

## Lecture 1~6

## Revision

**Microbiology Team - 430**



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## Otitis Media:

- 1- OM most commonly occurs in infants and pre-school age (until 4 years).
  - Why? Because of the horizontal position of the Eustachian Tube
- 2- OM is usually preceded by viral URTI or allergy.
- 3- Cleft palate is a risk factor for OM.
- 4- OM most commonly caused by *S.pneumoniae* then *H.influenza*
- 5- Chronic and serous OM has mixed collection of bacteria.
- 6- In serous OM most of the effusions "exudates" are sterile (negative on culture).
- 7- Serous OM represents a form of chronic OM with non purulent secretions.
- 8- A patient with OM will present with fever, irritability, earache and red bulging tympanic membrane.
- 9- Chronic OM can result in permanent hearing loss.
- 10- OM can be diagnosed by:
  - Clinical examination by otoscope
  - Tympanometry
  - Gram stain and culture
- 11- Acute OM should be treated with empirical therapy immediately even before investigation in infants and immune-compromised patients.
- 12- Amoxicillin used as empirical therapy for OM; if resistant we use 1st G Cephalosporin or Macrolides.
- 13- Meningitis, Hearing loss, Tympanic membrane perforation and Mastoiditis are the most common complications resulting from OM.

## Microbiology of Acute Pyogenic Meningitis:

1. Common causative organisms in adults are *N. meningitides*, *S. pneumonia*, and *H. influenza*.
2. Common organism in the neonate is *E.coli* & in children is *H.influenza*
3. Common signs and symptoms are Fever, Headache, Stiff neck, Nausea & vomiting and Sensitivity to light.
4. Diagnosis is reached :
  1. Clinically.
  2. Specimen:
    - Blood work [CBC] + [Blood culture]
    - CSF sample [ Lumbar Puncture ]
  3. Analysis of cells, protein, glucose, culture.
5. In the SCF analysis the glucose will be dropped & the protein will be high.

6. The **drugs of choice** for treating meningitis is **ceftriaxone** in all age group & **if we suspected S.pneumoniae**, add **Vancomycin**. If the Pt. is **neonate** or elderly **use ampicillin + Gentamicin**
7. **Prevent the infection by vaccination against N.meningitidis and all its groups except Group B. N. meningitides.**

## **Viral Infection of CNS:**

- ◆ Aseptic meningitis is caused by enteroviruses:
  - **Enterovirus.**
  - **Poliovirus.**
  - **Coxsackivirus.**
  - **Echovirus.**
  - **And also cause by HSV (type 2)**
- ◆ Infection is more common during **summer** in **children**, and **low hygiene is a risk factor.**
- ◆ They spread mainly by **oral-fecal route.**
- ◆ **90-95%** of **poliovirus infections** are **asymptomatic** with no illness, only **1-2%** of infections manifest as **major diseases** (Aseptic meningitis or Paralytic poliomyelitis) & about 4-8% are minor illness with no CNS involvements.
- ◆ Pathogenesis of **poliovirus** is from **blood** or **peripheral nerves** then it enters the CNS and damage the **AHCs** which might lead to paralysis.
  - Lab diagnosis of enteroviruses include:
  - **Isolation of virus (stool sample is taken).**
  - **CSF analysis.**
  - Serology (limited value – not very useful).
  - **Enteroviruses RNA detected by RT-PCR**

<b>Aseptic meningitis (CSF analysis )</b>	<b>Findings</b>
<b>color</b>	<b>Clear</b>
<b>Cells/mm<sup>3</sup></b>	<b>increase 100-1000 (mainly lymphocytes)</b>
<b>Protein</b>	<b>Normal/slightly high</b>
<b>Glucose</b>	<b>Normal</b>

- ◆ prevention of **polio** is by taking a vaccine :
    - **IPV (killed): given IM/S.C**
    - **OPV (live): given orally (contraindication to immune-compromised patients)**
- 
- ◆ **Viral encephalitis** is caused by:
    - **Enteroviruses**

- Herpes viruses (type 1)
- Rabies viruses
- Arboviruses (e.g. West Nile virus)
- ◆ Negri bodies are diagnostic feature of rabies encephalitis.

