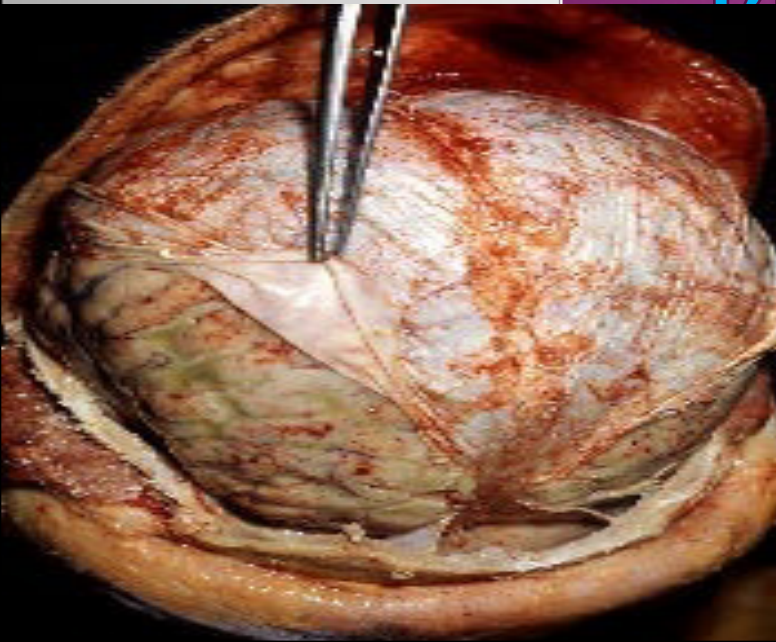


# DRUGS USED IN MENINGITIS

DR. ALIAH ALSHANWANI



# OBJECTIVES

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

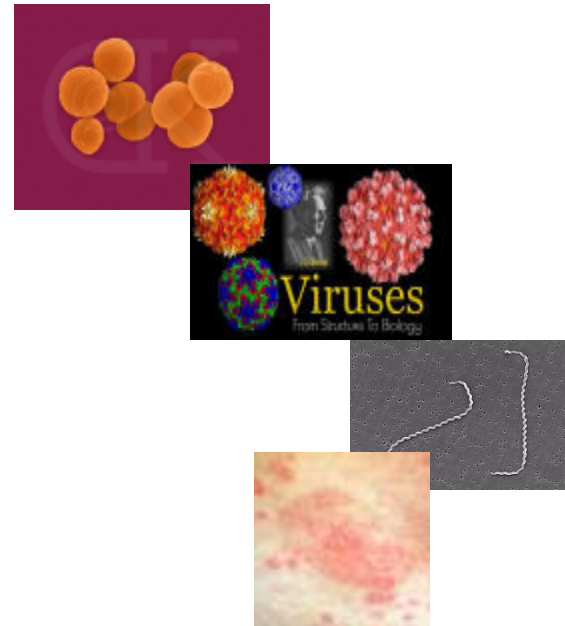
- ◉ Describe briefly common types of meningitis
- ◉ Describe the principles of treatment
- ◉ List the name of antibiotics used for the treatment of meningitis
- ◉ Describe the mechanism of action & adverse effects of the individual drugs.

# DEFINITION

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

# CAUSES OF MENINGITIS

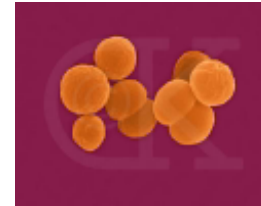
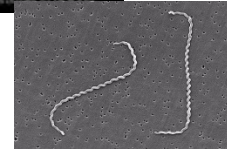
- Bacterial Infections
- Viral Infections
- Fungal Infections  
(*Cryptococcus neoformans*  
*Coccidioides immitis*)
- Inflammatory diseases (*SLE*)
- Cancer
- Trauma to head or spine.



