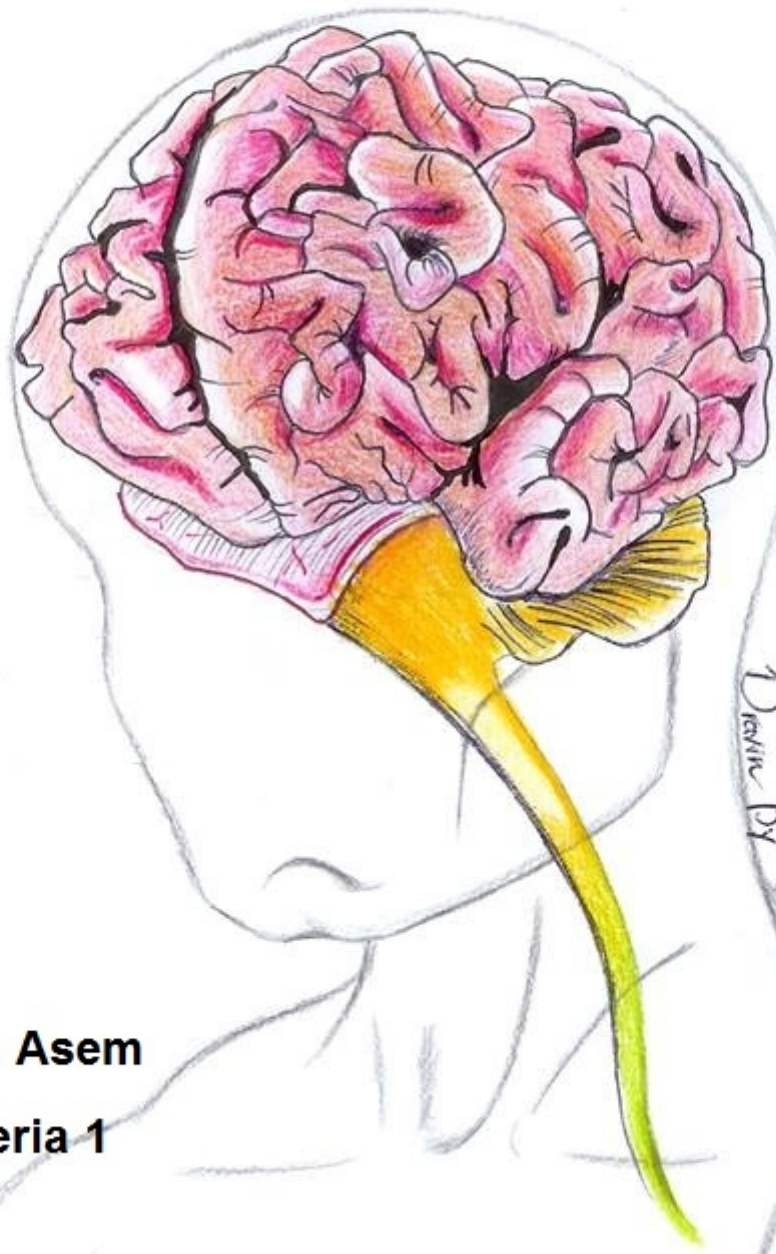


CENTRAL NERVOUS SYSTEM

- Handout
- Sheet
- Slide

- Anatomy
- Physiology
- Pathology
- Biochemistry
- Microbiology
- Pharmacology
- PBL



Drawn By Tariq Bushraaq...

Dr. Name: **Dr. Asem**

Lec #: **Bacteria 1**

Bacterial Infection of Central Nerve System

3rd Year Medical Students

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Meningitis & Encephalitis-1

- Bacterial Infections of the brain and spinal cord cause dangerous inflammation.. **Encephalitis/ Meningitis** or both **Meningoencephalitis**
- Acute bacterial meningitis is associated with a wide range of symptoms, including fever, headache, neck stiffness, confusion, vomiting, photophobia..within few hrs.. Mild/chronic..**mild and confusing symptoms.**
- **Meningitis** results from infection of meninges.. often through blood stream...Less respiratory tract or other body sites infection like **intravascular catheter**
- **Meningitis** is mostly caused by viruses (95%), bacteria (2-5%), Fungi (1%).. Affect all ages.. majority Infants & children aged < 5 years .