	HSV encephalitis	Rabies encephalitis	Arboviruses encephalitis
	ds DNA enveloped	Ss RNA enveloped (bullet shape)	Ss RNA enveloped - e.g. West Nile virus
<b>Reservoir</b>	Human	Dogs, cats and bats ( by bite)	Wild birds and mammals (mosquitoes are vectors)
<b>Diagnosis</b>	<ul style="list-style-type: none"> <li>- <b>MRI</b></li> <li>- <b>CSF analysis</b> (lymphocytosis, ↑ protein)</li> <li>- <b>PCR</b></li> </ul>	<ul style="list-style-type: none"> <li>- <b>IF</b> (detection of virus antigen)</li> <li>- <b>PCR</b> (rabies RNA in saliva)</li> <li>- <b>Histopathology</b> (<b>negri bodies</b>)</li> <li>- <b>Virus cultivation</b></li> </ul>	<ul style="list-style-type: none"> <li>- <b>Isolation</b> (Gold standard)</li> <li>- <b>IF and ELISA</b> (IgM antibodies)</li> <li>- <b>PCR</b></li> </ul>
<b>Treatment/prevention</b>	-Acyclovir	-Human anti-rabies immunoglobulin -Human Diploid Cell Vaccine	-Tick-borne encephalitis vaccine -Japanese encephalitis vaccine

# Fungal Infection of the Central Nervous System:

- Fungi can reach CNS by: **Hematogenous spread** or Local extension (paranasal sinuses, ear, orbits). And sometimes by Traumatic introduction (surgery, head trauma, lumbar puncture)
- Several fungal agents can cause CNS infections it could be: Yeast (Candida , Cryptococcus) , Mould (Aspergillus , Zygomycetes, Rhinocladiella mackinziei) or Dimorphic (Histoplasma)
- Cryptococcal Meningitis “Cryptococcus neoformans”: it’s capsulated yeast that **found mainly in AIDs patients**, it reach the CNS by **inhalation** & then cause **meningitis only**.
- Candidiasis “Candida albicans”: it usually diagnosed if the patient has catheter and fever with unresponsive to antibacterial agents, it **reach** the CNS mainly **by Catheters & Surgery**, and it also **cause both cerebral abscesses & meningitis**.
- Aspergillosis “Aspergillus fumigatus”: found mainly in patients with hematological malignancies or had cancer **chemotherapy or any transplantation**, it **reaches the CNS hematogenously or by adjacent sinuses**. It cause single or multiple **brain abscesses only**.
- Zygomycosis “Rhizopus”: it grow in acidic PH that’s why being **Diabetics with ketoacidosis is a risk factor**, the **Rhinocerebral Zygomycosis can reaches the CNS by starting as sinusitis**. It usually present with Facial edema & Angiotropism
- Pheohyphomycosis: it caused by dematiaceous fungi (such as: Rhinocladiella mackinziei). **It cause both brain abscesses & chronic meningitis**
- Lap Investigation:

CNS infection	Direct microscopy	Culture	Serology*
<b>Cryptococcal meningitis</b>	Yeast cells <b>Capsulated (india ink)</b>	Yeast	<b>cryptococcal Ag</b> (capsule) Latex agglutination
<b>Candidiasis</b>	Yeast cells and pseudohyphae	Yeast	Mannan Ag (cell wall)
<b>Aspergillosis</b>	Septate branching hyphae	Hyaline mould	Galactomannan Ag
<b>Zygomycosis</b>	Broad non-septate hyphae	Hyaline mould Fast growing	<b>No serology available</b>
<b>Pheohyphomycosis</b>	Brown septate hyphae	Dematiaceous mould	



- To treat Cryptococcal meningitis, Candidiasis, Zygomycosis we mainly use **Amphotericin B**.
- The drug of choice to treat **Aspergillosis** is **Voriconazole**

## **Cerebral Malaria:**

- Malaria Species: ***Plasmodium falciparum***, ***Plasmodium vivax***, ***Plasmodium ovale*** & ***Plasmodium malariae***
  - The main complications of malaria are
    - **Coma**, Convulsion, Renal failure, cerebral malaria, **Anemia** & Pulmonary edema.
  - Cerebral malaria is an unrousable coma with Positive blood film → you will see some bodies of P.falciparum (**Falciparum malaria**).
  - **There is 2 main pathophysiological mechanism:**
    - Anemia
    - Impairment of microcirculations.
- \*\* Both of them leading to tissue hypoxia.**
- **The main pathological stage is blood stage.**
  - The main clinical features of Cerebral Malaria are:
    - **Opisthotons.**
    - **Disconjugate gaze.**
  - **Cerebral Malaria management is done by:**
    - Diagnosis → **Hypoglycemia & Meningitis.**
    - Treatment
      - Antimalaria drugs
      - General management of coma → nursing on side, insert urethral catheter, fluid intake & monitor level of consciousness.

