FACULTY OF MEDICINE
MANSOURA NATIONAL UNIVERSITY

MICROBIOLOGY

Bacterial Meningitis

Meningitis:

Inflammation of the meninges (protective membranes covering the central nervous system).

Clinical types of meningitis:

MCQ ☒ **Purulent meningitis:** infections of the meninges associated with a marked, acute inflammatory exudates usually caused by a bacteria.

☒ **Chronic meningitis:** caused by slow-growing agents (mycobacteria or fungi) that produce granulomatous inflammatory changes.

MCQ ☒ **Aseptic meningitis:** commonly caused by virus

Routes of CNS infection

A. Blood-borne spread:

☒ Most CNS infections result from blood-borne spread; for example, bacteremia or viremia resulting from infection outside the CNS may result in penetration of the blood–brain barrier.

☒ Examples of infectious agents that commonly infect the CNS by this route are *H. influenzae*, *N. meningitidis*, *S. pneumoniae*, *M. tuberculosis*, and viruses such as enteroviruses.

meningitis بيعمل virus أشهر

B. Direct spread:

☒ Occurs from adjacent infected focus such as middle ear infection (otitis media), mastoiditis, and sinusitis.

☒ Traumatic, surgical, or congenital lesions may give direct access. For example, fractures of the base of the skull

☒ The blood–brain barrier is the special defense mechanism of the CNS which serves to minimize passage of infectious agents and toxic metabolites into CSF

Causative organisms of acute purulent meningitis:

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- is usually caused by one of these organisms:
  - *Haemophilus influenzae* type b (Hib).
  - *Neisseria meningitidis (meningococci).*
  - *Streptococcus pneumoniae (pneumococci).*
  - *Listeria monocytogenes*
- Acute purulent meningitis is caused by encapsulated pathogen.
- However, many other bacteria can occasionally cause the disease if they gain access to the meninges.

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- N. meningitidis causes epidemic disease.

Bacterial causes according to the age group

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- **Neonates:** *Group B Streptococci, Streptococcus pneumoniae, Listeria monocytogenes, Escherichia coli.*
- **Infants and young children**: *S. pneumoniae, Neisseria meningitidis, Haemophilus influenzae type B (Hib), Group B Streptococci.*
- **Teens and young adults**: *N. meningitidis, S. pneumoniae*
- **Older Adults**: *S. pneumoniae, N. meningitidis. Hib, group B Streptococcus, Listeria monocytogenes*

Mode of transmission (How It Spreads)

- *Hib, S. pneumoniae and N. meningitidis:* Transmitted by droplet infection during coughing or sneezing
- Group B *Streptococcus, E. coli and L. monocytogenes:* Mothers can pass these bacteria to their babies during birth.
- *E. coli and L. monocytogenes* by eating contaminated food.

Neisseria

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- Gram-negative diplococci
- All Neisseria are oxidase positive
- The genus contains:
  - ☒ Many commensal species, most of which are harmless inhabitants of the upper respiratory and alimentary tracts.
  - ☒ Two pathogenic species:
    - ○ Neisseria meningitidis (meningococcus), a major cause of meningitis and bacteremia.
    - ○ Neisseria gonorrhoeae (gonococcus), the cause of gonorrhea

Neisseria meningitidis (Meningococci)

- **Morphology**

  Gram negative kidney-shaped diplococci ,non motile ,non-sporulated and have polysaccharide capsule Mcq مهم

- **Culture characters**
  - ☒ Aerobic, optimum temperature is 37°C.
  - ☒ 10 %Carbon dioxide enhances growth. Capnophilic
  - Fastidious ☒ Cannot grow on ordinary media
  - Mcq ☒ Grow on chocolate agar or selective media (Thayer-Martin media). Mcq
- **Antigenic composition of Neisseria meningitidis**
  - ☒ Polysaccharide capsule: classified into 12 serogroups according to the capsular polysaccharides
  - ☒ The most important disease-producing serogroups are A, B, C, W-135, and Y. Mcq

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☒ Group A strains can cause widespread epidemics.

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☒ The group B polysaccharide differs from that of the other groups in failing to stimulate the production of bactericidal antibody due to the similarity of its sialic acid polymer to human brain antigens.

☒ Recently, in sub-Saharan Africa, (X)

Virulence factors of Neisseria meningitidis

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1. Polysaccharide capsule (the most important)
   - antiphagocytic.
   - enables meningococci to resist complement-mediated bactericidal activity and subsequent neutrophil phagocytosis
2. Pili and outer membrane proteins for adhesion.
3. IgA proteases which inactivate IgA.
4. Endotoxin damage the ciliated cells.

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Type of endotoxin : Lipooligosaccaride

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Pathogenesis of meningococcal meningitis

☒ Source: Case or Carrier

☒ Meningococci are found in the nasopharyngeal flora of approximately 10% of healthy individuals

☒ Transmission:

- Transmitted by inhalation of respiratory droplets, then spread from the nasopharynx to blood causing bacteremia, endotoxemia and meningitis.
- Most common age of infection is between 6 months and 2 years of age, which is the time between loss of trans-placental antibody and the appearance of naturally acquired antibody

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- Complement deficiencies enhance risk

Clinical Manifestations

- Fever
- headache
- Stiff neck or back (rigidity)
- Nausea, and vomiting
- N. meningitidis infections may be accompanied by rash, thrombocytopenia, and other manifestations associated with endotoxemia.

Laboratory diagnosis of meningococcal meningitis

☒ **Samples:**

- CSF is the proper sample for diagnosis (3-10 ml), obtained by lumbar puncture under complete aseptic precaution.
- blood, or skin lesions samples can be also used for diagnosis.

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- nasopharynx: carrier or early in the disease.