Common Cause of Acute Bacterial Meningitis

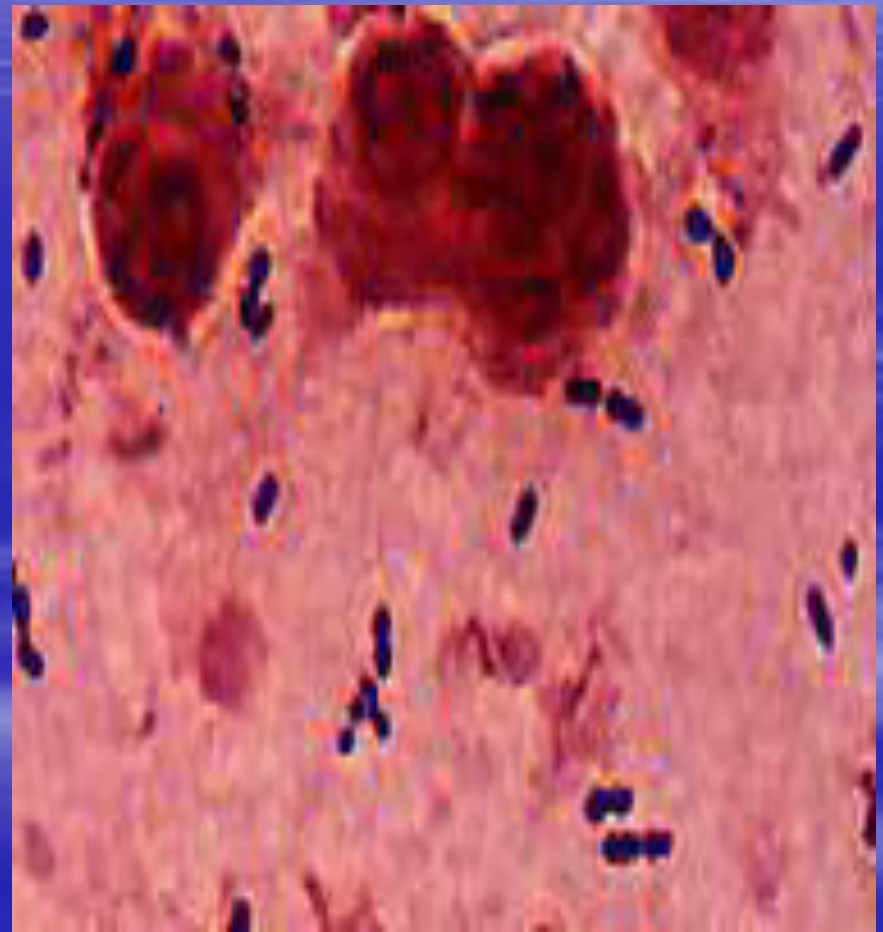
- **Pneumococcal meningitis** / *S. pneumoniae*.. Gram+ve diplococcus.. Alpha-Hemolytic..Large polysaccharide capsule..numerous serotypes..
- Most **Pneumococcal invasive infections** endogenous.. More serious than all causes of bacterial meningitis.. High mortality without rapid diagnosis & treatment
- **Pneumococcal meningitis** followed acute /sub acute pneumonia, septicemia, middle ear and nasal sinus infections
- **High risk factors:** Children under age 5-year, elderly persons with immunodeficiencies, malignancy, sickle cell anemia, diabetes melitlitus, splenectomy, ischaemic heart disease..**severe viral infections..**
Measles, Influenza

S. pneumoniae-2

- **Treatment:** Most *S. pneumoniae* strains in developing countries are Highly Penicillin-R, less resistance to erythromycin & tetracycline.. Mostly susceptible to vancomycin & Cefotaxime / ceftriaxone
- **Prevention: Pneumovax/Adults** contains 23-serotypes polyvalent polysaccharide bound to a protein, protection 60%–80% for one-year.
- **Prevenar /Children** (2 months to 2 year).. contains 13-selected polysaccharides serotypes.. 2 doses .. 90% protection.. Each 2-3 years.

