



CNS REVISION



كلية الطب - جامعة المنصورة الأهلية
Faculty Of Medicine - MANSOURA NATIONAL UNIVERSITY



Lecture outline

- Bacterial meningitis
- Viral meningitis
- Viral encephalitis
- Fungal encephalitis

Meningitis

Clinical types of meningitis

- **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).
- **Aseptic meningitis**: commonly caused by virus

Routes of CNS infection

- Direct spread
- Blood borne
- droplet infection : Hib, S. pneumoniae and N. meningitidis
- vertical transmission : Group B Streptococcus, E. coli and L. monocytogenes
- food borne infection : E. coli and L. monocytogenes

Causative organisms of acute purulent meningitis

- Is usually caused by one of these organisms:
 - *Haemophilus influenzae* type b (Hib).
 - *Neisseria meningitidis* (meningococci).
 - *Streptococcus pneumoniae* (pneumococci).
 - *Listeria monocytogenes*
 - **encapsulated** pathogens cause **Acute purulent** meningitis
 - ***N. meningitidis*** causes **epidemic** disease.
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Bacterial causes of meningitis according to the age group

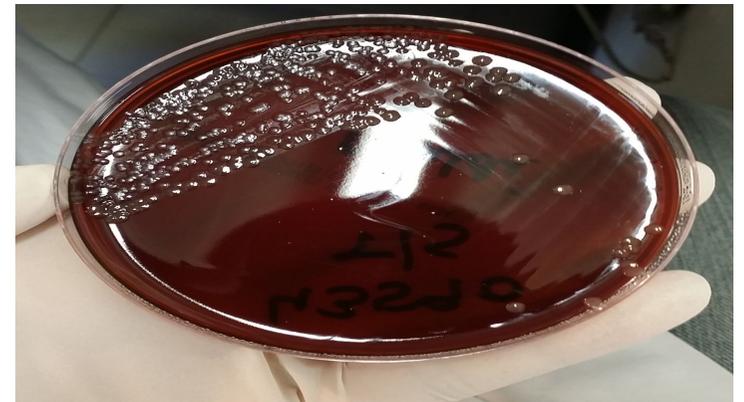
- **Neonates:** Group B Streptococci, Streptococcus pneumoniae, Listeria monocytogenes, Escherichia coli.
 - **Infants and young children:** S. pneumoniae, N. meningitidis, Haemophilus influenzae type B (Hib), Group B Streptococci.
 - **Teens and young adults:** N. meningitidis, S. pneumoniae
 - **Older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

- All Neisseria are **oxidase positive, glucose and maltose fermenters**
- **The genus contains:**
 - **Many commensal species**, most of which are harmless inhabitants of the upper respiratory and alimentary tracts.
 - **Two pathogenic species:**
 1. **Neisseria meningitidis** (meningococcus), a major cause of meningitis and bacteremia. **Gram-negative diplococcic.** kidney-shaped, non motile, non-sporulated and have polysaccharide capsule
 2. **Neisseria gonorrhoeae** (gonococcus), the cause of gonorrhea

Culture characters

- **Aerobic or facultative anaerobe**, optimum temperature is **37°C**.
- **10 %** Carbon dioxide enhances growth.
- Cannot grow on ordinary media
- Grow on **chocolate agar** or selective media (**Thay**



Antigenic composition of *Neisseria meningitidis*

- **Polysaccharide capsule: 12 serogroups**
- The most important disease-producing serogroups are **A, B, C, W-135, and Y.**
- **Group A strains** can cause widespread epidemics.
- 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*

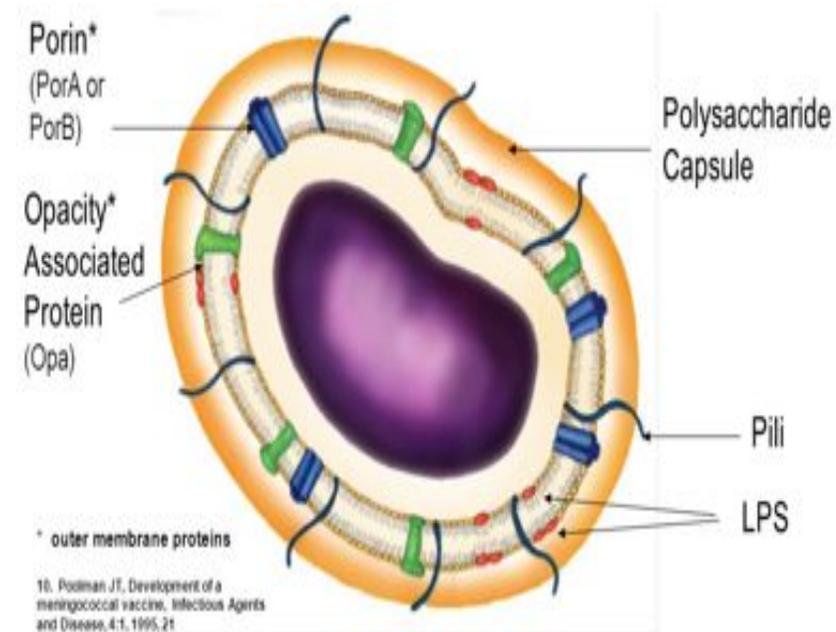
1- Polysaccharide capsule (the most important)