☒ **CSF is examined for:**

- Physical (pressure , turbidity)
- chemical (protein, and glucose)
- Haematological (cells)
- Bacteriological characters (microscopy and culture)

A. In acute bacterial meningitis, CSF is

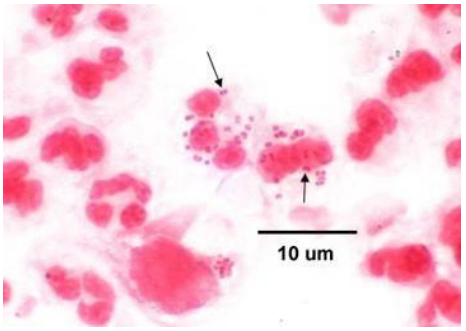
Mcq
- Turbid, under tension, low glucose value, high protein level, and contains polymorphonuclear cells

NB : Polymorphonuclear cells are not usually seen in normal CSF

B. Direct film

- Direct Gram smears of CSF in meningitis usually demonstrate the typical bean-shaped, Gram-negative diplococci inside and outside the polymorphonuclear cells.
- Detection of intracellular Gram negative diplococci is diagnostic of meningococcal meningitis.

C. Culture



1. Culture characters:

- Aerobic.
- Optimum temperature: 37 °C, with narrow temperature range (30-38°C), no growth at 22°C.
- 10% Co2 and moist atmosphere are required for growth.

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2. Media:

- cannot grow on ordinary media
- can grow on chocolate agar.
- Thayer-Martin media is selective media for Pathogenic Neisseria, contains antimicrobials which inhibit the growth of organisms other than pathogenic *Neisseria*.
  - **V**ancomycin kill most gram-positive bacteria
  - **C**olistin kill most gram-negative bacteria including the commensal *Neisseria* spp.,except pathogenic *Neisseria*
  - **N**ystatin kill most fungi.

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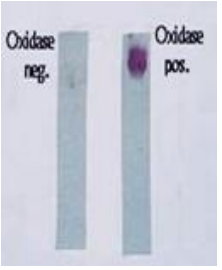
D. Biochemical reactions: MCQ



1. **Oxidase test:** all pathogenic Neisseria are oxidase positive.
2. **Sugar fermentation:** *N. Meningitidis* ferment glucose and maltose with acid production.

E. Serological test

Detection of meningococcal antigen

☒ Rapid diagnosis: may be obtained by detection of meningococcal antigen in CSF.

☒ Help if patient started antibiotics MCQ

☒ Latex agglutination available for N. meningitidis groups A,B,C,Y and W135 Mcq

Prevention of meningococcal meningitis

☒ **Meningococcal Vaccines**

- Meningococcal conjugate vaccines (MenACWY vaccines).
- Serogroup B meningococcal vaccines (MenB vaccines).

☒ **Chemoprophylaxis**

MCQ : For prophylaxis only

- In case of close contact with meningococcal meningitis case.
- Rifampicin or Ciprofloxacin is the chemoprophylactic agent of choice.
- Ceftrixone, an alternative

Treatment:

☒ Penicillin, Ampicillin and Ceftriaxone are used to treat meningitis

Mcq ☒ Ceftriaxone is the drug of choice during epidemics because of its antimeningococcal activity and good CSF penetration .

Laboratory diagnosis of other causes of bacterial meningitis

- **Sample:** CSF.
- **Direct film stained by Gram stain:** usually demonstrate inside and outside the polymorphonuclear cells the causative organism:
  - ☒ H. influenzae: Gram-negative cocco bacilli.
  - ☒ Streptcoccus pneumoniae : Gram - positive capsulsated diplococci
  - ☒ Listeria: Gram positive bacilli arranged in short chains.
  - ☒ Mycobacterial meningitis:
    - CSF is less turbid.
    - CSF contains lymphocytes; low glucose and high protein levels.
    - Direct film of CSF is examined by Ziehl-Neelsen stain to demonstrate acid fast bacilli

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Listeria monocytogenes

Natural habitat

- Listeria species are widely distributed in nature.
- Found in humans, animals, birds, fish, oysters & ticks.
- It is carried in intestinal tract of 2 to 12% of humans without any symptoms.
- It causes listeriosis in animals and humans.

Morphology:

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Small gram positive rods, arranged in short chains, non- sporing, non-capsulated, motile at 22–25°c, but are non-motile at 37°c as peritrichate flagella are produced at room temperature but not at 37°c . Mcq

Cultural characters: Mcq

- Grows on ordinary medium.
- Produces β- hemolysis on blood agar.
- The optimal growth temperature for is 30-35° C.
- Can grow slowly in the cold even at temperatures as low as 1°C, so can grow in contaminated food stored in the refrigerator .

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Virulence factors of L. monocytogenes

☒ **Growth at low temperatures:** L. monocytogenes can grow at low temperature so it can accumulate in contaminated food stored in the refrigerator.

☒ **Motility:** Which may help in attachment and penetration of the intestinal mucosa

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☒ **Adherence and Invasion:** Listeria can attach to and enter mammalian cells using a surface protein called internalin. The bacteria are then taken up by phagocytes.

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☒ **Facultative intracellular bacteria:** After engulfment, the bacterium may escape from the phagosome before phagolysosome fusion occurs by toxin, which also acts as a hemolysin (listeriolysin O).

Listeriosis

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Infection is transmitted by:

☒ Eating contaminated meat, vegetables, and milk products as L. monocytogenes can multiply at low temperatures, so it can contaminate food stored in the refrigerator

☒ Congenital transmission across the placenta (Intrauterine infection)

☒ Birth canal transmission can occur during labor by bacteria colonizing the genital tract of the mother.

☒ The risk of disease is increased at the extremes of life (in infants less than 1 month of age or adults over 60 years of age and immunocompromised individuals as well as women in late pregnancy .

