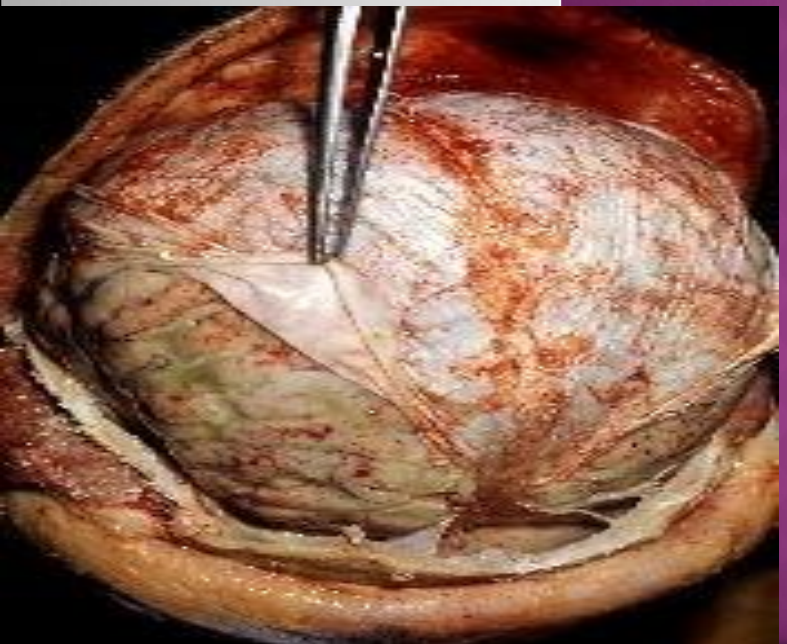
DRUGS USED IN MENINGITIS

PROF. HANAN HAGAR



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

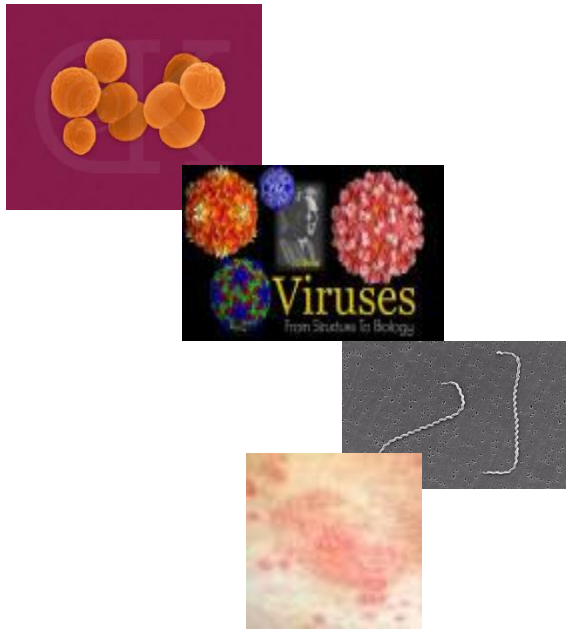
(Cryptococcus neoformans

Coccidiodes immitus)

-Inflammatory diseases *(SLE)*

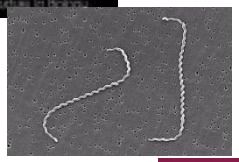
- Cancer

-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 BACTRIAL 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 and 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.**

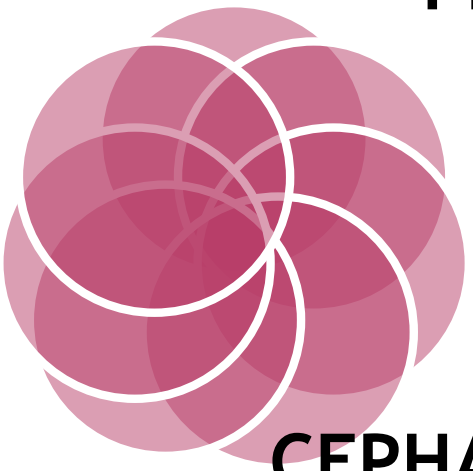
- **Regimen chosen must have potent activity against known or suspected pathogens & exert a bactericidal effect (Empiric?)**

ANTIBIOTICS FOR TREATMENT OF BACTERIAL MENINGITIS

INHIBITORS OF CELL WALL SYNTHESIS (B-LACTAMS)

