β-lactamases**

PHARMACOKINETICS

- Not absorbed orally, **given by I.V route**.
- Inactivated by **dehydropeptidase** in renal tubules to a nephrotoxic metabolites, so it is given with a dehydropeptidase inhibitor drug for clinical use (**Imipenem/cilastatin).**
- Penetrates body tissues and fluids including C.S.F.
- Excreted primarily by the kidney.
- Doses must be reduced in renal failure.
- Half- life about 1 hr.

ADVERSE EFFECTS

- Nausea, vomiting, diarrhea
- Skin rash and reaction at the site of infusion
- High doses may **cause seizure** in patients with renal failure
- Patients allergic to penicillins may be allergic to carbapenems .

OTHER CELL WALL SYNTHESIS INHIBITORS

VANCOMYCIN

VANCOMYCIN

- Bactericidal
- Cell wall inhibitor
- Poorly absorbed orally
- Used orally to treat GIT infections caused by clostridium difficile e.g. pseudomembranou colitis.
- Given intravenously for the treatment of meningitis

VANCOMYCIN

- **Active only against Gm+ve bacteria**
- **Used against Methicillin resistant S. aureus (MRSA).**
- **Used in combination with 3rd generation cephalosporins for treatment of meningitis caused by penicillin resistant pneumococci.**
- **May be combined with ampicillin or ceftazidime as an initial therapy of meningitis in infant, elderly and immunocompromised patients .**

ADVERSE EFFECTS

- **Phlebitis at site of injection**
- **Ototoxicity**
- **Nephrotoxicity**
- **Histamine release due to nonspecific mast cell degranulation leading to:**
  - **"Red man syndrome" or "red neck syndrome"**
  - **Hypotension (minimized if injected slowly over 60 minutes).**

AMINOGLYCOSIDES

e.g. Gentamicin,i.v.

Antibacterial Spectrum

Bactericidal (exclusive for **aerobic G-bacteria**).

Mechanism of action

Inhibit protein synthesis (30s subunit)

ADVERSE EFFECTS OF GENTAMICIN

Ototoxicity & nephrotoxicity
(directly related to serum conc.)
Neuromuscular blockade (very high dose)

PREVENTION BETTER THAN CURE

- Haemophilus influenzae type b **(Hib)** bacterium, is a leading **cause of bacterial meningitis in children.**

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(protects against meningitis caused by S.pneumonia)**
- **Meningococcal conjugate vaccine, used for people going to Hajj(protects against meningitis caused by N. meningitides)**