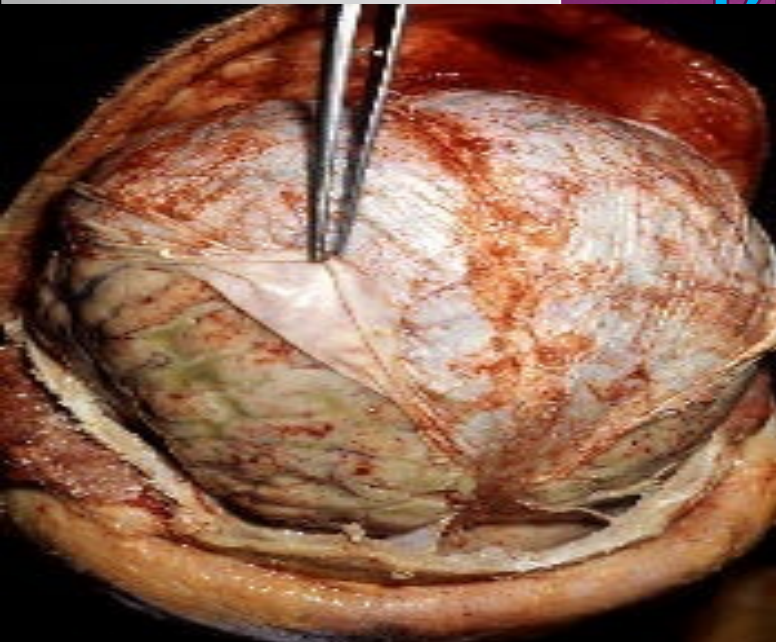


DRUGS USED IN MENINGITIS

DR. ALIAH ALSHANWANI



OBJECTIVES

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

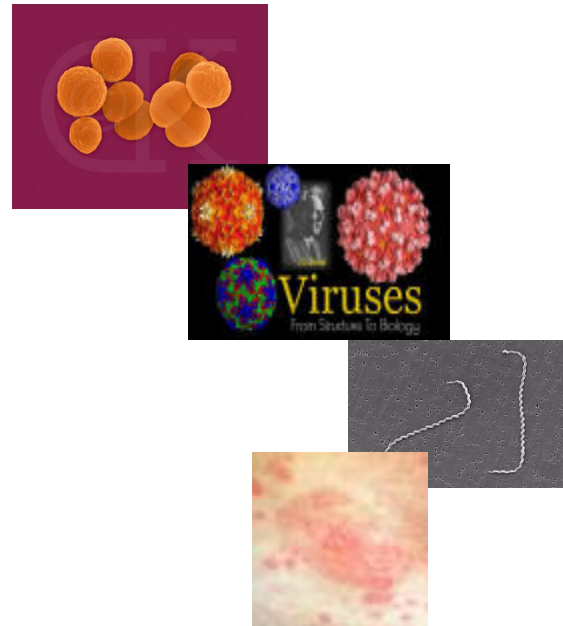
- ◉ Describe briefly common types of meningitis
- ◉ Describe the principles of treatment
- ◉ List the name of antibiotics used for the treatment of meningitis
- ◉ Describe the mechanism of action & adverse effects of the individual drugs.

DEFINITION

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

CAUSES OF MENINGITIS

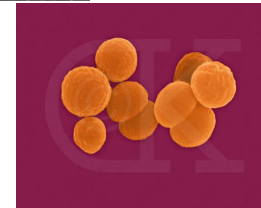
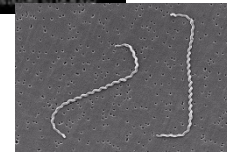
- Bacterial Infections
- Viral Infections
- Fungal Infections
(*Cryptococcus neoformans*
Coccidioides immitus)
- Inflammatory diseases (*SLE*)
- Cancer
- Trauma to head or spine.



CAUSES OF MENINGITIS

Infectious

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



Non-infectious

- **Cancer (malignant meningitis)**
- **Inflammatory diseases (SLE)**
- **Trauma to head or spine**

WHAT ARE CAUSES OF BACTERIAL MENINGITIS?