PENICILLINS

Penams



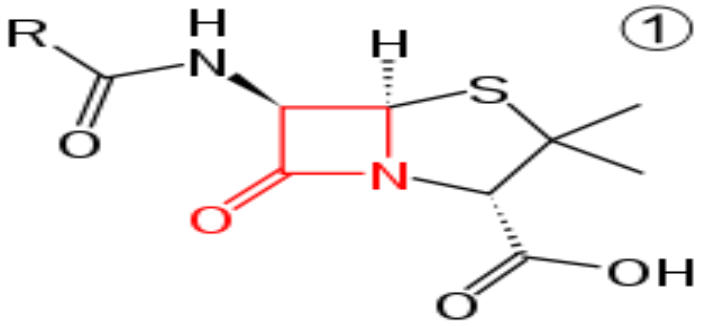
Carbapenems

CEPHALOSPORINS

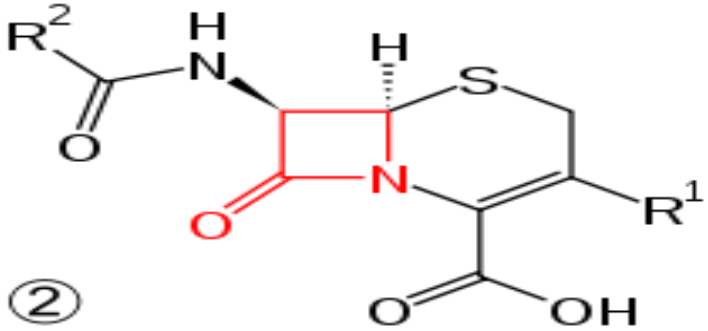
cephems

B-LACTAM ANTIBIOTICS

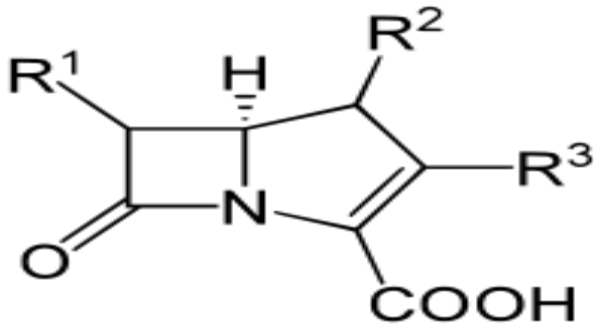
1) PENICILLINS



2) CEPHALOSPORINS



3) Carbapenems



PENICILLINS

Mechanism of action:

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

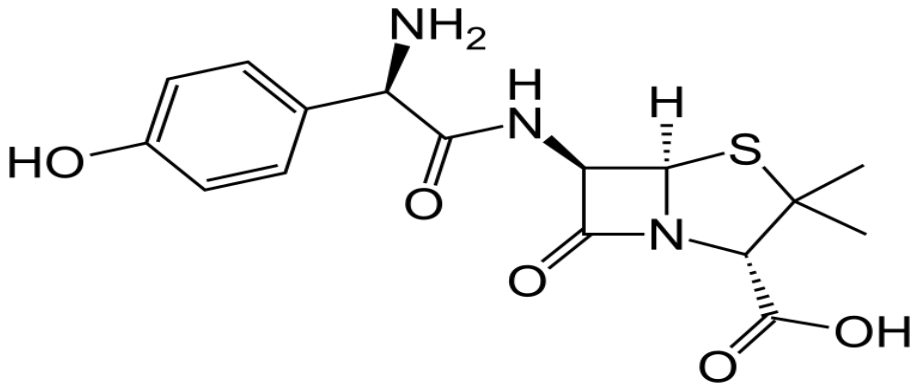
NARROW SPECTRUM PENICILLIN

Penicillin G (benzyl penicillin)

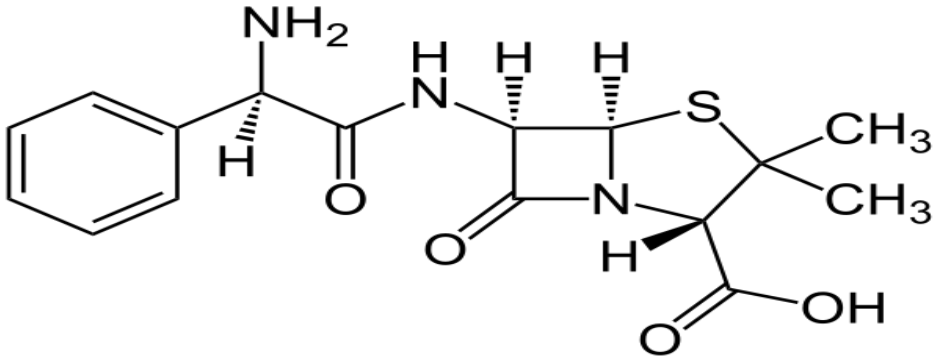
- **Narrow spectrum of activity**
- **Has poor oral absorption.**
- **Destroyed by gastric acidity**
- **Given by intravenous infusion**
- **β- lactamase sensitive (penicillinase sensitive)**
- **Short acting (4-6 hrs)**
- **Half- life 30-60 min.**

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 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**
  - **e.g. Ampicillin + Sulbactum**
- **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**

- **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.***
- **Used for treatment of bacterial meningitis caused by pneumococci, meningococci, and 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 and gram positive bacteria, including pseudomonads)
- Resistant to most **β-lactamases**

PHARMACOKINETICS

- Not absorbed orally, **taken by I.V**.
- Penetrates body tissues and 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?