Clinical features

☒ Range from mild influenza-like symptoms to meningitis

☒ Congenital listeriosis causes: abortion, stillbirth, delivery of infant with signs of congenital infection

☒ When infection is acquired during labor by bacteria colonizing the genital tract of the mother, meningitis occurs.

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☒ Immunocompromised hosts are more susceptible to serious generalized infections

Diagnosis of listeriosis

- Sample: CSF, blood, or focal lesions.
- Direct Gram stained smear: In meningitis, Gram-positive rods arranged in short chains in CSF
- Culture:

- Culture on blood agar produces β- hemolytic colonies. Mcq
- Blood and CSF culture reveals Gram-positive rods arranged in short chains . Mcq

Treatment:

- L. monocytogenes is susceptible to penicillin G, ampicillin, and trimethoprim/sulfamethoxazole, all of which have been used effectively.
- Ampicillin combined with gentamicin is considered the treatment of choice for fulminant cases.
- Erythromycin is also effective.

Control

- No vaccines are currently available
- Hygienic food processing and storage
- Individuals in high-risk groups should avoid uncooked food.
- A safe water supply and proper disposal of feces is important.

Viral meningitis

Also known as aseptic meningitis, is a type of meningitis due to a viral infection. It results in inflammation of the meninges (the membranes covering the brain and spinal cord).

Signs and symptoms:

- **Fever**
- **headaches**
- **Neck stiffness**.

In contrast to bacterial meningitis, symptoms are often less severe and do not progress as quickly.	**Nausea, vomiting, photophobia (light sensitivity), muscle aches and malaise due to meningeal irritation.** **Increased cranial pressure**	**In severe cases, people may experience concomitant encephalitis (meningoencephalitis), which is suggested by symptoms such as altered mental status and seizures.**

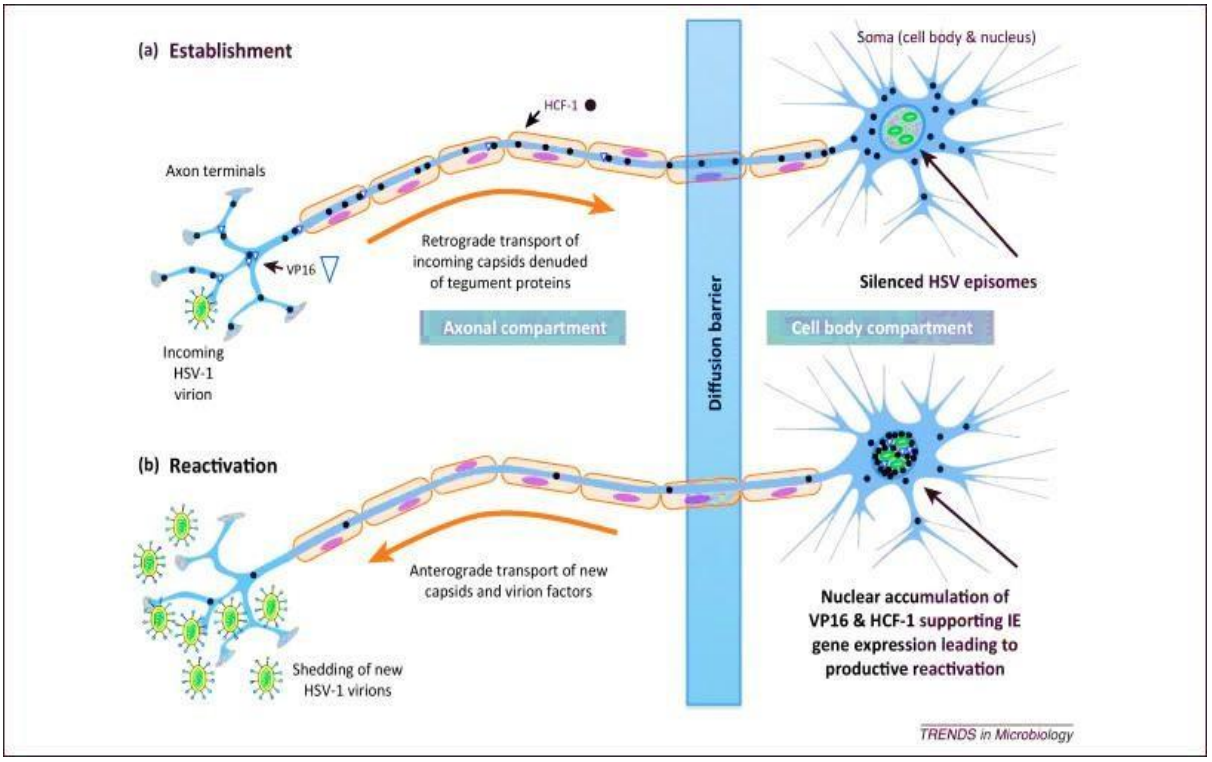
Causative agents of viral meningitis: مهمه

- Enteroviruses: Echovirus, Poliovirus, Coxsackie A virus
- Herpes: Herpes simplex virus type 1 (HSV-1 / HHV-1) or type 2 (HSV-2 / HHV-2), Varicella zoster (VZV / HHV-3); also causes chickenpox and shingles (herpes zoster), Epstein–Barr virus (EBV / HHV-4), Cytomegalovirus (CMV / HHV-5).
- Measles, Mumps, influenza.
- Human immunodeficiency virus (HIV).
- Lymphocytic choriomeningitis virus (LCMV).
- St. Louis encephalitis virus, West Nile virus.