Bacterial meningitis is caused by several different types of bacteria, including:

- ◉ *Streptococcus pneumoniae* ** (Pneumococcal)
- ◉ *Neisseria meningitidis* ** (Meningococcal)
- ◉ *Haemophilus influenzae*, also called Hib
- ◉ *Pseudomonas aeruginosae*
- ◉ *Staphylococcus aureus*
- ◉ *Listeria monocytogenes*
- ◉ *Mycobacterium tuberculosis* (*tuberculous*)

ROUTE OF TRANSMISSION

Most bacteria that cause this form of infection are spread through close personal contact, such as:

- ⦿ coughing
- ⦿ sneezing
- ⦿ Kissing
- ⦿ Infection occurs when the pathogens spread from the respiratory tract to the blood stream and to the nervous system and cause **bacterial meningitis** .

SYMPTOMS OF BACTERIAL MENINGITIS

- ◉ **High fever**
- ◉ acute onset of severe **headache**
- ◉ **Stiff neck**
- ◉ **Nausea**
- ◉ **Vomiting**
- ◉ **Photophobia Sensitivity to bright light**
- ◉ **Confusion**
- ◉ **a rash of purple discoloration.**

TREATMENT PRINCIPLES

- ⊙ Meningitis, caused by a bacteria, is life threatening and requires urgent medical attention & treatment with antibiotics
- ⊙ **Emergency hospitalization**
- ⊙ **Antibiotics**
- ⊙ **Measures for treatment of complications.**

BACTERIAL MENINGITIS

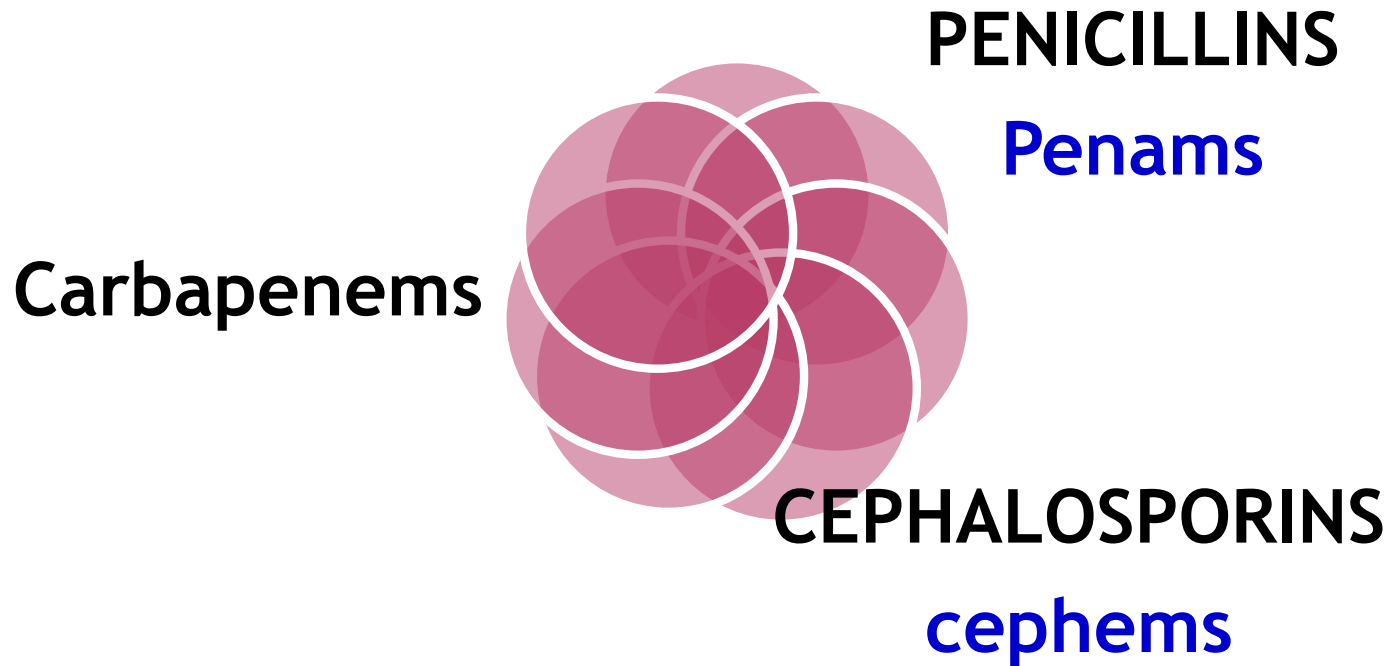
- **Is a serious, life threatening disease.**
- **Without treatment, bacterial meningitis can cause serious consequences**
 - Cognitive deficits
 - Deafness
 - Hydrocephalus
 - paralysis
 - stroke, seizures, sepsis, and even death.

