pharmacology
Team 438

MED438
KING SAUD UNIVERSITY

Reviewed by Razan AlRabah & Ibrahim AlDakhil

Neuropsychiatry Block

Pharmacology Team 438

Drugs Used in Meningitis

Objectives

By the end of the lecture , you should know:

- 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.

Color index:

Black : Main content
Red: Important
Blue: Males' slides only

Pink: Females' slides only
Grey: Extra info or explanation
Green: Dr. notes

Editing File

Meningitis

An inflammation of the protective membranes covering the **brain** and the **spinal cord** (meninges).

Causes of Meningitis

Infectious:

- Bacteria
- Viruses
- Fungal

Non-Infectious[1]:

- spread of cancer to meninges (malignant meningitis)
- Inflammatory disease (SLE)
- Trauma to head or spine

Bacterial Meningitis

- Is a serious , **life threatening disease**.
- May lead to serious consequences without treatment (e.g. deafness, limb loss, epilepsy, paralysis, hydrocephalus & cognitive deficits ,stroke ,seizures, sepsis and even death,).

Causes of Bacterial Meningitis

Most common causes:

1) Streptococcus pneumoniae. (Pneumococcal)

2) Neisseria meningitides. (Meningococcal)

Other causes:

1) Haemophilus influenzae
2) Staphylococcus aureus
3)Pseudomonas aeruginosa
4)Listeria monocytogenes
5) Mycobacterium Tuberculosis→ (tuberculous meningitis)

Route of transmission

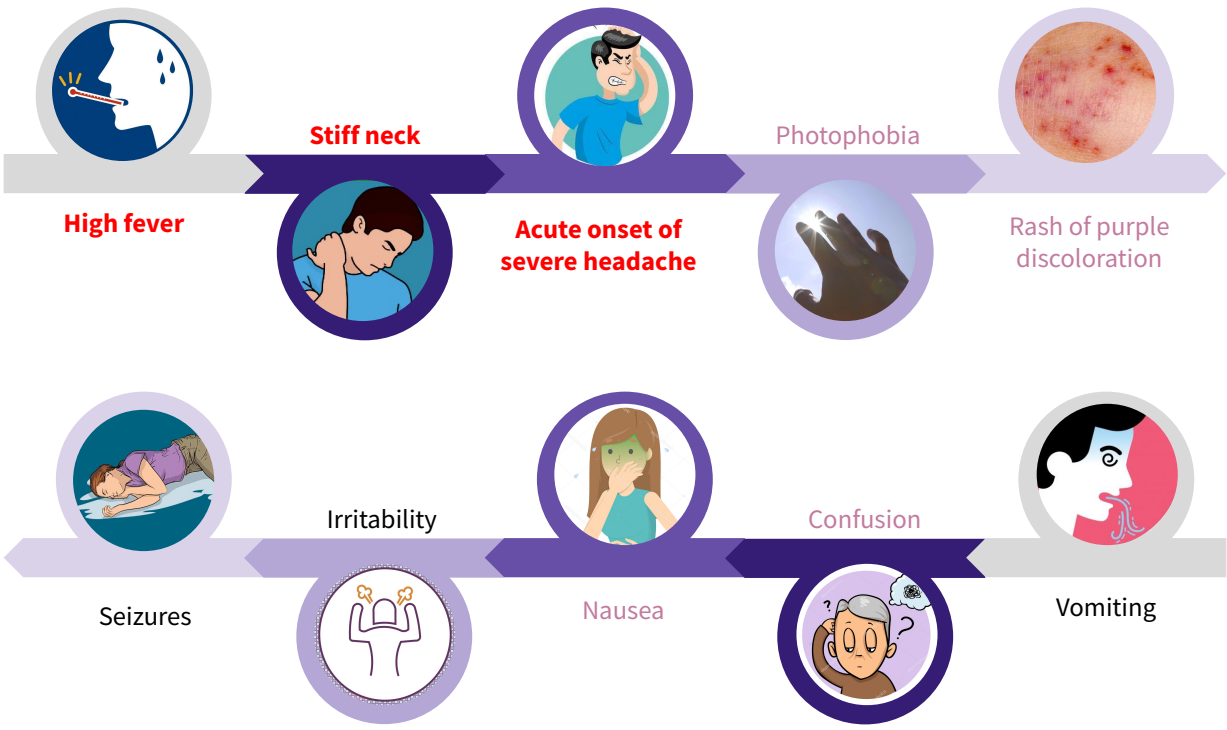
Most bacteria that cause this form of infection are spread through close personal contact, such as: **coughing , sneezing & kissing**,sharing eating utensils.

