

Drugs used in meningitis

- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE



Objectives



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.

Meningitis

Definition

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

Causes

Infectious: Viruses, Bacteria and Fungi (*Cryptococcus neoformans*, *Coccidioides immitis*).

Non-Infectious: Cancer (malignant meningitis), Inflammatory disease (SLE) and Trauma to head or spine

Bacterial Meningitis

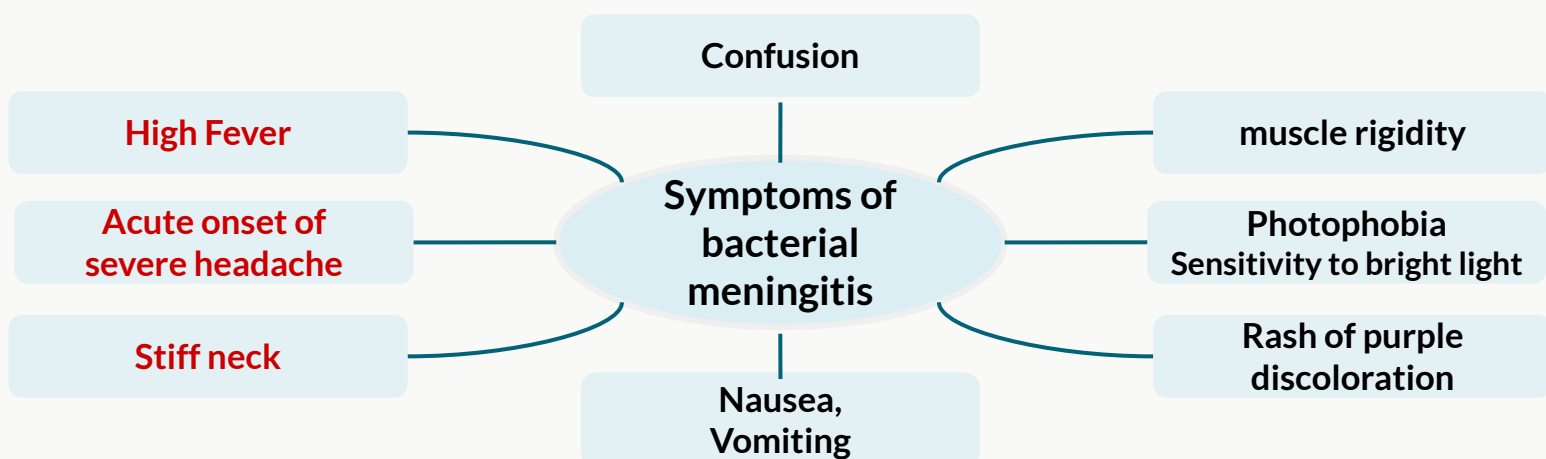
A serious, **life threatening** disease that may lead to serious consequences without treatment (e.g. Cognitive deficits, deafness, hydrocephalus, paralysis, stroke, seizures, sepsis and even death)

Causes :

- **Streptococcus pneumoniae (Pneumococcal).**
- **Neisseria meningitidis (meningococcal).**
- Haemophilus influenzae (Hib).
- Staphylococcus aureus.
- Pseudomonas aeruginosa.
- Listeria monocytogenes.
- Mycobacterium tuberculosis (tuberculous)

Route of transmission:

- Most bacteria that cause form of infection are spread through close personal contact, such as: coughing, sneezing, kissing.
- The pathogens spread from the **respiratory tract** to the **bloodstream** and to the nervous system and cause **bacterial meningitis**.



Treatment of Meningitis

Treatment principles

Meningitis, caused by a bacteria, is life threatening & requires urgent medical attention & treatment with antibiotics.

Emergency hospitalization

Antibiotics

Measures for treatment of conditions

Antibiotic selected must penetrate adequately into CSF.
 inflamed meninges → ↑ permeability → drug will penetrate BBB easily”

Regimen chosen must have potent activity against known or suspected pathogens & exert a bactericidal effect (Empiric “medical treatment based on experience”).

Prevention better than cure

Haemophilus influenzae type b (Hib) vaccines

- Hib is a leading cause of bacterial meningitis in **children**.
- Vaccines available as part of the routine childhood immunization schedule have greatly reduced cases of this type of meningitis.