# 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

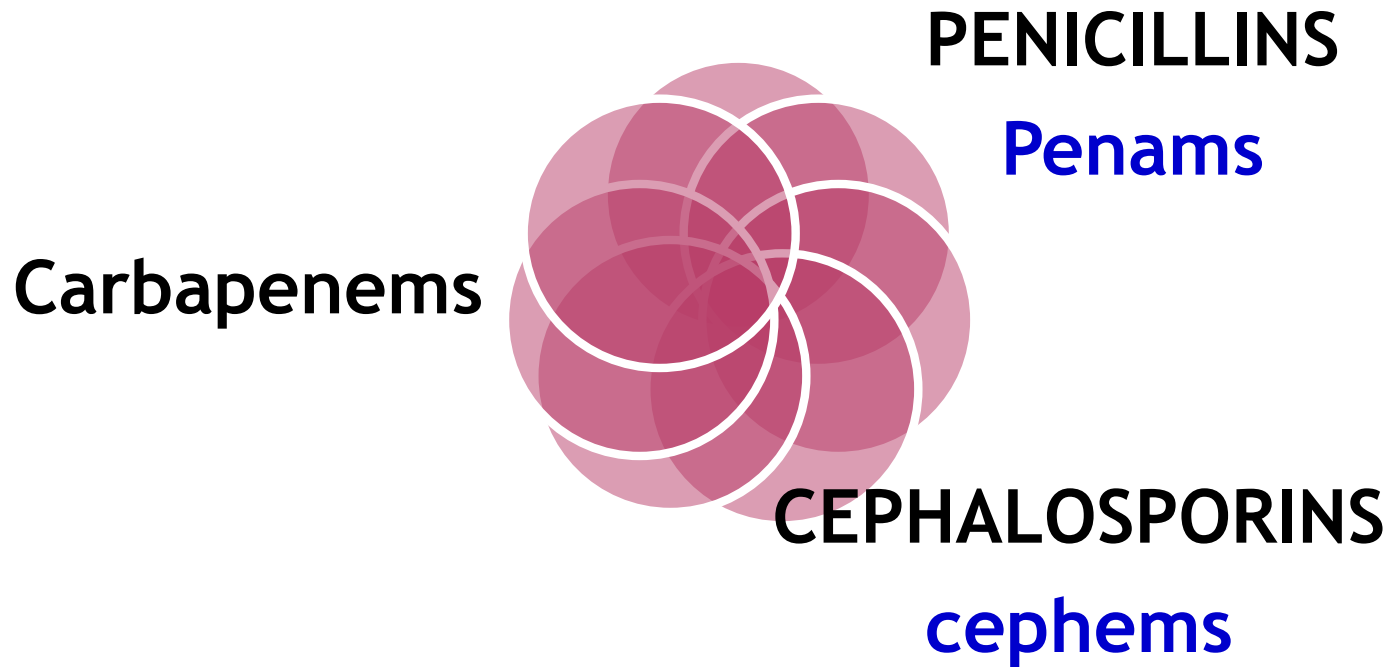
- **Is a serious, life threatening disease.**
- **Without treatment, bacterial meningitis can cause serious consequences**
  - Cognitive deficits
  - Deafness
  - Hydrocephalus
  - paralysis
  - stroke, seizures, sepsis, and even death.