## Cerebral TB and Chronic Cerebral infection:

- The most important causes of chronic bacterial cerebral and meningeal infections in KSA are: TB & Brucellosis.
- TB & Brucellosis can be differentiated through history, symptom, occupation, affected organs & CSF findings.
- **Brucellosis** affects people who are in contact with domestic animals or those who consume raw milk and milk products.
- **Brucellosis** present with **fever (> 3 weeks) & the patient feels ok between fever attacks.**
- **Tuberculosis** is caused by M.tuberculosis, the patient is presented with fever for long time and coughing blood when the chest is affected.
- If the neurological syndrome exists for > 4 weeks it usually diagnosed as **Chronic** Cerebral or Meningeal infection, in acute infection we have rapid onset of symptoms & signs.
- In **acute infections** there is increased WBC with **predominance of polymorphs**, but in **chronic infection** the differential cell count shows **lymphocytosis.**
- In case of chronic cerebral or meningeal infection you will notice increased intracranial pressure, increased protein level and reduced glucose level and lymphocytosis.
- Z-N Stain can show AFB of T.B while modified Z-N can show Nocardia and we use India ink for Cryptococcus neoforman.
- Gram stain and culture can help differentiate between bacterial and viral infection, Specially the CSF culture to diagnose Brucella, T.B.
- To Treat TB we use: Isoniazide (INH), Rifamycin , Ethambutol, Pyrazinamid “ 2 months “ then only INH & Rifampicin “ 4 – 6 months “. In case of Brucellosis we use: Rifampicin & Cotrimoxazole.

Notice that we use Rifampicin to treat both TB and Brucellosis

## Cases:

### Case1:

A 10 years old male presented with fever, irritability, earache & history of URTI. On otoscopic examination, a red tympanic membrane was shown.

He was diagnosed having Otitis media. For treatment he was given Amoxicillin

What are the most likely pathogens?

S.pneumoniae

H.influenzae

### Case2:

People who want to perform Hajj this year, they should be vaccinated against:

1. N. meningitis.
2. S.pneumoniae
3. H.influenza

### Case3:

Newborn child was diagnosed with Meningitis, the most common causing organism is:

1. E.coli.
2. N.meningitis.
3. S.aureus.

### Case4:

21 years old male had a traffic accident, he suffered from internal bleeding, the doctors managed him by splenectomy, and the doctor also told him that he has a risk to have Meningitis, what is the most common causing organism:

1. N. meningitis, S.pneumoniae, H.influenza.



2. E.coli.
3. S.epidermidis

## Case5:

Neonate was diagnosed with Meningitis; he should be managed by giving him:

1. Ampicillin + Gentamicin.
2. Ceftriaxone + Vancomycin.

## Case6:

A 9 years old male presented to the ER with fever, headache & vomiting. On examination he showed neck stiffness. CSF sample was taken, it was clear with elevated WBC (lymphocytes), glucose & protein levels were within normal range.

The pt was diagnosed with aseptic meningitis. What is the best sample to take for Isolation?  
Stool.

## Case7:

A 20 years old female, was exposed to a dog bite, presented with headache, fever, malaise, nausea & vomiting. On microscopic examination an intracytoplasmic inclusions (Negri bodies) was shown.

The pt was diagnosed having viral encephalitis. What is the most likely virus causing encephalitis in this case?

- Rabies virus.

## Case8:

A 33 –years – old diabetic male comes to emergency with **facial edema and loss of his vision**. Few days earlier, he suffered from **sinusitis**. Direct microscopy showed **broad non – septate hyphae** .in addition, there was **no serology** available. The disease was rapid and progressive

**What organism is likely the cause of this disease?**

- Zygomycetes e.g. **Rhizopus**.

## Case9:

Patient presented with **Opisthotons**, **Disconjugate gaze** and fever, he is having:

1. Meningitis.
  2. **Cerebral malaria**.
- The most common complications are:
    - Coma, severe anemia, acute renal failure and acute pulmonary edema.

## Case10:

- A 30-year-old woman presented with headache, vomiting and fever of (104°F) [40c] less oriented and attentive. Lateral rectus palsy (abducent nerve is affected) along with bilateral papilloedema.
  - Neck rigidity and kernig's sign were positive.
  - Chest x-ray showed miliary shadows in both lungs.
  - CSF revealed **elevated opening pressure**, proteins **248 mg/dl** (normal is 15 to 60 mg/dL), sugar **34 mg/dl** (corresponding blood sugar was 98 mg/dl); 204 cells/ml, **15% polymorphs rest lymphocytes**. CT head showed multiple small enhancing lesions in brain parenchyma.
- ✓ The patient was given **antituberculous** treatment and corticosteroids. She showed significant improvement in all her symptoms after 15 days.