S.pneumoniae Lab diagnosis

Blood culture-Optochin/ Gram-stain



Meningococcal meningitis

- ***Neisseria meningitidis***: Gram-negative diplococci..
- Serotypes A, B, C, Y, W-135.. Nasopharynx.. Human only host.. Few% Respiratory Healthy carriers
- Highly susceptible to harsh conditions outside body.
- **highly contagious disease**.. Causing outbreak in schools, military camps. Endemic in tropics & subtropics countries in Africa and South America.
- **High-risk groups** include infants & children aged of 6 months - 3 year, Young adults & persons with suppressed immune systems..
- Non-pathogenic *Neisseria* species in nasopharynx contribute to host protection.

- **Clinical features:** Mild sore throat..Headache, High fever, Neck stiffness, vomiting within 2 days.. Later without treatment.. Thrombosis small blood vessel, Disseminated Intravascular Coagulation (DIC), Hemorrhagic Skin Rash, Adrenal hemorrhage, Circulatory collapse & Death within hours.
- 10 -15 % of cases are fatal.. Another 10-15 % causing brain damage and other serious side effects.
- **Capsular polysaccharide vaccine** > 2 years & more
- **Treatment:** Generally low percentage of resistance to Penicillin, Cefotaxime / Ceftriaxone.. Rifampicin should be used in treatment of carriers/contact persons.