- 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.



Laboratory diagnosis of meningococcal meningitis

1-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.
- ✓ **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)

In acute bacterial meningitis, CSF is

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

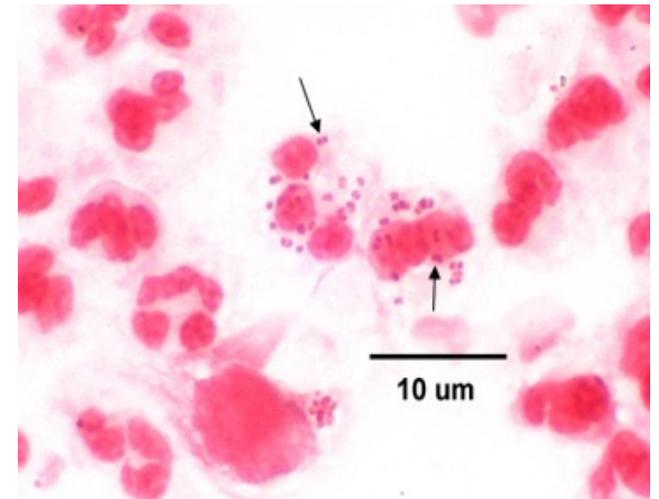
NB : Polymorphonuclear cells are not usually seen in normal CSF

Laboratory diagnosis of meningococcal meningitis

2- Direct film

- Direct Gram smears 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.



Laboratory diagnosis of meningococcal meningitis

3- Culture

A- 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.**

B- Media:

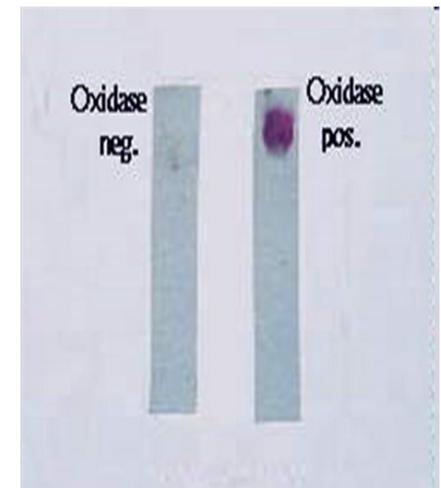
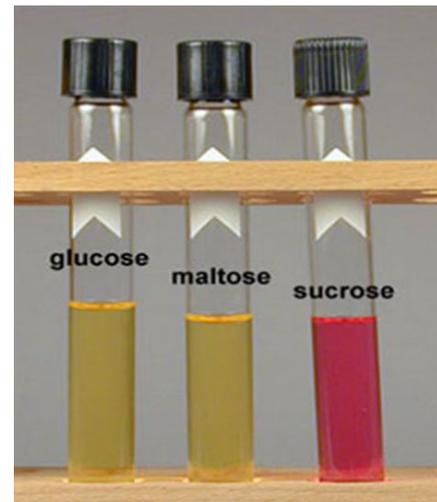
- cannot grow on ordinary media
 - can grow on **chocolate agar**.
 - **Thayer-Martin media** is selective media for Pathogenic Neisseria,
contains antimicrobials which inhibit the growth of organisms other than pathogenic Neisseria.
 - o Vancomycin kill most gram-positive bacteria
 - o Colistin kill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

Laboratory diagnosis of meningococcal meningitis

4-Biochemical reactions:

A- Oxidase test: all pathogenic *Neisseria* are **oxidase positive**.