Herpes viruses

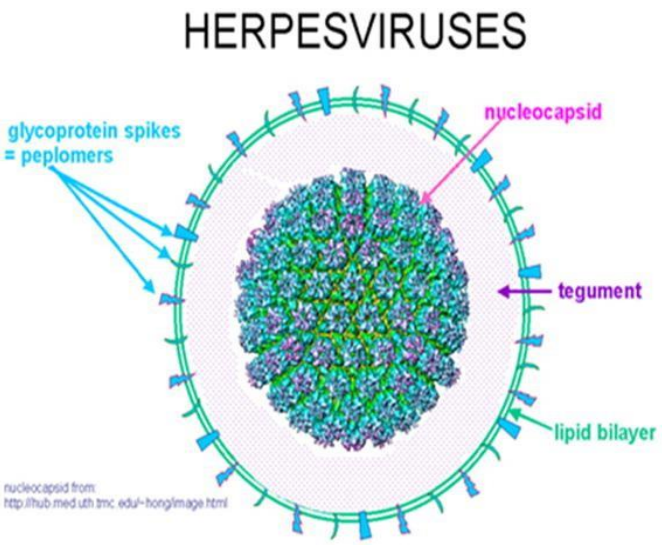
Eight human herpesvirus species are known.

- **All have the ability to enter a latent state following primary infection and to be reactivated at a later time.**



Structure:

- Virion: icosahedral
- Genome: Double stranded DNA, linear
- Envelope: Contains glycoprotein spikes



Classification of Herpesviruses

They have been divided into three subfamilies:

Alpha herpesvirinae	*Gamma herpesvirinae*	*Beta herpesvirinae*
Herpes simplex virus types 1 (HSV-1 or HHV-1)	Epstein-Barr virus (HHV-4).	Cytomegalovirus (HHV-5)
Herpes simplex virus types 2 (HSV-2 or HHV-2)	Kaposi's sarcoma-associated herpes virus (KSHV) or (HHV-8).	Human herpes viruses types 6 (HHV-6)
Varicella – Zoster virus (VZV or HHV-3).		HHV-7.

Herpes simplex viruses

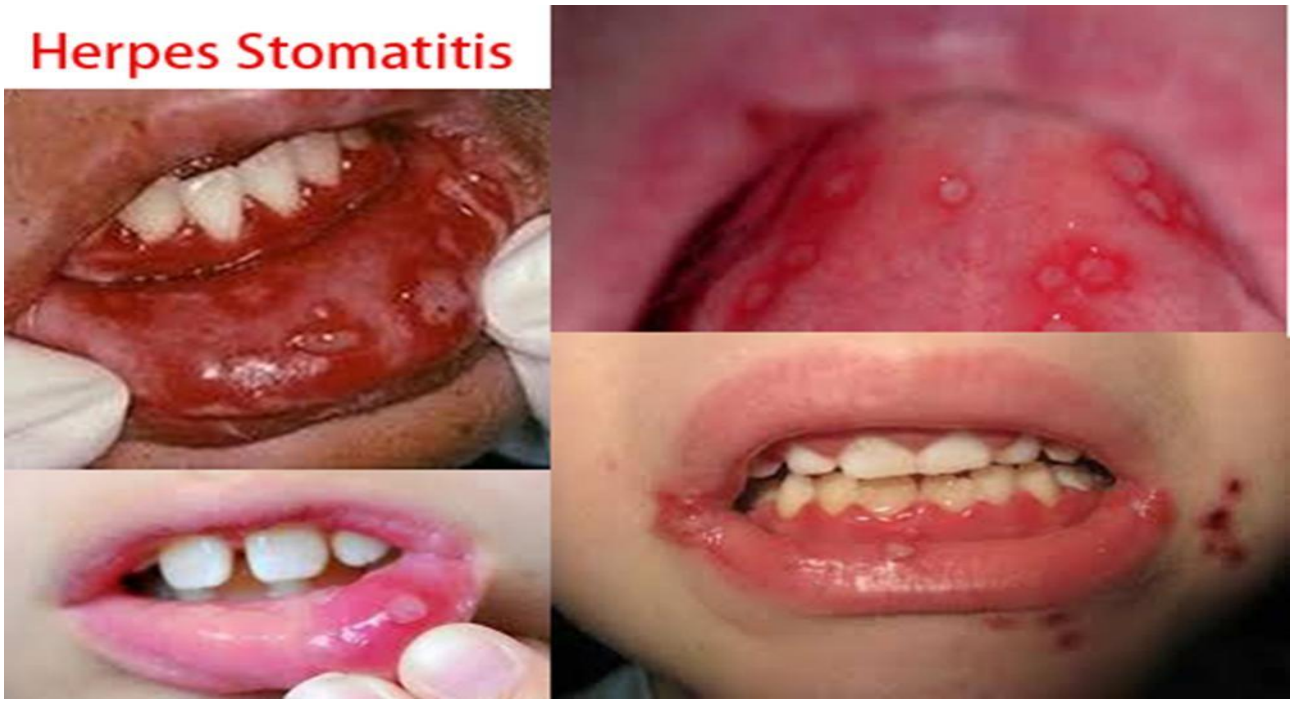
- There are 2 distinct herpes simplex viruses, type 1 and type 2.
- The two viruses cross-react serologically but some unique proteins exist for each type.

Transmission and pathogenesis:

	HSV-1	HSV-2
Mode of transmission	Primarily in saliva (kissing)	by sexual contact
• Multiplies locally in the mucous membrane or a braded skin causing vesicular lesion.		
Site of lesion	Mainly orofacial lesions	Genital lesions
However, both types of HSV can infect oral or genital mucosa depending on regions of contact.		

Clinical syndromes

	HSV-1	HSV-2
Primary infection	- Acute gingivostomatitis. - Herpes libialis (cold sores - Herpetic whitlow: is a pustular lesion of the skin of finger or hand of medical personnel. - Keratoconjunctivitis, encephalitis. - Disseminated infections, such as esophagitis and pneumonia in immuno-compromised.	- Genital herpes: vesiculo-ulcerative lesions on external genitalia as well as the cervix. - Neonatal infection: Originates chiefly from contact with vesicular lesions within the birth canal. Neonatal herpes varies from a severe generalized disease often involving the CNS, through milder local lesion to asymptomatic infection. - Aseptic meningitis.



