Lecture 9

Drugs used in Meningitis

Objectives:

1. Describe briefly common types of meningitis
2. Describe the principles of treatment
3. List the name of antibiotics used for treatment of meningitis
4. Describe the mechanism of action & adverse effects of the individual drugs

- Additional Notes
- Important
- Explanation –Extra-

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

1. **Infectious:**

- Viruses
- **Bacteria**: Is a serious , life threatening disease. May lead to serious long –term consequences (e.g. deafness, epilepsy, ,hydrocephalus & cognitive deficits).

Causes:

1. **Neisseria meningitidis**
2. **Streptococcus pneumoniae**
3. Haemophilus influenzae (in children)
4. Staphylococcus aureus
5. Pseudomonas aeruginosae (very resistant organism)
6. Listeria monocytogenes
7. Mycobacterium tuberculosis(tuberculous meningitis)

Symptoms: High fever, Severe headache, Stiff neck (rigidity in muscles = patient can't touch his chest with his chin) , Irritability, Seizures and Vomiting.

Route of transmission:

- The bacteria are carried by humans in the nose and throat and spread by coughing and/or sneezing, kissing, sharing eating utensils.
- The pathogens spread from the respiratory tract to the blood stream and to the nervous system and cause bacterial meningitis .

2. **Non-infectious** e.g, spread of cancer to meninges (malignant meningitis),etc.

Treatment principles:

1. Emergency hospitalization
2. Measures for treatment of complications
3. Antibiotics:
   - Antibiotic selected must penetrate adequately into the CSF.
   - (in this case the drug don't have to be lipid soluble because the BBB in this case is inflamed & destroyed. (e. g. penicillin).
   - We never use bacteriostatic antibiotic in the treatment of meningitis because it's serious disease.
   - Regimen (treatment) chosen must have potent activity against known or suspected pathogens & exert a bactericidal effect. (Empiric? You start *broad spectrum antibiotic* immediately before getting culture results)
   - **β- lactamase** is an enzyme produced by some bacteria's (e.g. Pseudomonas aeruginosa, Haemophilus influenzae, and Neisseria gonorrhoeae) that has the ability to destroy some antibiotics (e.g. penicillin).

Prevention better than cure:

1. **Haemophilus influenzae type b** (**Hib**) bacterium, a leading **cause of bacterial meningitis in children**. **New Hib vaccines** — available as part of the routine childhood immunization schedule have greatly reduced cases of this type of meningitis.

2. **Pneumococcal polysaccharide vaccine** (PPSV) for older children & adults.
3. **Meningococcal conjugate vaccine** ,people going **to Hajj**.

Inhibitors of cell wall synthesis (β -Lactams)

Group	Penicillin's			Cephalosporin's 3rd generation		Carbapenems
Drug	**Penicillin G**	**Amoxicillin**	**Ampicillin**	**Ceftazidime**	**Ceftriaxone**	**Imipenem**
Spectrum	Narrow (not used as empiric)	– Extended – Active against gram positive and negative.		– Highly effective against Gram negative – Anaerobic microbes – Pseudomonas **(ceftazidime)**		– aerobic and anaerobic – gram positive and negative including pseudomonads
MOA	Inhibit bacterial cell wall synthesis by inhibiting the peptidoglycan layer of bacterial cell wall (bactericidal).			Inhibitors of cell wall synthesis (bactericidal) (it's named drug with champion action cause it's strong) Wide spectrum		
Inactivation by β-lactamase	YES	YES		NO		
P.K	Destroyed by gastric acidity Short acting (4-6 hrs)	acid stable (effective orally) I.V or I.M Amoxicillin is better absorbed from the gut and not affected by food.		IV only (they penetrate CNS better than 1st & 2nd generations, inhibit bacteria cell wall, Highly effective against Gram –ve bacilli 2- Anaerobic microbes)		IV Inactivated by **dehydropeptidases** in renal tubules. Penetrates body tissues and fluids including C.S.F.
Combination	-	**Amoxicillin + Clavulanic acid** (β- lactamase inhibitors)	**ampicillin + salbactum** (β- lactamase inhibitors)	-	-	**Imipenem + cilastatin** (inhibitor of dehydropeptidase in kidney)
ADRs	Hypersensitivity (anaphylactic reaction), diarrhea (only if taken orally), nephritis, neurotoxicity (with high doses).			Allergy, thrombophlebitis at the site of injection, renal toxicity (in high dose), superinfections (common).		Seizures (high doses in patient with renal failure), GIT effects Skin rash and reaction at the site of infusion.

*** Patients allergic to penicillin's may be allergic to Carbapenems.**

Other inhibitor of cell wall synthesis

Drug	Vancomycin
Spectrum	Active only against Gram positive bacteria.
MOA	Cell wall inhibitor (Bactericidal).
P.K	Poorly absorbed orally (IV)
indication	Used orally to treat GIT infections caused by *clostridium defficile* (a type of bacterium that infects immunocompromised patients & those who use broad spectrum antibiotic for long time) e.g. colitis. against Methicillin resistant S. aureus (**MRSA**).
combination	• With ampicillin or ceftazidime as an initial therapy of meningitis in infant, elderly and immunocompromised patients. • With 3rd generation cephalosporins for **treatment of meningitis** caused by penicillin resistant pneumococci • Pencillin work in initial step while vancomycin in final step.
ADRs	• Phlebitis at site of injection • Ototoxicity • Nephrotoxicity • Histamine release (flushing of upper body) [red man (red neck) syndrome]. • hypotension (minimized if injected slowly).

1)Which one of the following is a broad spectrum ?

A. Penicillin G
B. Vancomycin
C. Ampicillin
D. Ciprofloxacin

2)Which on of the following inhibits DNA gyrase?

A. Imipenem
B. Penicillin
C. Gentamicin
D. Ciprofloxacin

3)what is the MOA of ceftriaxone?

A. Inhibit bacterial cell wall synthesis
B. Inhibit DNA synthesis
C. Protein synthesis inhibitor
D. Non of above

4)For beta lactamase enzyme producing pathogens, which combination do we use with Ampicillin?

A. Calvulanic acide
B. Salbactam
C. Cilastatine

5)it is highly effective against pseudomonas.

A. Ceftazidime
B. Amoxicillin
C. Vancomycine
D. Imipenem

6)Regarding fluroquinolones:

A. Inhibit cell wall synthesis
B. They have poor oral bioavailability
C. May damage growing cartilage in children
D. B+C

7)which on of the following is used against methicillin resistant S.aureus?

A. fluroquinolones
B. Vancomycine
C. Ceftazidime
D. Extended spectrum ampicillin

8)In high doses may cause seizure in patient with renal failure?

A. Vancomycin
B. Carbapenems
C. Ciprofloxacin

9)12years old male has meningitis caused by S.pneumoniae , what is the appropriate treatment for him?

A. Ampicillin
B. Vancomycin
C. Ciprofloxacin
D. ceftriaxone

1:C 2:D 3:A 4:B 5:A 6:C 7:B 8:B 9:D

Good luck!

Done by Pharmacology team 434

- Reema Alnasser
- Maha Al-Rabiah
- Nada Alomari
- Asma Alrusaiss
- Moneera Aldraihem

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com