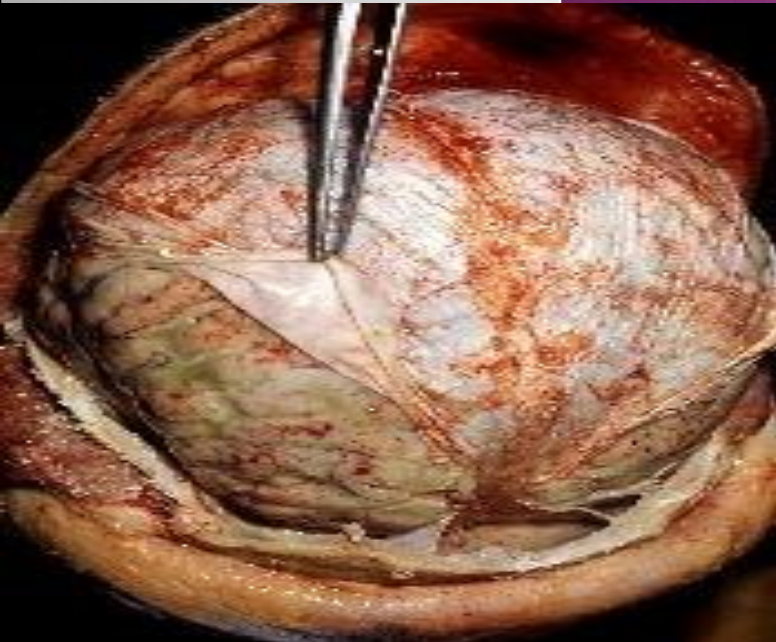


DRUGS USED IN MENINGITIS

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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
 - Limb loss
 - 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 BACTERIAL MENINGITIS

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

TREATMENT PRINCIPLES

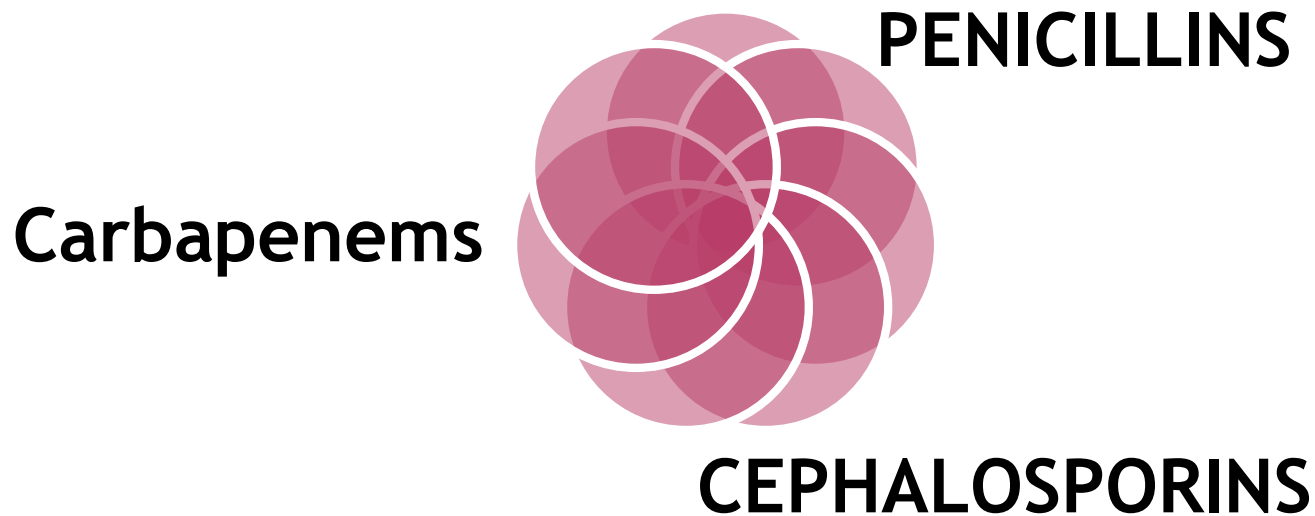
- ⦿ **Emergency hospitalization**
- ⦿ **Antibiotics**
- ⦿ **Measures for treatment of complications**

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

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 + sulbactam (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
- ⦿ Seizure(high dose in renal failure).

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/cilastatin

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 (**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
- ◉ Inhibit Cell wall synthesis
- ◉ Poorly absorbed orally
- ◉ Used orally to treat GIT infections caused by clostridium difficile e.g. pseudomembranous 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.**

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

- ◉ **Hib vaccines**(protects against meningitis caused by *Haemophilus influenzae* type b (Hib) bacterium)
- ◉ **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*)