Meningococcal conjugate vaccine

- Used for people going to Hajj (protects against meningitis caused by **N.meningitidis**)

Pneumococcal polysaccharide vaccine (PPSV)

- For older children and adults (protects against meningitis caused by **S.pneumoniae**)

Antibiotics for treatment of bacterial meningitis

Inhibitors of cell wall synthesis

Inhibitor of protein synthesis

β-lactams

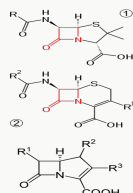
Other

Binding to 30S subunit

I. Penicillins (Penams)

II. Cephalosporins (Cephems)

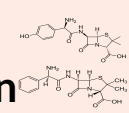
III. Carbapenem



Vancomycin

Aminoglycosides: Gentamicin

I. Penicillins

Drug	Penicillin G / "benzylpenicillin"	Aminopenicillins: Amoxicillin, Ampicillin 
M.O.A	Inhibit bacterial cell wall synthesis by inhibiting the peptidoglycan layer of bacterial cell wall (bactericidal).	
Spectrum	Narrow	<ul style="list-style-type: none"> ● Broad (active against gram +ve and -ve) ● Not active against pseudomonas aeruginosa.
P.k	<ul style="list-style-type: none"> ● Poor oral absorption (destroyed by gastric acidity). ● Given IV infusion/ Half life 30-60 min. ● Short acting (4-6 hrs) ● β-lactamase sensitive (penicillinase sensitive). 	<ul style="list-style-type: none"> ● They are acid stable (effective orally) ● Can also be given I.V or I.M ● Amoxicillin is better absorbed from gut and not affected by food.
β -lactamase <small>* (only for Aminopenicillins)</small>	<ul style="list-style-type: none"> ● Inactivated by β-lactamase enzyme. ● Combination with β-lactamase inhibitors are available: <ol style="list-style-type: none"> 1. Amoxicillin + Clavulanic acid "Augmentin" 2. Ampicillin + Sulbactam ● This combination is intended to: <ul style="list-style-type: none"> ○ Prevent enzymatic hydrolysis by β-lactamase ○ Extend antimicrobial activity. 	
ADRs	<ul style="list-style-type: none"> ● Hypersensitivity (Anaphylactic reactions). ● Antibiotic associated diarrhea. "GI upset" ● Super-infections or secondary infections (candidiasis, oral thrush). (due to alteration of normal flora) ● Nephritis ● High dose in renal failure (seizure). 	

II. Cephalosporins (3rd Generation)

Ceftriaxone - Ceftazidime - Cefotaxime

M.O.A	-Inhibit bacterial cell wall synthesis (bactericidal) "same MOA as Penicillins" -Vs gram -ve & +ve organisms
P.k	Given I.V by infusion
Spectrum	<ul style="list-style-type: none"> ● Highly effective against gram -ve bacilli. ● Highly resistant to β-lactamase. "difference from penicillins" ● Against Pseudomonas (Ceftazidime) "difference from penicillins" ● Used for treatment of bacterial meningitis caused by: pneumococci, meningococci, H.influenzae.
ADRs "same as penicillins"	<ul style="list-style-type: none"> ● Allergy ● GIT upset and diarrhea ● Super-infections ● Thrombophlebitis at site of injection "irritation" ● Renal toxicity

III. Carbapenems

Imipenem + Cilastatin

M.O.A	Inhibit bacterial cell wall synthesis (bactericidal) "same MOA as previous drugs"
P.k	<ul style="list-style-type: none"> ● Not absorbed orally, taken by I.V & 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 for clinical use (Cilastatin) "↓toxicity" ● Cilastatin has no antibacterial action, like b-lactamase inhibitors it only prolongs the action of the antibiotic ● Penetrates body tissues and fluids including CSF. ● Excreted primarily by the kidney, doses must be reduced in renal failure.
Spectrum	<ul style="list-style-type: none"> ● Has a wide spectrum of activity (aerobic & anaerobic Gram +ve & -ve bacteria, including pseudomonads). ● Resistant to most β lactamases. "related to cephalosporins"
ADRs "same as previous drugs"	<ul style="list-style-type: none"> ● Skin rash & reaction at the site of infusion ● Nausea, vomiting, diarrhea "GI upset" ● Patients allergic to penicillins may be allergic to carbapenems ● High doses may cause seizure in patients with renal failure

2. Other inhibitor of cell wall synthesis

Vancomycin

M.O.A	Inhibits cell wall synthesis (bactericidal) "in a way different from previous drugs"
P.k	<ul style="list-style-type: none">● Poorly absorbed orally, only used orally to treat GIT infections caused by clostridium difficile associated colitis "it will work locally without absorption"● Given I.V for the treatment of meningitis.
Uses	<ul style="list-style-type: none">● Active only against gram +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 patient.
ADRs	<ul style="list-style-type: none">● Ototoxicity & Nephrotoxicity● Phlebitis at the site of injection● Histamine release due to nonspecific mast cell degranulation leading to: "vasodilation"- Red man or Red neck syndrome, Hypotension (minimized if injected slowly over 60 minutes).