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?**)**

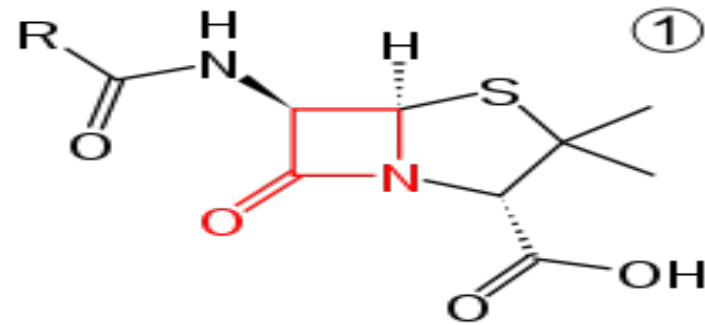
ANTIBIOTICS FOR TREATMENT OF BACTERIAL MENINGITIS

INHIBITORS OF CELL WALL SYNTHESIS (B-LACTAMS)

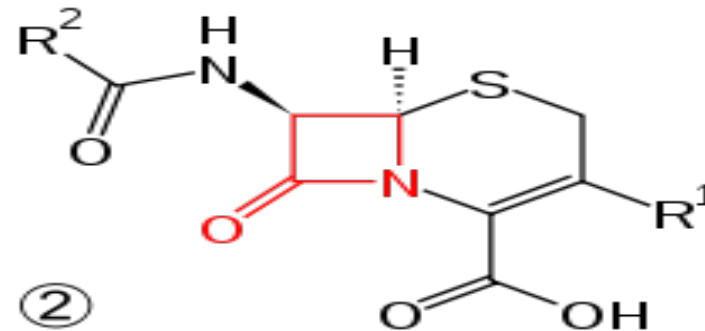


B-LACTAM ANTIBIOTICS

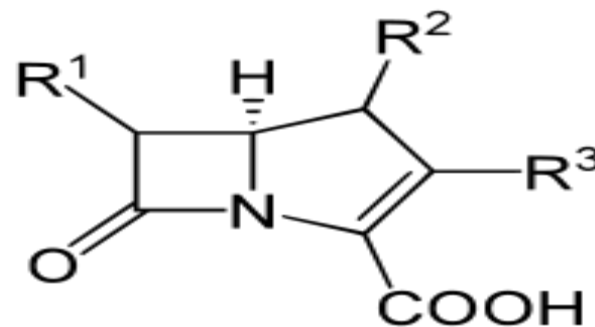
1) PENICILLINS



2) CEPHALOSPORINS



3) Carbapenems



PENICILLINS

Mechanism of action:

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

NARROW SPECTRUM PENICILLIN

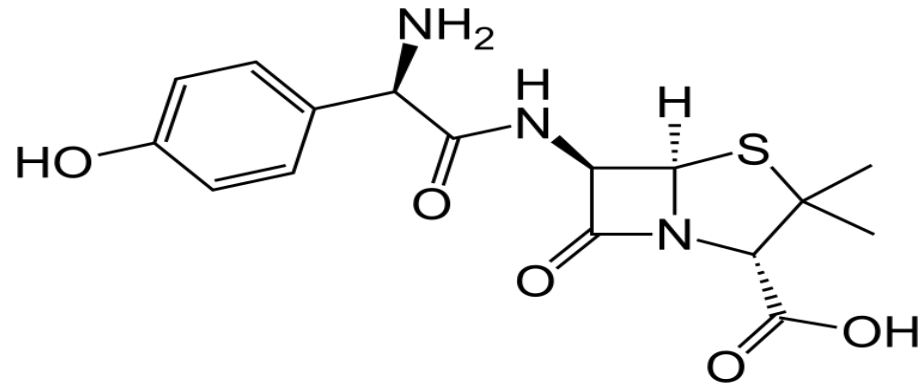
Penicillin G (benzyl penicillin)