B- Sugar fermentation: *N. Meningitidis* **ferment glucose and maltose with acid production.**



Laboratory diagnosis of meningococcal meningitis

5- Serological test

Detection of meningococcal antigen

- **Rapid diagnosis: may be obtained by detection of meningococcal antigen in CSF.**
- **Help if patient started antibiotics**
- **Latex agglutination available for *N. meningitidis* groups A,B,C,Y and W135**

Prevention of meningococcal meningitis

Meningococcal Vaccines

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

Chemoprophylaxis

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

Treatment

- **Penicillin, Ampicillin and Ceftriaxone** are used to treat meningitis
- **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 coccobacilli.
 - ✓ Streptococcus pneumoniae : Gram - positive capsulated 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

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:

- 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.

Gram Stain Listeria

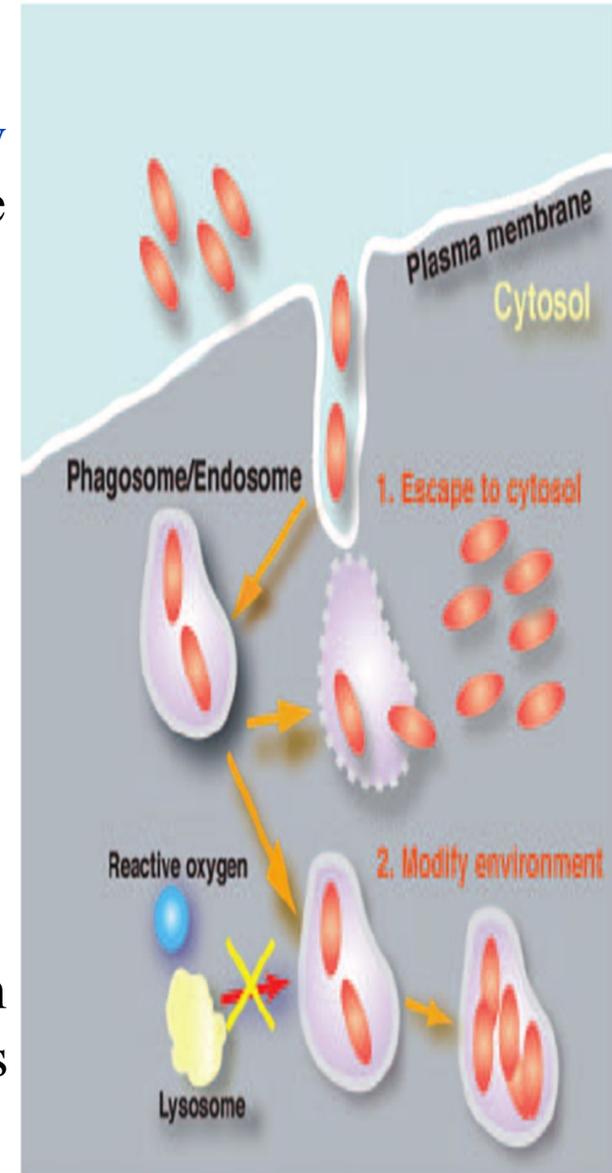


Cultural characters

- 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.

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
- **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.
- **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

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.

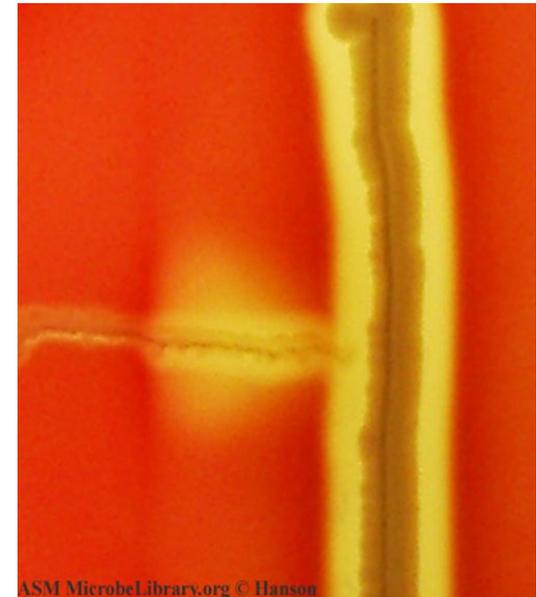
The risk of disease is increased at the extremes of life (in infants less than 1 month of age or adults over 60 years of age and immunocompromised individuals as well as women in late pregnancy).