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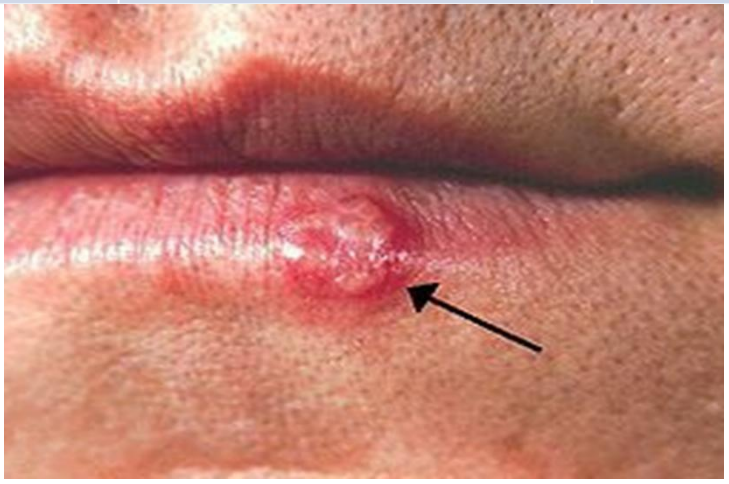
	HSV-1	HSV-2
Latency	• Trigeminal ganglia.	• Sacral ganglia.
Reactivation:	• In response to stimuli as common colds, hormonal changes and sunlight.	
	• Cold sores. • Keratitis	• Occur more frequently. • Often asymptomatic but still results in viral shedding.



Diagnosis:

- Detection of viral particles.
- Virus isolation from herpetic lesions
- Serologic diagnosis.
- Histological staining (Giemsa stain) of scrapings or swabs from the base of skin lesions.

Treatment:

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- Acyclovir, Famciclovir, and Valacyclovir are the treatment of choices.
- It shortens the duration of the lesion and decreases shedding of the virus.
- No drug treatment prevents recurrences.
- No effect on the latent state.

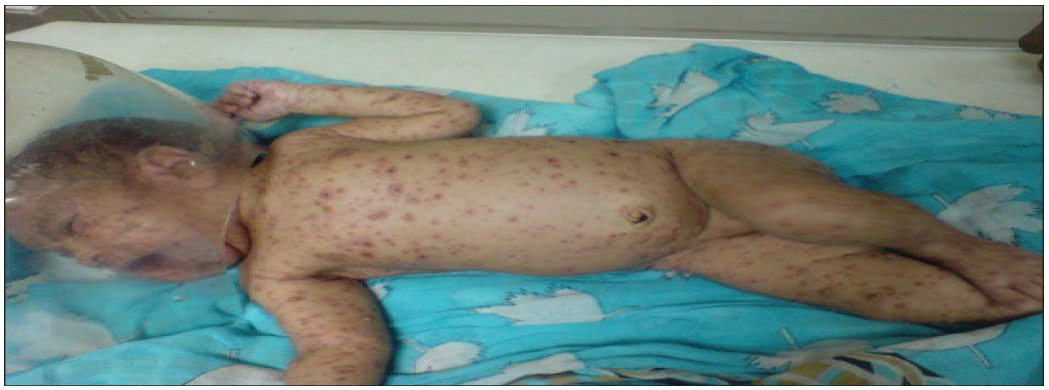
Varicella-Zoster virus

A. Primary infection: Varicella or chicken pox.

I.P: 14-21 days **Transmission and pathogenesis:** by droplets and by direct contact with the lesions	**Clinical findings:** A mild febrile illness with a characteristic vesicular rash which starts on the trunk and spreads to the limbs and face. Vesicles appear in successive waves so that the lesions of different stages are present together. **Complications of Varicella** are rare as meningitis, encephalitis and pneumonia.

Neonatal Varicella

- Early in pregnancy: fetal infection is uncommon, but can result in multiple developmental abnormalities (damage to the lens, retina and brain).
- Near the time of birth: fetal infection is more common and may exhibit typical varicella at birth or shortly thereafter.
  - The severity of the disease depends on whether the mother has begun to produce anti-VZV IgG by the time of delivery or not.



B. Latency

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- Trigeminal and dorsal root ganglia being most common sites of latency.

C. Reactivation (Zoster or shingles)

- Zoster is a sporadic disease of adults or immunosuppressed patients.
- Painful vesicles along the course of a sensory nerve of the head or the trunk (a belt of roses from hell). The pain can last for weeks and post-zoster neuralgia may exist.
- In immunocompromised, disseminated infection as pneumonia can occur.

Diagnosis:

- Mainly clinically. But, laboratory diagnosis can be done as on the same line used for HSV.
- A rise in antibody titer can be used to diagnose varicella, but is less useful in diagnosis of zoster, since antibody is already present.

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Treatment:

- No antiviral therapy is necessary for chicken pox in normal
- Systemic disease in immunocompromised patients can be treated with acyclovir.