# 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?**)**

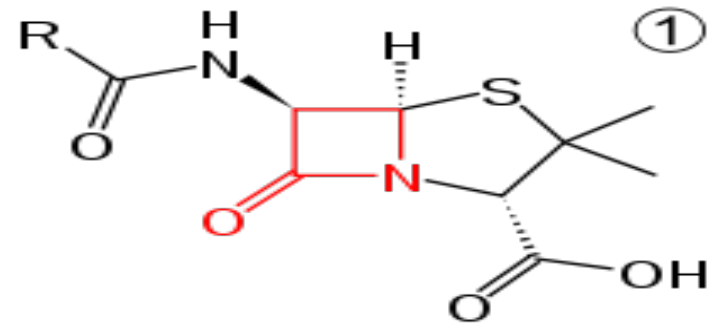
# ANTIBIOTICS FOR TREATMENT OF BACTERIAL MENINGITIS

## INHIBITORS OF CELL WALL SYNTHESIS (B-LACTAMS)

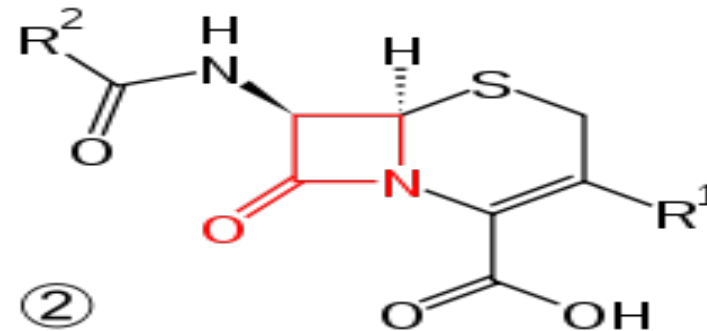


# B-LACTAM ANTIBIOTICS

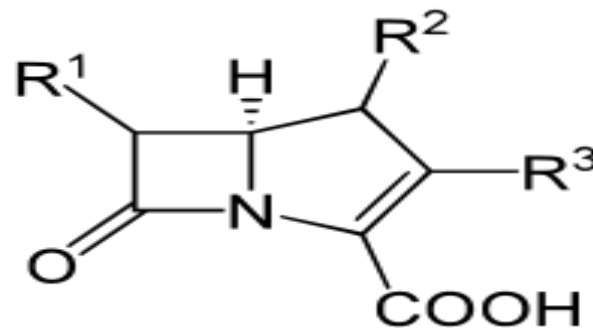
## 1) PENICILLINS



## 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

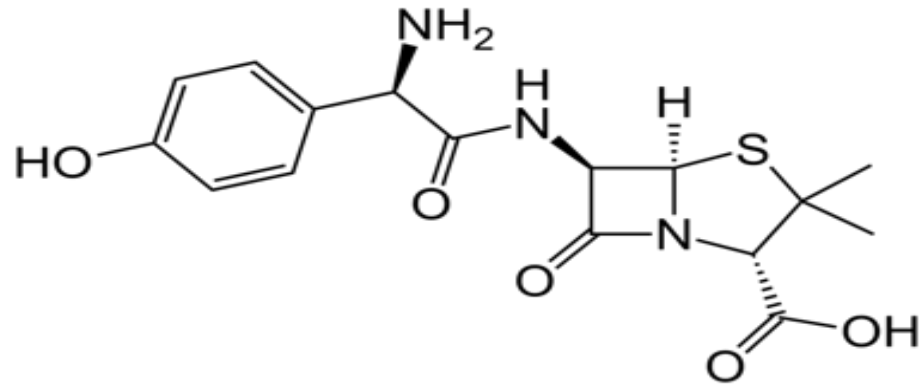
## Penicillin G (benzyl penicillin)

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

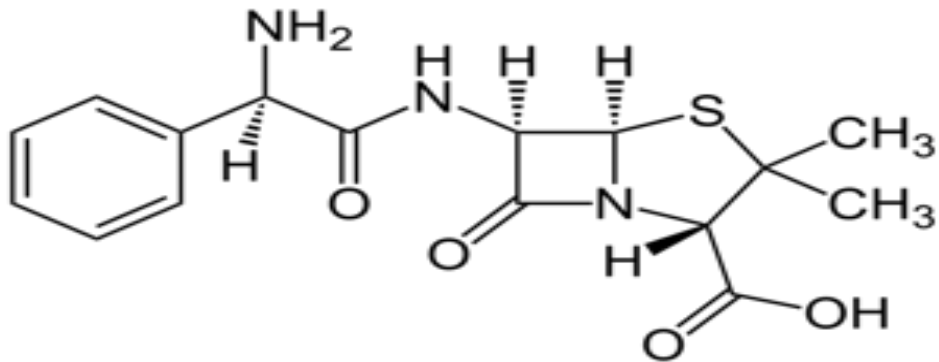
# EXTENDED SPECTRUM PENICILLINS

## 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  $\beta$ -lactamase enzyme**
- ⊙ **combination with  $\beta$ -lactamase inhibitors are available**
  - e.g. Amoxicillin + Clavulanic acid
  - e.g. Ampicillin + Sulbactam
- ⊙ **This combination is intended to:**
  - Prevent enzymatic hydrolysis by  $\beta$ -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 3<sup>RD</sup> GENERATION CEPHALOSPORINS

- ⊙ **Highly effective against Gm –ve bacilli**
- ⊙ **Against Pseudomonas (ceftazidime)**
- ⊙ **Highly resistant to  $\beta$ -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  **$\beta$ -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?**