N.meningitidis-Pili

Gram-stain/intracellular



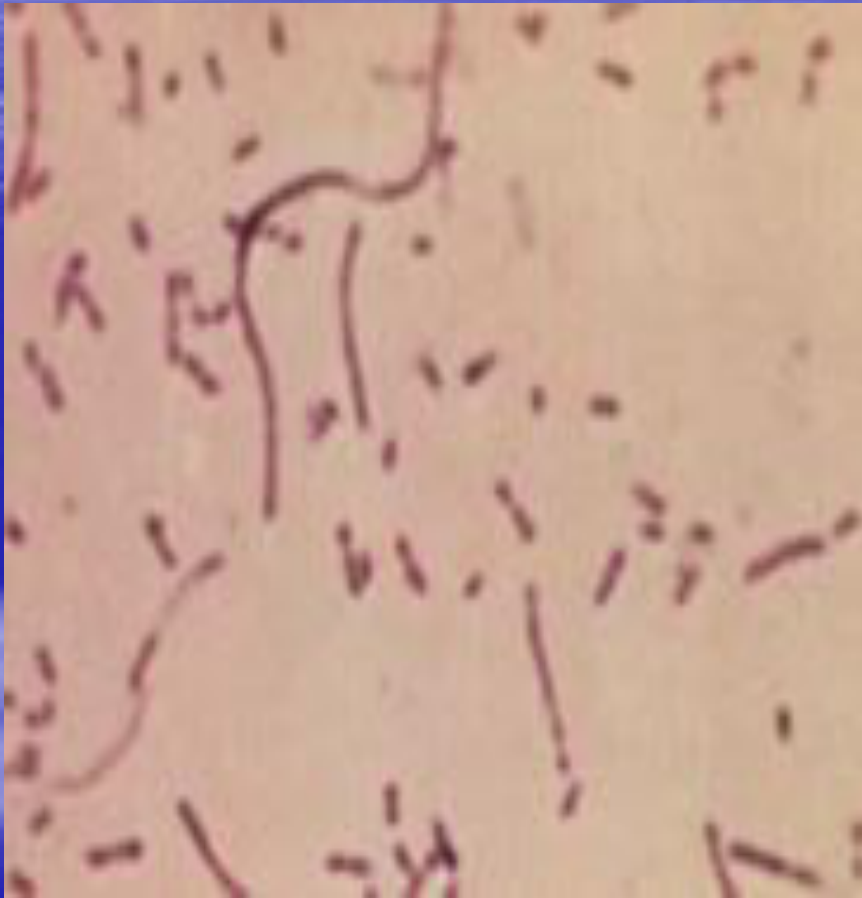
Haemophilus *influenzae*

- **H. influenzae** Nasopharynx.. Low % Healthy carriers for encapsulated type b.. More virulent & invasive than Other capsulated & non-capsulated strains.. High-risk children ages 5 months-5 years.. Rare adults.
- **Acute meningitis followed** .. Mild sore throat / pneumonia, chronic bronchitis, empyema, sinusitis, otitis media, conjunctivitis in children
- Most common form of bacterial meningitis among young children worldwide before introduction **Hib vaccine 1990**.. reduced the incidence of meningitis & carrier rate up to 95%.. Immunization children at age 2, 4, 6 months. **Treatment:** Ceftriaxone, Cefotaxime

Virulence of Common meningitis Pathogens

Virulence Factors	<i>S. pneumonia</i>	<i>N.meningitidis</i>	<i>H. Influenzae</i> Type b
Capsule	+ Large	+ Thin	+ Thin
IgA Protease	+	+	+
Pili	-	+	+
Endotoxin & outer membrane proteins	-	+	+

H. influenzae/ Coccobacilli-Short filaments - Listeria monocytogenes



Less Common bacterial Meningitis

- **Group B Hemolytic Streptococci (GBS)..**
S. agalactiae .. Colonize 10-30% adult women vagina/ intestine.. common cause acute fatal **neonatal pneumonia/ early-onset sepsis & meningitis.**
- Infection is spread to infants mostly during delivery.. often swallow amniotic fluid during delivery.. higher among preterm infant.
- Any rupture of uterus following delivery may cause acute **Endometritis.. Septicemia, Puerperal fever..**
- **Lab Diagnosis+ Treatment:** CSF + Blood Culture ,Vaginal and rectal swabs women before delivery
- Amoxicillin, 2G-Cephalosporins

Listeria monocytogenes

- **Gram-positive intracellular small bacilli**.. Common in animals intestine.. Human Infection by contaminated milk/ dairy products.. Most infection found in immune suppressed host.
- **Colonizing intestine**.. May cause enteritis, mesenteric lymphadenitis, blood sepsis & meningitis in all ages.
- Rarely colonize female genital tract.. can cross the placental barrier..causing **abortion** in pregnant women or **sepsis-meningitis** in neonatal..High fatality without treatment..Difficult to detect infection.
- Lab Diagnosis+ Treatment: Blood /CSF Culture, Treatment: Co-trimoxazole, floroquinlones, aminoglycosides.

Less Common bacterial Meningitis-2

- **Enteric Bacteria**: Klebsiella, Enterobacter, Pseudomonas aeruginosa.. Gram-ve bacilli.. Following surgical procedure in spinal cord, Sepsis, Burn cases.. Mostly **Nosocomial Infection, Multidrug Resistance**
- ***E. coli*** : Common cause of sepsis & meningitis in **new born baby**.. Infant < 6 months.
- **Brucellosis**: Common *B. melitensis*.. intracellular Gram-ve coccobacilli.. Septicemia.. few % associated with chronic meningitis & abscess in any body part .
- **Treatment**: combination Rifampin+Monocycline or ciprofloxacin.. Children co-trimoxazole .. 8 weeks.