Prevention:

- Varicella-Zoster immunoglobulin (VZIG): Can be used to prevent varicella and disseminated zoster in immunocompromised people exposed to the virus.
- VZV vaccine: a live attenuated vaccine, one dose is recommended for children 1 to 12 years of age. It prevents varicella, but zoster still occurs in those previously infected because the vaccine does not eliminate the latent state.

characters	Chicken pox (varicella)	Shingles (Zoster)
Symptoms	Fever itching rash	Painful vesicles along the course of a sensory nerve of the head or the trunk (a belt of roses from hell). The pain can last for weeks and post-zoster neuralgia may exist.
Rash	Itching Non grouped vesicles.	Painful Grouped vesicles
Complications	rare	More often

characters	Chicken pox (varicella)	Shingles (Zoster)
Definition	Contagious disease causes by infection with varicella-zoster virus	Infection of nerve and skin around them, caused by reactivation of Varicella-zoster virus
Age of the patient	All ages are susceptible but, much more common in children	Occur in adults
Transmission	By air droplet pathway.	After chicken pox, the virus remains latent in the nerve ganglia. Under certain conditions, the virus is activated
Type of the infection	Primary infection	Reactivation of old infection

Cytomegalovirus (CMV)

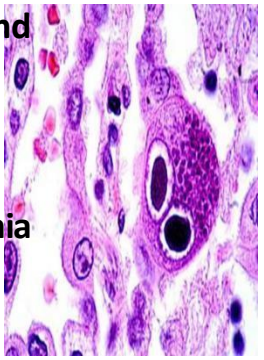
Transmission and pathogenesis:

Early in life:	Later in life:
- Transplacentally - within birth canal - Via breast milk.	- Saliva (most common route), - Sexually, - Blood transfusion - Organs transplant.

Clinical Significance:

A. Primary infection:

In healthy individuals may cause:



- **Asymptomatic infection with intermittent shedding in saliva and urine.**

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- **Infectious mononucleosis –like syndrome: similar to EBV infection but heterophil antibodies negative.**
- **Infection of immunodeficient patiants. Hepatitis and pneumonia are common,**

Mcq

- **Congenital infections: the most common intrauterine viral infection:**
- In-utero it causes abortion, still birth or cytomegalic inclusion disease. Mental retardation, microcephaly blindness and deafness.
- Perinatal infection from the birth canal or from the milk usually subclinical infection.

B- Latency and reactivation:

Mcq

- Latency is established in monocytes, macrophages and kidney.
- Repeated episodes of asymptomatic virus shedding over prolonged periods of times.

Diagnosis:

- Virus isolation in cell culture, CPE is 2-3 weeks (typical swollen and translucent cells with intranuclear inclusion bodies.
- Fluorescent antibody & histological staining of inclusions in giant cells in urine and in tissue. The inclusion bodies are intranuclear oval (owls eye) shape
- PCR for detection of CMV nucleic acid in tissues or body fluid as CSF.
- Serological test to detect rising IgG titer or IgM.

Treatment: Gancyclovir **Mcq**

Preventive measures:

- For pregnant women, the saliva and urine of infected children are the main sources of CMV infection.
- Secondary source is sexual contact.

Prevention behaviors:

Hygiene and behavioral measures that may be taken in order to reduce the viral spread:

- Hand washing whenever there is contact with a child saliva or urine,
- Do not sharing drinking glasses or eating utensils with young children,
- Do not kissing young children on the mouth or cheek.
- All women who are CMV seronegative and are planning to become pregnant or are pregnant should be informed about the risks of fetus infection and transmission.

Epstein Barr virus (EBV)

Mcq

- EBV is structurally and morphologically identical to other herpesviruses but is genetically different
- **Transmission** of EBV occurs by intimate contact with infected saliva.
- Viral replication occurs in oropharyngeal epithelium.
- Then some of progeny virus infect B lymphocytes → polyclonal B cells proliferation & non-specific increase of IgM, IgG and IgA.

- **Infected B cells are rejected by cytotoxic T cells which change in shape and appear as atypical T lymphocytes in peripheral blood**

Clinical Significance:

1. **Infectious mononucleosis:**
   - Disease is manifested by fever, headache, malaise,
   - Lymphadenopathy and increased level of liver enzymes

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   - EBV and malignancies:
   - Burkitt's lymphoma (jaw malignancy in African children)
   - Nasopharyngeal carcinoma.

3- Latency and reactivation: in B lymphocytes,

- reactivation, results in lytic cycle

Laboratory diagnosis:

- Blood smear to detect lymphocytosis.

- Detection of EBV in patieint's peripheral lymphocytes by DNA hybridization.

مهم - Detection of heterophile antibodies.

- Detection of EBV specific antibodies.
- Virus isolation from saliva.

No drug available to treat EBV. Vaccine is being developed.

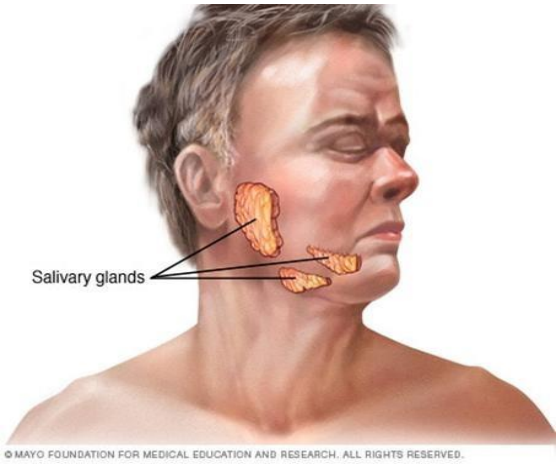
Mumps Virus

Mode of transmission:

Spread by the respiratory route, and has a relatively long incubation of (21 days).

Clinical picture:

It causes a febrile illness and inflammation of the salivary glands, classically the parotid and submaxillary glands.



Complications: SAQ

- **Aseptic meningitis:** fairly common complication. In about half of the mumps meningitis cases, parotitis will not be apparent.

- **Mumps meningoencephalitis:** is rare but a more serious development.
- **Orchitis:** can occur, more often after puberty, but is rarely followed by infertility. Other glandular tissue is very occasionally involved e.g.. pancreatitis, oophoritis or thyroiditis.

Diagnosis:

- Isolation of the virus from saliva, CSF or urine by culture on monkey kidney cells.
- Serologically: Confirmed Diagnosis by positive IgM antibodies by using CF, HI and ELISA.

