

Pharmacology Team 431

(CNS BLOCK)

Antibiotics used in meningitis

Done by :

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❖ **Definition:**

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

❖ **Causes:**

-Infectious

- ▶ *Fungi*
- ▶ *Parasites*
- ▶ **Bacteria** →
- ▶ *Viruses*

Bacterial meningitis:

- ▶ It is a serious, life threatening disease.
- ▶ May lead to serious long-term consequences (e.g. deafness, epilepsy, hydrocephalus & cognitive deficits).

-Non-infectious

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

❖ **Causes of bacterial meningitis:**

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

❖ **Route of transmission:**

- ▶ The bacteria are carried by humans in the nose and throat and spread into the air by coughing and/ or sneezing.
- ▶ 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***
 - ▶ **Severe headache***
 - ▶ **Stiff neck***
- } Triad
- ▶ Irritability
 - ▶ Seizures
 - ▶ Vomiting

❖ Treatment principles:

- ▶ Emergency hospitalization
- ▶ Antibiotics
- ▶ Measures for treatment of complications.

-Antibiotic selected must penetrate adequately into the CSF.

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

Empiric therapy is a medical term referring to the initiation of treatment prior to determination of a firm diagnosis. It may be thought of as taking the initiative against an anticipated and likely cause of infectious disease. It is most often used when antibiotics are given to a person before the specific bacterium causing an infection is known.

Antibiotics for treatment of bacterial meningitis

1-Cephalosporins

E.g: Ceftriaxone, i.v; Cefotaxime, i.v, Ceftazidime, i.v

Third generation cephalosporins, they are mainly **effective against** gram negative bacteria and they really **cover wide range** of gram negative bacteria, so if the patient is suspected with meningitis **ceftriaxone is the first choice medication.**

2-Penicillins

E.g: penicillin G, i.v; Ampicillin, i.v

It is preferred with **pediatric or immunocompromised patients.**

3-Glycopeptides

E.g: Vancomycin, i.v

Used with **staph. aureus gram positive**, especially that which produce **beta-lactamase (MRSA).**

4-Aminoglycosides

E.g: Gentamicin, i.v

Mainly against **gram negative (aerobic) bacteria.**

1-Cephalosporins

- Ceftriaxone (children & adults).
- Cefotaxime (preferred in neonates).
- Ceftazidime (excellent against **p. aeruginosae**)

❖ Mechanism of action

Inhibits bacterial cell wall synthesis (**bactericidal**)

❖ Side effects

1. **Hypersensitivity reactions**-Most common
2. Thrombophlebitis (**inflammation of veins**)
3. Superinfections
4. Diarrhea (**happens if it is orally taken, rarely with I.V**)

2-Penicillins

- Penicillin G (**narrow spectrum**),i.v.
- Ampicillin (**broad spectrum**),i.v.

❖ Mechanism of action:

Inhibits bacterial cell wall synthesis(**bactericidal**)

❖ Side effects:

- 1-**Hypersensitivity**
 - 2-Superinfections
 - 3-Diarrhea
 - 4-May cause **convulsions** after **high doses by i.v** or in **renal failure**.
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3-Vancomycin

- Active **ONLY** against **Gm+ve bacteria**.
- In combination with **3rd generation cephalosporins** for treatment of meningitis caused by **penicillin resistant pneumococci**.
- Against **Methicillin resistant S. aureus (MRSA)**.
- Combined with ampicillin or ceftazidime as an initial therapy of meningitis in infant, elderly and immunocompromised patients .
- **Not** effective against G-ve bacteria
- Given by **slow i.v infusion**.

❖ Mechanism of action:

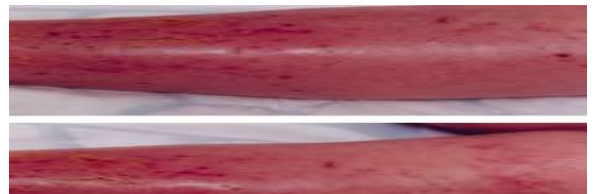
Inhibits bacterial cell wall synthesis

❖ Side Effects:

- 1-Phlebitis at the site of injection
- 2-Ototoxicity & Nephrotoxicity (high conc.)
- 3-**Red man or red neck syndrome+hypotension**
(with rapid infusion)

Rapid infusion:

Histamine release (flushing of upper body
(**Red man or red neck syndrome**) &
hypotension {minimized if injected slowly}.



4-Aminoglycosides

E.g: **Gentamicin, i.v.**

(**Antibacterial Spectrum**), **Bactericidal** (exclusive for **aerobic G-ve bacteria**)

❖ Mechanism of action:

Inhibit protein synthesis (**30s subunit**)

❖ Side Effects:

- 1-Ototoxicity
- 2-Nephrotoxicity
- 3-**Neuromuscular blockade**.(very high dose)

(directly related to serum conc.)

▼The drug needs Oxygen to enter the bacterial cytosol and binds to the ribosomes. As we know anaerobes live in the absence of Oxygen, **so anaerobic bacteria are resistant to Aminoglycosides**

Prevention better than cure

1-**Haemophilus influenzae type b (Hib) vaccines**
routine childhood immunization.

2-**Pneumococcal polysaccharide vaccine (PPSV)**
for older children and adults.

3-**Meningococcal conjugate vaccine**
people going to Hajj.

Drugs	Against	Mechanism of action	Adverse effects
Cephalosporins (Ceftriaxone, i.v; Cefotaxime, i.v, Ceftazidime,i.v)	Mainly gram(-)	Inhibits bacterial cell wall synthesis	1. Hypersensitivity reactions - most common 2. Thrombophlebitis 3. Superinfections 4. Diarrhea
Penicillins (Penicillin G, i.v; Ampicillin,i.v)	Mainly gram(+)	Inhibits bacterial cell wall synthesis	.1-Hypersensitivity .2-Super infections .3-Diarrhea .4-May cause convulsions after high doses by i.v or in renal failure
Glycopeptides (Vancomycin, i.v)	Gram(+)	Inhibits bacterial cell wall synthesis	1-Phlebitis at the site of injection 2-Ototoxicity+Nephrotoxicity(high conc.) 3-Red man or red neck syndrome- Hypotension(with rapid infusion)
Aminoglycosides (Gentamicin, i.v)	Aerobic gram(-)	Inhibit protein synthesis (30s subunit)	1-Ototoxicity & nephrotoxicity (directly related to serum conc.) 2-Neuromuscular blockade (very high dose)

MCQs

1-Which of the following drugs can cause red neck syndrome after rapid (IV) infusion:

- A- Gentamicin
- B- Vancomycin
- C- Ampicillin
- D- Ceftriaxone
- E- Ceftazidime

2-Which of the following drugs can act against Methicillin resistant S. aureus (MRSA):

- A- Gentamicin
- B- Vancomycin
- C- Ceftriaxone
- D- Ceftazidime
- E- Penicillin G

3- Mechanism of action of Aminoglycoside:

- A- Inhibit bacterial cell wall synthesis
- B- Inhibit protein synthesis (30s subunit)
- C- Inhibit protein synthesis (50s subunit)

GOOD LUCK ..