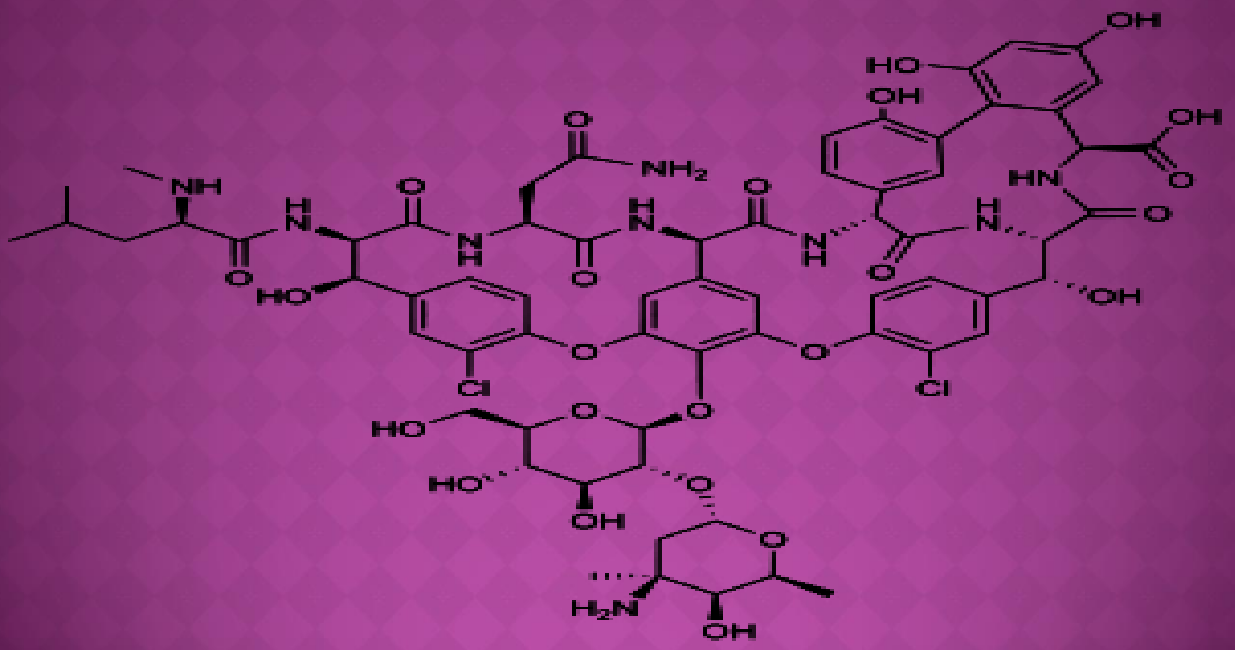
Inactivated by **dehydropeptidase** in renal tubules to a nephrotoxic metabolites, so it is co formulated with the **dehydropeptidase inhibitor** cilastatin for clinical use (Imipenem/cilastatin)

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 synthesis 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

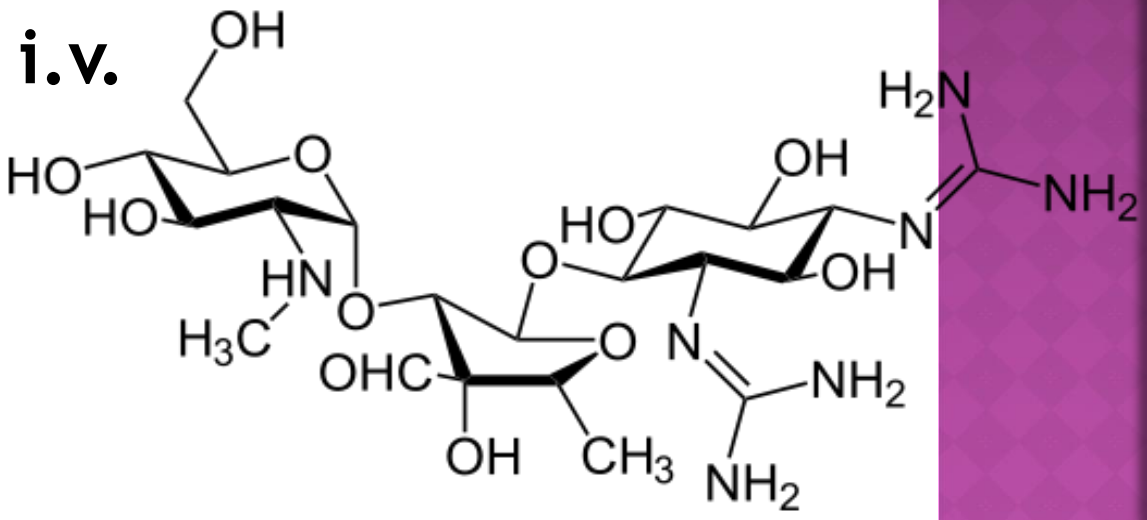
- **Phlebitis at site of injection**
- **Ototoxicity**
- **Nephrotoxicity**
- **Histamine release due to nonspecific mast cell degranulation leading to:**
  - **"Red man syndrome" or "red neck syndrome"**
  - **Hypotension (minimized if injected slowly over 60 minutes).**

AMINOGLYCOSIDES

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 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)**


The End