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

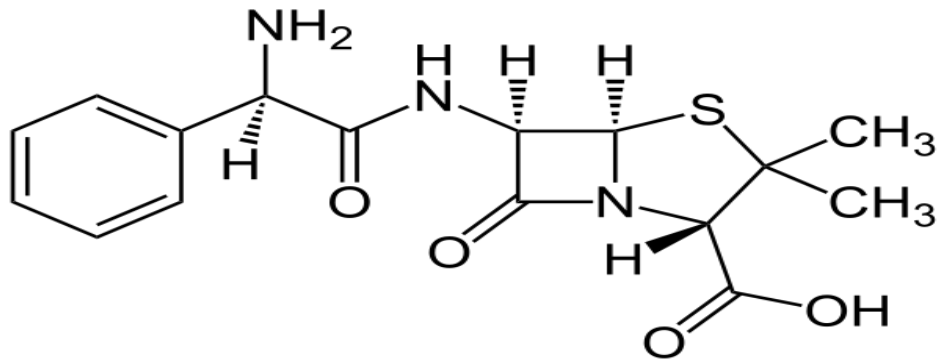
EXTENDED SPECTRUM PENICILLINS

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 & 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
 - e.g. Ampicillin + Sulbactam
- ⊙ **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

- **Cefotaxime**
 - **Ceftriaxone**
 - **Ceftazidime**
-
- **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.**
- ⊙ **Used for treatment of bacterial meningitis caused by pneumococci, meningococci, & Haemophilus influenzae.**

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 & gram positive bacteria, including pseudomonads)
- ⦿ Resistant to most β -lactamases.

PHARMACOKINETICS

- ⊙ Not absorbed orally, **taken by I.V.**
- ⊙ Penetrates body tissues & fluids including CSF
- ⊙ Excreted primarily by the kidney
- ⊙ Doses must be reduced in renal failure
- ⊙ Half- life about 1 hr.

- It should be used in combination with cilastatin? **Why?**

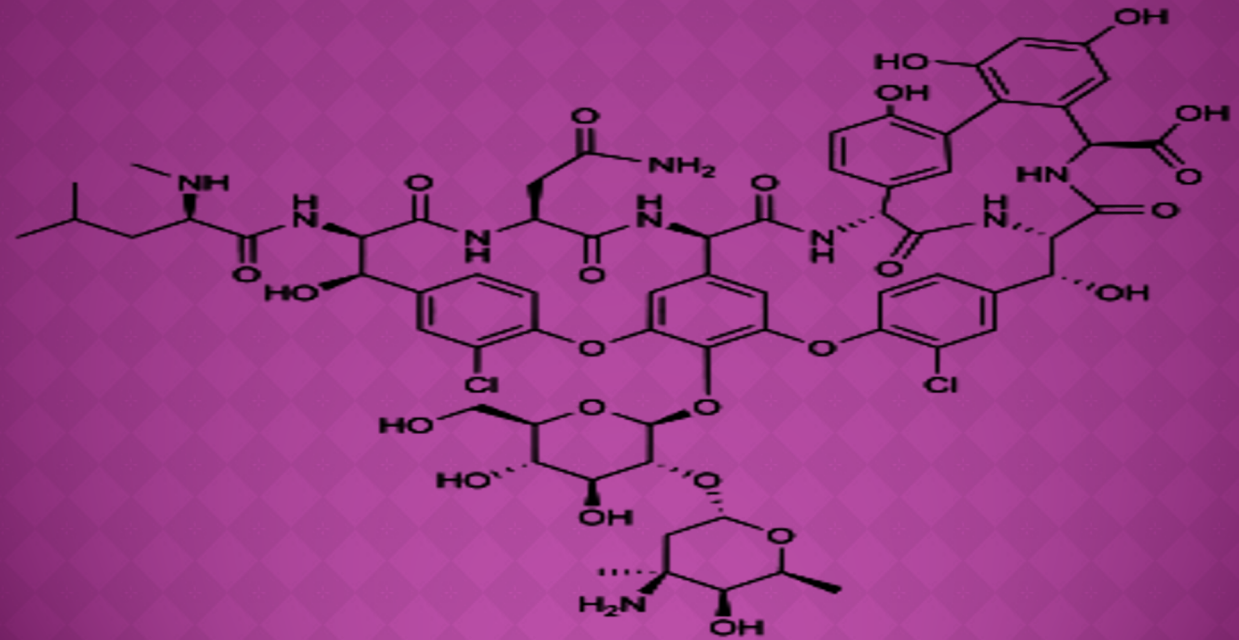
Inactivated by **dehydropeptidase** in renal tubules to a less active & **nephrotoxic metabolite**, so it is co-formulated with the **dehydropeptidase inhibitor** cilastatin for clinical use (Imipenem/cilastatin).