Prevention:

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- Live attenuated virus vaccine given in MMR vaccine.

Measles Virus

Mode of transmission:

- Measles is **one of the most infectious diseases** known.
- **Transmission is by respiratory droplets.** After infecting the cells lining the upper respiratory tract, the virus enters the blood and spreads to the skin. The virus can also infect via the eye and multiply in the conjunctivae.
- **Incubation period:** 10-12 day.

Clinical manifestations:

- Prodromal phase is characterized by fever, dry cough, sore throat, conjunctivitis, and Koplik's spots (raised red spots with white centers in the mouth). Mcq
- After few days, the characteristic red, maculopapular rash starts on the head and then spreads to body.

Complications: SAQ

- Bronchopneumonia and otitis media (with or without secondary bacterial infections).
- Encephalitis occurs in ~1:2000 cases.
- Subacute sclerosing pan-encephalitis: It is a chronic infection in which the virus multiplies in the brain resulting in neurodegenerative disease.

Diagnosis

- Measles is easy to diagnose clinically. Laboratory diagnosis is rarely needed.

Prevention

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- Trivalent live attenuated vaccine (MMR) is usually given by subcutaneus injection. It is given at 12 – 15 months age. A single dose of the MMR vaccine gives around 90% protection against measles and mumps and 95-99% against rubella.

Treatment

- No specific drugs.
- Symptomatic treatment only.

Case scenario, Clinical Correlate, Practice points:

- A 16 year-old boy presented with a one week history of sore throat, fever and profound fatigue. Physical examination revealed a fever of 39.5°C, cervical lymphadenopathy, exudative pharyngitis and mild hepatosplenomegaly. His WBCs was 12.500/µl with 20% neutrophils, 24% monocytes, 42% lymphocytes, 12% atypical lymphocytes. A rapid serologic test performed at physician office revealed the presence of heterophil antibodies.
- What is the cause of this body illness?
- Define the most likely case diagnosis?
- What is the most likely causative organism?
- Identify the pathogenesis of the causative organism?

Viral and Fungal encephalitis

ILO1: - List the causative organisms of encephalitis (viral, fungal, bacterial).

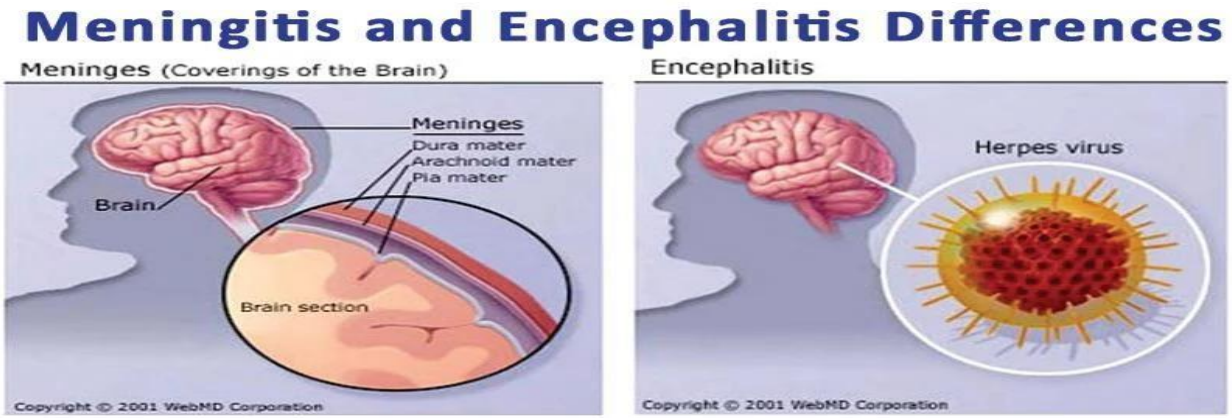
Definitions

Encephalitis

Inflammation of the brain parenchyma associated with clinical evidence of brain dysfunction usually a result of viral infection.

Meningitis: Inflammation of the meninges.

Meningoencephalitis: Inflammation of the meninges and brain parenchyma.



Causes of Encephalitis: Mcq

Viral:

1. **Common Viruses**

- Herpes Simplex Virus (HSV-1 & HSV-2): Most common cause, especially HSV-1. Can be severe and life-threatening.
- Varicella-Zoster Virus (VZV):
- Epstein-Barr Virus (EBV):
- Cytomegalovirus (CMV):

2. Arboviruses (Mosquito- or Tick-Borne Viruses)

- West Nile Virus: Leading
- Japanese Encephalitis Virus:
- Zika Virus: Can cause encephalitis, especially in newborns.
- St. Louis Encephalitis Virus:
- Tick-borne Encephalitis Virus:

3. Enteroviruses

- Coxsackievirus & Echovirus.:
- Poliovirus: Rare due to vaccination but can cause encephalitis.

4. Rabies Virus

5. Measles, Mumps, and Rubella Viruses

- Rare due to vaccination but can cause post-infectious encephalitis.
- Subacute Sclerosing Panencephalitis (SSPE): A late complication of measles.

6. Human Immunodeficiency Virus (HIV)

Fungal: Candida, Mucor, Aspergillus, Cryptococcus.

Bacterial: N. Meningitidis, Mycoplasma, Pneumococcus, Treponema pallidum.

ILO2: - Differentiate between primary and secondary viral encephalitis.