→

The pathogens spread from the **respiratory tract** to the **bloodstream (septicemia)** and to the nervous system and **cause bacterial meningitis.**

1. Basically caused by any chemical that initiates an inflammatory reaction within the CSF.

Symptoms of Bacterial Meningitis



Treatment Principles

1. Emergency hospitalization
2. Antibiotics
   a. Antibiotic selected must penetrate adequately into the CSF
   b. Regimen chosen must have potent activity against known or suspected pathogens & exert a bactericidal effect. (Empiric[1])
3. Measures for treatment of complications

Antibiotics For Treatment of Bacterial Meningitis

Inhibitors of cell wall synthesis (B-LACTAMS [2]):

Penicillin — Carbapenem — Cephalosporin

1. Empiric Means : without knowing the cause, I give antibiotics immediately.
2. All b- lactams excreted by kidney

Penicillins [1]

Drug	Penicillin G	Aminopenicillins: • Amoxicillin • Ampicillin
MOA	Inhibit bacterial cell wall synthesis by inhibiting the peptidoglycan layer of bacterial cell wall (bactericidal).	
Spectrum	Narrow " Gram + only"	• Broad(against gram +ve and –ve) • Not active against *pseudomonas aeruginosa*.[3]
P.K	• Poor oral absorption → It destroyed by gastric acidity. • Given IV infusion. • Short acting (4-6 hrs) • Half- life 30-60 min. • β- lactamase sensitive (penicillinase sensitive)	• They are acid stable (effective orally) • Route of administration: I.V or I.M • Amoxicillin [4] is better absorbed from the gut and not affected by food
B-lactamase	-	Inactivated by β-lactamase enzyme. (now a days combination with B- lactamase inhibitors are available) 1) Amoxicillin + Clavulanic acid = orally 2) Ampicillin + sulbactam = IV **This combination is intended to:** **- Prevent enzymatic hydrolysis by β-lactamase.** **- Extend antimicrobial activity.**
ADRs	• Hypersensitivity (anaphylactic reaction)[2] • Antibiotic-associated diarrhea • Nephritis • Super-infections or secondary infections (candidiasis, oral thrush [5]) • High dose in renal failure [6] (seizure)	

Cephalosporins (3rd Generation)

Drug	• Ceftriaxone • Ceftazidime • Cefotaxime
MOA	Inhibit bacterial cell wall synthesis (bactericidal).
P.K	Both of them are given by **intravenous** infusion.
Spectrum	• Highly effective against **Gm –ve bacilli.** ★ **Ceftazidime → against *P. aeruginosa*.** ★ used for treatment of bacterial meningitis caused by pneumococci, meningococci, H.influenzae • Highly resistant to B-lactamase
ADRs	• Allergy • Thrombophlebitis (at injection site) • Renal toxicity • Super-infection • GIT upset & diarrhea

1. It cross the BBB because of inflamed condition, inflammatory mediators, like IL-1, IL-6, TNF-alpha cause vasodilation and increase permeability. Note that penicillin is unique is that it causes all 4 hypersensitivity reactions (I: Systemic Anaphylaxis, II: Hemolytic anemia (kidney failure occur as complication), III: Glomerulonephritis, IV: Contact Dermatitis)
2. Management with adrenaline and glucocorticoids, allergy causes release of histamine, and adrenaline is the physiological antagonist of histamine.
3. Pseudomonas resist bactericidal activity by: (1) decrease membrane permeability, (2) penicillinase, (3) active pumping of drug
4. Amoxicillin is better because ampicillin affected by food
5. White patches in the tongue
6. Penicillin excreted by kidney , so in high dose with patient have kidney problems seizure could happen.