ADVERSE EFFECTS

- ⊙ Nausea, vomiting, diarrhea
- ⊙ Skin rash & 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 synthesis inhibitor**
- ◉ **Poorly absorbed orally**
- ◉ **Used orally to treat GIT infections caused by clostridium difficile associated 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 & immunocompromised patients.**

ADVERSE EFFECTS

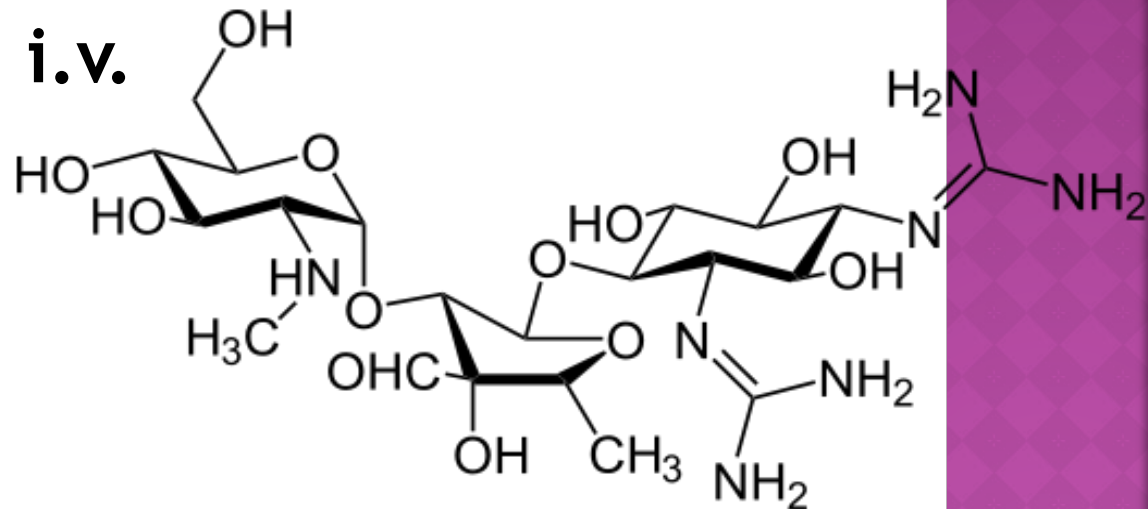
- ⊙ **Phlebitis at site of injection**
- ⊙ **Ototoxicity**
- ⊙ **Nephrotoxicity**
- ⊙ **Histamine release due to nonspecific mast cell degranulation leading to:**
 - **“Red man syndrome” or “red neck syndrome”**
 - **Hypotension (minimized if injected slowly over 60 minutes).**

AMINOGLYCOSIDES

Gentamicin

Mechanism of action

- Inhibit protein synthesis (30s subunit).
- Bactericidal.
- Not absorbed orally
- Given by injection i.v.



ADVERSE EFFECTS OF GENTAMICIN

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



The End