3. Inhibitors of protein synthesis: Aminoglycosides

Gentamicin

M.O.A	Inhibit protein synthesis (30S subunit) (bactericidal)
P.k	<ul style="list-style-type: none">● Not absorbed orally so given by injection I.V
ADRs	<ul style="list-style-type: none">● Ototoxicity & Nephrotoxicity "high doses", Neuromuscular blockade "very high dose".

Summary

Drug	Cell wall inhibitor					Inhibit protein synthesis (30s ribosomal subunit)
	Penicillin G	Aminopenicillin (Amoxicillin, Ampicillin)	Cephalosporins Ceftriaxone Ceftazidime Cefotaxime	Carbapenems Imipenem/ Cilastatin	Vancomycin	Gentamicin
spectrum	Narrow +ve	Broad +ve & -ve	Gram -ve bacilli	-ve & +ve aerobic and anaerobic	+ve MRSA	aerobic G-ve bacteria
ADRs	<ul style="list-style-type: none"> -Hypersensitivity (anaphylactic) -Diarrhea -Super infections or secondary infections -Nephritis -High dose in renal failure (seizure) 		<ul style="list-style-type: none"> -Thrombophlebitis -Allergy -GIT upset -Super infections -Renal toxicity 	<ul style="list-style-type: none"> -Nausea, vomiting, diarrhea -Skin rash -High dose in renal failure (seizure) -Patients allergic to penicillins may be allergic to carbapenems 	<ul style="list-style-type: none"> -Ototoxicity -Nephrotoxicity -Phlebitis at the site of injection -Histamine release leading to <ol style="list-style-type: none"> 1- Red man or Red neck S 2- Hypotension (minimized if injected slowly over 60 minutes) 	<ul style="list-style-type: none"> -Ototoxicity -Nephrotoxicity -Neuromuscular blockade



MCQ

1.What is the mechanism of action of Gentamicin?			
A.Inhibiting synthesis of proteins	B.Inhibiting bacterial wall synthesis	C.Inhibiting nucleic acid synthesis	D.Alteration of cell membrane
2.Which one of these antibiotics could lead to anaphylactic reaction?			
A.Penicillins	B.Aminoglycoside	C.Cephalosporins	D.Carbenems
3.If a patient took Vancomycin which one of these is the most adverse side effects?			
A.Bone marrow suppression	B.Anemia	C.Red man syndrome	D.Hepatotoxicity
4.Patient treated by antibiotic previously, now he is Suffering from ototoxicity and nephrotoxicity which one of these antibiotics could lead to those symptoms?			
A.Vancomycin	B.Gentamicin	C.Ceftriaxone	D.A & B
5.Prescribing HIGH dose Imipenem for patients with renal failure Cause			
A. Seizure	B.Hepatitis	C.Hypertensive reaction	D.none
6.Imipenem Inactivated by dehydropeptidase in renal tubules to a nephrotoxic metabolites so we give:			
A.Penicillin	B.Cilastatin	C.Ceftazidime	D.Beta blocker



SAQ

01

Ahmad, an 8 year old boy, was suffering from a high fever and neck stiffness . When he woke up in the morning he also had a sudden headache and he was abnormally sensitive to bright light. He went to the emergency room and he was diagnosed with bacterial meningitis and doctor give him Amoxicillin + clavulanic acid. Ues this case to answer the following two questions

- 1-Describe this drug's mechanism of action
- 2-What is the reason behind the combination of drugs you mentioned above?

- 1-Inhibit bacterial cell wall synthesis by inhibiting the peptidoglycan layer of bacterial cell wall (bactericidal)
- 2-Prevent enzymatic hydrolysis by β -lactamase, Extend antimicrobial activity.

02

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

Aminoglycosides (Gentamicin)

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