Chronic meningitis & Brain Abscess-1

- **Mycobacteria tuberculosis**Less other types .. Acid-fast bacilli ..causes meningitis in young children with malnutrition more than adults following disseminated tuberculosis.. Less following lung tuberculosis.
- Culture growth: 2-6 weeks
- **Nocardiosis:** *N. asteroides*, Gram+ve coccobacilli slightly Acid-fast bacilli, Common in soil.. Inhalation, Chronic Lung lesions.. Immune suppressed..Chronic meningitis with brain abscess
- Culture growth :1-2 weeks
- Treatment: ciprofloxacin, Co-trimoxazole

Chronic meningitis & Brain Abscess-2

- **Syphilis:** *Treponema pallidum*.. Tertiary stage or Congenital syphilis may cause **Neurosyphilis** with meningitis .. Diagnosed by serological test.. Difficult to be cured..Fatal
- **Lyme disease:** *Borrelia burgdorferi*.. Transmitted by Tick bites from animal skin/Deer.. skin rash mild sepsis.. Later involve joints, heart, CNS.
- **Complication** Meningitis-Encephalitis.. Common in USA, Canada, North Europe.
- **Lab Diagnosis:** Dark-field microscopy, Special fluid culture, Specific antibodies (IgG, IgM) ELISA, PCR
- Macrolides, Doxycyclines, Ceftriaxone

Fungal meningitis-1

- **Cryptococcosis:** *C.neoformans*..& other species..
This encapsulated yeast is found in the environment worldwide, particularly in soil contaminated with **bird droppings**. Enters the body most commonly through inhalation, start as lesion in sinuses/lung tissues. Infection develop slowly often in **immuno-suppressed patients**.. advanced AIDS, Lymphomas, Long-term corticosteroid & Toxic drugs therapy.
- Cryptococcus may spread from lung to meninges, skin, prostate gland.. Fatal without treatment.
- **Cryptococcal meningitis & brain abscess** develop very slow, chronic, CNS vague symptoms, mild/sever headache, fever. Clinical & laboratory diagnosis.

Fungal meningitis-2

- **Candidiasis**: *C.albicans*, *C.glabrata*, Others.. Lung.. blood Infection.. Rare meningitis.. compromised host.
- **Histoplasmosis**: *H. capsulatum*, **Blastomycosis**: *B. dermatitidis*.. Inhalation, mostly asymptomatic infection
Diamorphic fungi (Yeast & filamentous forms).. Lung, Systemic, Oral mucosa ..Skin lesions..Meningitis, Immune deficiency, Both infection may ended in chronic meningitis.
- **Lab Diagnosis**: Direct CSF exam, Culture Sabouraud Dextrose agar, Blood agar.. Incubation 1-4 weeks.
- Serological methods are not useful.
- **Treatment**: Systemic Amphotericin B+ Flucytosine, fluconazole No Vaccine.

Laboratory Diagnosis of Bacterial meningitis

- **All CSF specimens** should be sent rapidly for the following investigation: WBC count, Level of glucose+ protein
- **Bacterial meningitis:**
- Cloudy fluid, glucose level \leq 40 mg/dL (normal: 45-85), Protein level $>$ 50 mg/dL (normal:15-45), numerous WBCs /predominance neutrophils $200 >$ 20000/uL
- **Fungal meningitis:**
- Mild/not cloudy fluid, little change in glucose + protein levels.. 100-1000 uL WBCs.. mostly Lymphocytes.
- **Tuberculosis meningitis:** Mild cloudy fluid, little change in glucose + protein levels.. 100-1000 uL WBCs/ Lymphocytes
- **Late CNS Syphilis:** Clear fluid.. Normal Glucose.. slight elevation Protein.. Few WBCs

Bacterial Antigen Test

- **Direct Antigen Tests** are available to detect bacterial antigens in the CSF for diagnosis of *S. pneumoniae*, *N. meningitidis*, *H. influenzae* type b, group A, B *Streptococcus*, *Listeria*, *Mycobacteria*
- These tests should be confirmed by **positive Gram-stain or culture**
- Therefore, negative results for a specific bacterial antigen do not rule out bacterial meningitis.
- **Molecular methods (PCR)** detect bacterial DNA now available mostly in reference laboratories.