Viral Encephalitis

Primary Encephalitis:

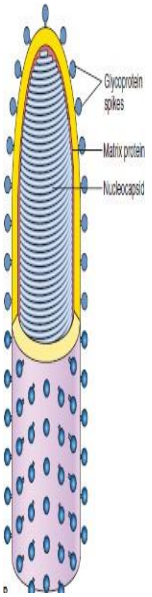
Mcq

- Direct infection of the brain & spinal cord.
- Eastern equine encephalitis virus, Western equine encephalitis virus (rare in Egypt due to cross immunity with West Nile Fever Virus) and Rabies virus and La Crosse encephalitis virus

Secondary encephalitis:

- An infection first occurs elsewhere in the body then travels to the brain. May results from a faulty immune system reaction to an infection elsewhere in the body (post-infection encephalitis).
- Measles, rubella and Varicella zoster Virus.

ILO3: - Identify morphology, pathogenesis, laboratory diagnosis, treatment and vaccination of rabies.



Rhabdoviruses

SAQ

- Rhabdo in Greek means 'rod-shaped'.
- Virus particles have unique bullet-shaped appearance.
- Nucleocapsid: (-) sense ss RNA associated with nucleoprotein.
- Virus has lipid enveloped with prominent glycoprotein spikes on surface (G protein- hemagglutinates RBCs) & the matrix protein lining the envelope.

Rabies Pathogenesis

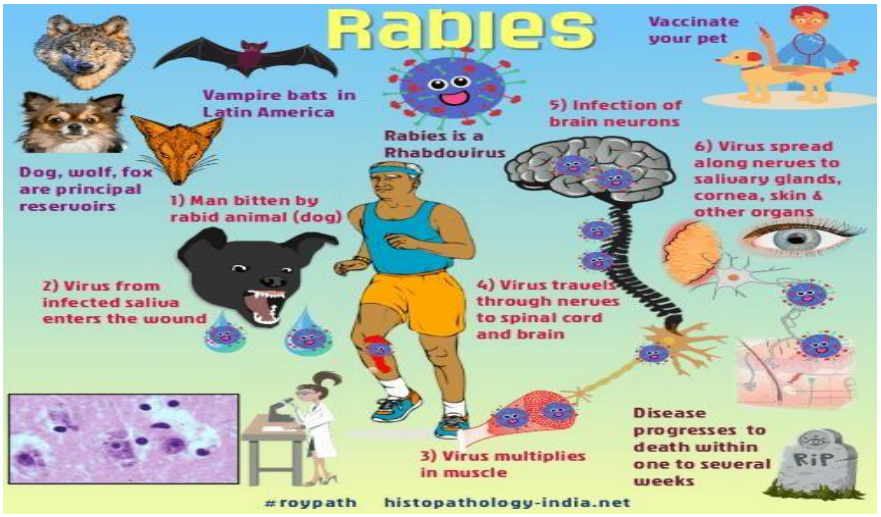
- Rabies **(the word is from the Latin for rage or madness).**

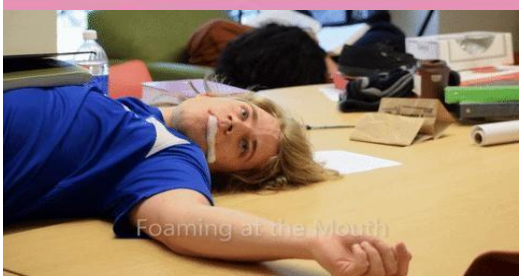
- Transmission **occurs by bite of an infected rabid animal (Rabies virus in dog's saliva, Zoonotic infection).**
- Normal hosts: **foxes, dogs, cats, bats, camels.**
- I.P: **varies from 3-8 weeks to 1 year depending on size & site of inoculation (head/face/neck vs. hands or feet).**
- Viral multiplication and spread

Viral entry occurs from wound or abrasion of skin (site of the bite) directly into blood.

Primary replication of the rabies virus occurs locally in muscle & connective tissue (no symptoms).

Virus then infects peripheral nerves {PNS} then travels along neuronal axons to CNS, to produce photophobia, hydrophobia, severe and fatal encephalitis. Few cases escape these severe consequences.





Rabies Diagnosis

- Specimen: saliva, serum, spinal fluid, and skin biopsies of hair follicles at the nape of the neck and infected brain (postpartum and in animals). **Gold standard test is : IF**
- Detection of viral antigens or nucleic acid: IF & RT-PCR.
- Histopathological diagnosis by detection of Negri bodies in the brain or the spinal cord.

- Isolation of the virus: infected tissue is inoculated into a suckling mice result in encephalitis & death.

Rabies treatment and Vaccination

In veterinary medicine: rabies vaccines are used as a preventive measure.

Vaccination of humans: **Mcq**

- Takes place mainly after exposure to a rabid animal (not to prevent infection but to moderate the severity of the disease).
- In the case of severe exposure: vaccination is often accompanied by injection of rabies immunoglobulin (IG).

SAQ

Rabies Human Vaccines

- ✓ Nerve Tissue Vaccine: Culture the virus on infected sheep, goat, or mouse brain then inactivated, causes post vaccination encephalitis.
- ✓ Duck embryo Vaccine: culture the virus in embryonated duck eggs then inactivated, 21 injections.
- ✓ Human diploid fibroblast vaccine: culture the virus on human fibroblasts then inactivated, safe, effective but expensive, 6 injections.

في البوربوينت مش في الكتاب

Arboviruses (RNA viruses)

- Transmitted primarily by Arthropod (mosquitoes, sand-flies, fleas, ticks, lice).e.g: Togaviruses
- There are 4 major clinical patterns of disease:-
  - ❖ No clinical illness.
  - ❖ Febrile systemic illness.
  - ❖ Encephalitis.
  - ❖ Hemorrhagic fever.

Arboviruses Causing Encephalitis

Togaviridae

- Eastern equine encephalitis virus.
- Western equine encephalitis virus.

Flavivirdiae

- Japanese encephalitis virus.
- St. Louis encephalitis virus
- West Nile fever virus.

Bunyaviridae

- La crosse encephalitis

Mosquito Borne Infections