Carbapenems
(Most powerful)

Drug	Imipenem/cilastatin
MOA	Inhibits bacterial cell wall synthesis (bactericidal).
P.K	• Not absorbed orally, taken by I.V. & Half- life about 1 hr. ★ Inactivated by **dehydropeptidase** in renal tubules to a nephrotoxic metabolites, so it is given with a dehydropeptidase inhibitor **cilastatin** for clinical use. ⟶ it is given by combination of **imipenem + cilastatin**. • Penetrates body tissues and fluids including CSF • Excreted primarily by the kidney. • Doses must be reduced in renal failure.[1]
Spectrum	• Has a wide spectrum of activity (aerobic & anaerobic GM +ve & GM -ve bacteria, including pseudomonads) • Resistant to most β lactamases.
ADRs	• 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 inhibitor of cell wall synthesis

Drug	Vancomycin
MOA	Cell wall inhibitor (bactericidal)
P.K	★ **Poorly** absorbed **orally,** only used **orally**[2] to treat GIT infections caused by *clostridium difficile* e.g.**pseudomembranous colitis**.[3] • Given intravenously for the treatment of meningitis.
Spectrum	• It is active **only against gram positive bacteria**. (narrow spectrum)
Uses	★ 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 patient

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

1- check creatinine clearance
2-has high molecular weight , we give patient orally only for Git infectious because drug will stay in Git , in case of meningitis give IV
3-Pseudomembranous colitis is an inflammatory condition of the intestines, believed to be caused by changes to the normal flora of the intestines after antibiotics use, a newer and a much more efficient treatment for this disease is fecal transplant, yes, feces from a healthy donor by infusion or orally. This helps restore normal flora balance.

Aminoglycoside

Drug	Gentamicin
MOA	• Inhibit protein synthesis (30S subunit) • Bactericidal [1]
Spectrum	• exclusive for aerobic G-bacteria
P.K	• Not absorbed orally • Given I.V
ADRs	• Ototoxicity & Nephrotoxicity (Directly related to serum Conc.) • Neuromuscular blockade (very high dose)

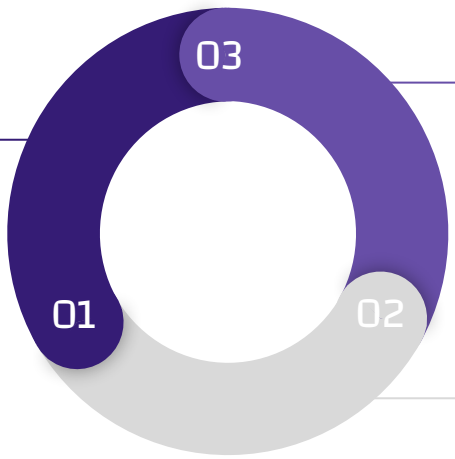
Prevention Better Than Cure

Haemophilus influenzae type b (Hib) vaccines

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

Hib causes bacterial meningitis in children.

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)

1. All antibiotics that act by inhibit protein synthesis are bacteriostatic except Gentamicin

Quiz

MCQ

1- which of the following is the drug of choice in cases of meningitis by pseudomonas aeruginosa ?

A- Penicillin G B- Ceftriaxone C- Amoxicillin + Clavulanic Acid D- Ceftazidime

2- Salah was commenced on antibiotics but developed thrombophlebitis at the site of injection. which of the following is the most likely antibiotic to have caused this ?

A- Ceftriaxone B- Ampicillin + Sulbactam C- Gentamicin D- Penicillin G.

3- Vancomycin taken orally can be used for the treatment of ?

A- Meningitis B- Sinusitis C- Pseudomembranous colitis G D- Otitis media

4-Which of the following can cause red man syndrome?

A- Ceftriaxone B- Imipenem C- Vancomycin D- Ceftazidime

SAQ

-A 20-year-old female presents to the ER with headache, stiff neck, and fever for 2 days after investigations she is diagnosed with meningitis caused by a gram -ve bacilli.

1-What is the best choice for the treatment of meningitis in this patient?

2-What is the MOA of this drug?

3-What is the contraindicated drug to 50-year-old female with a history of myasthenia gravis came to the ER suffering from meningitis?

-A 39-year-old male came to the ER with a high fever and headache after investigations he was diagnosed with a meningitis caused by gram +ve bacteria.

4-If the patient is allergic to penicillin, what is the most appropriate drug in this case?

5-Mention 2 ADRs of this drug.

Answers:

MCQ

Q1	D
Q2	A
Q3	C
Q4	C

SAQ

Q1	Cephalosporins (3rd generation)
Q2	Inhibit bacterial cell wall synthesis (bactericidal).
Q3	Aminoglycosides (Gentamicin)
Q4	Vancomycin
Q5	Ototoxicity - Nephrotoxicity

pharmacology

Team 438

Good Luck , Future Doctors!

Team Leaders:

May Babaeer

Zyad Aldosari

This Stunning Work Was Done By:

May Babaeer

Fay AlBuqami

Nouf AlShammari

Njoud AlMutairi

Noura AlMazrou

Shahad AlSahil

Share with us your ideas !