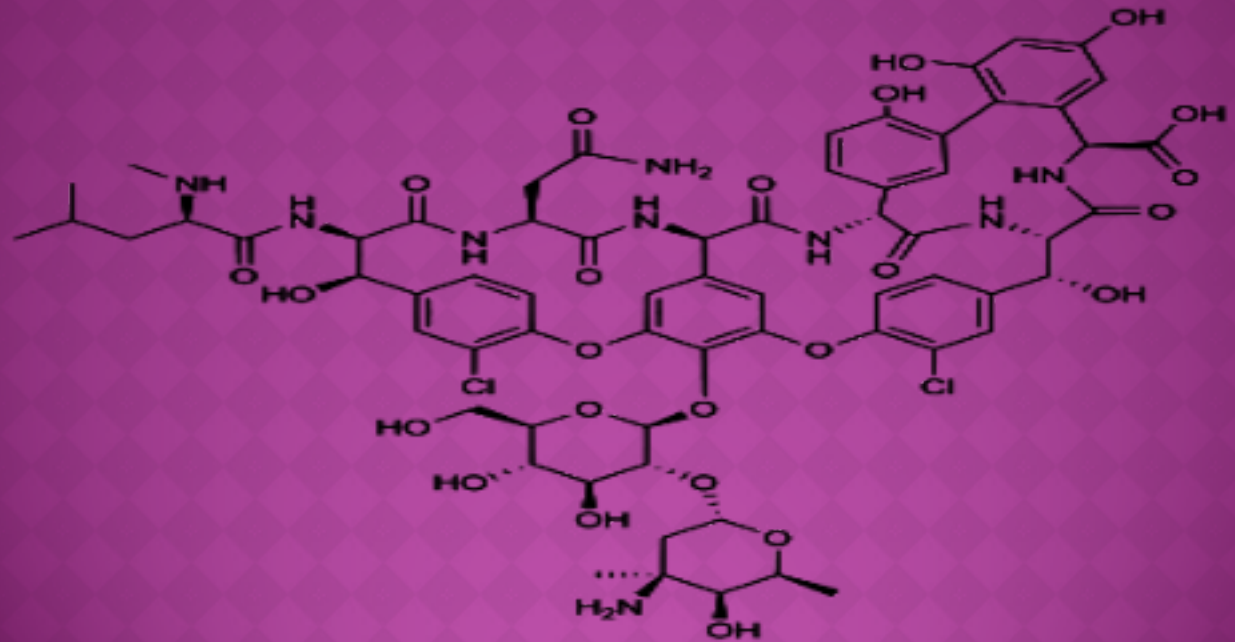
Inactivated by **dehydropeptidase** in renal tubules to a nephrotoxic metabolites, so it is co formulated with the **dehydropeptidase inhibitor** cilastatin for clinical use (Imipenem/cilastatin)

# 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. 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.**
- ◉ **May be combined with **ampicillin or ceftazidime** as an initial therapy of meningitis in infant, elderly and immunocompromised patients .**

# ADVERSE EFFECTS

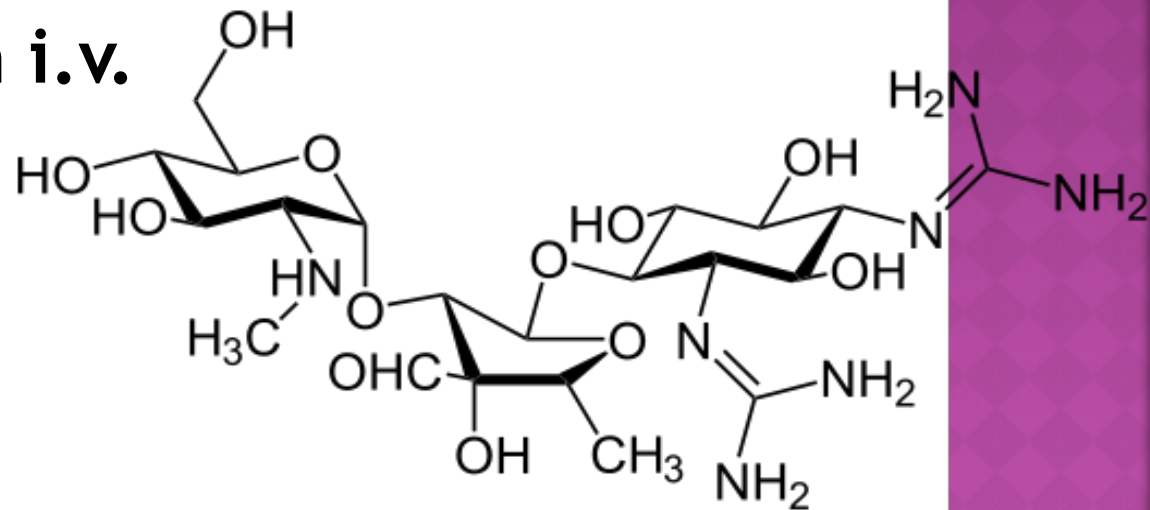
- ⊙ **Phlebitis at site of injection**
- ⊙ **Ototoxicity**
- ⊙ **Nephrotoxicity**
- ⊙ **Histamine release due to nonspecific mast cell degranulation leading to:**
  - **“Red man syndrome” or “red neck syndrome”**
  - **Hypotension (minimized if injected slowly over 60 minutes).**

# 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*