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.
- **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.**
 - Blood and CSF culture reveals **Gram-positive rods arranged in short chains.**



Q 2

The following simple test is diagnostic of Neisseria meningitides:

- a. Detection of gram negative diplococci
- b. Culture on ordinary medium
- c. Oxidase negative
- d. PCR for CSF
- e. Detection of antigen by ELISA

Viral meningitis



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:

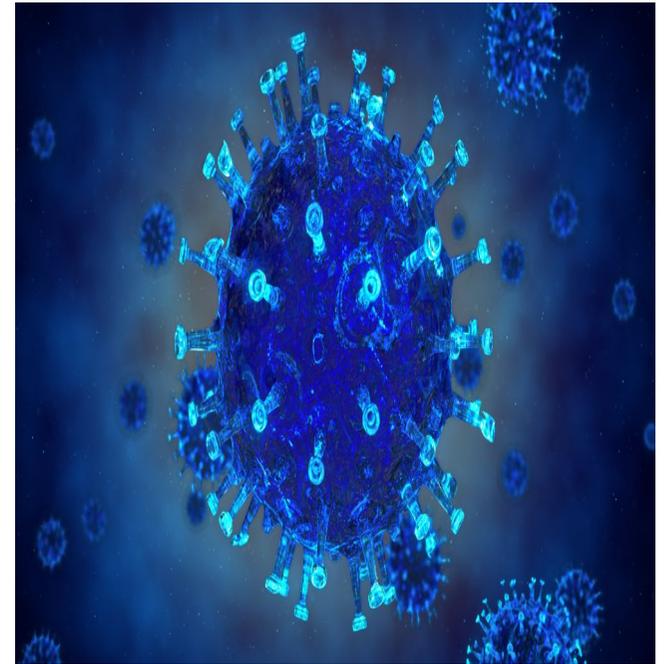
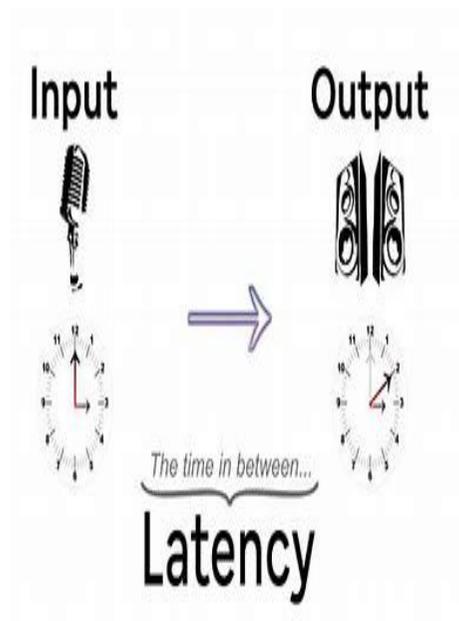
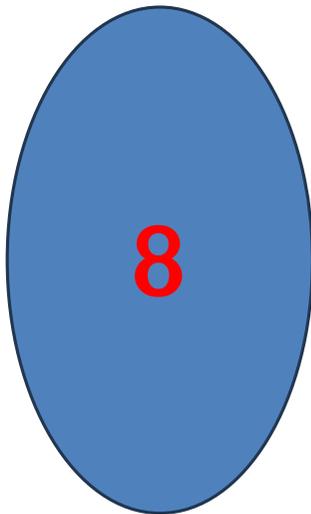
- **Enteroviruses:** Echovirus, Poliovirus, Coxsackie A virus
- **Herpes:** Herpes simplex virus type 1 (HSV-1 / HHV-1) or type 2 (HSV-2 / HHV-2), Varicella zoster (VZV / HHV-3); also causes chickenpox and shingles (herpes zoster), Epstein–Barr virus (EBV / HHV-4), Cytomegalovirus (CMV / HHV-5).
- **Measles,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



Herpes viruses

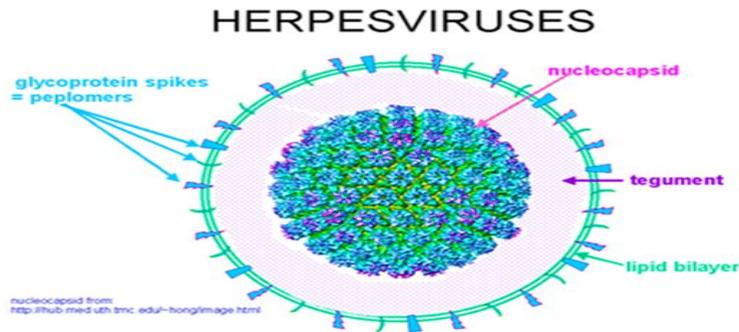
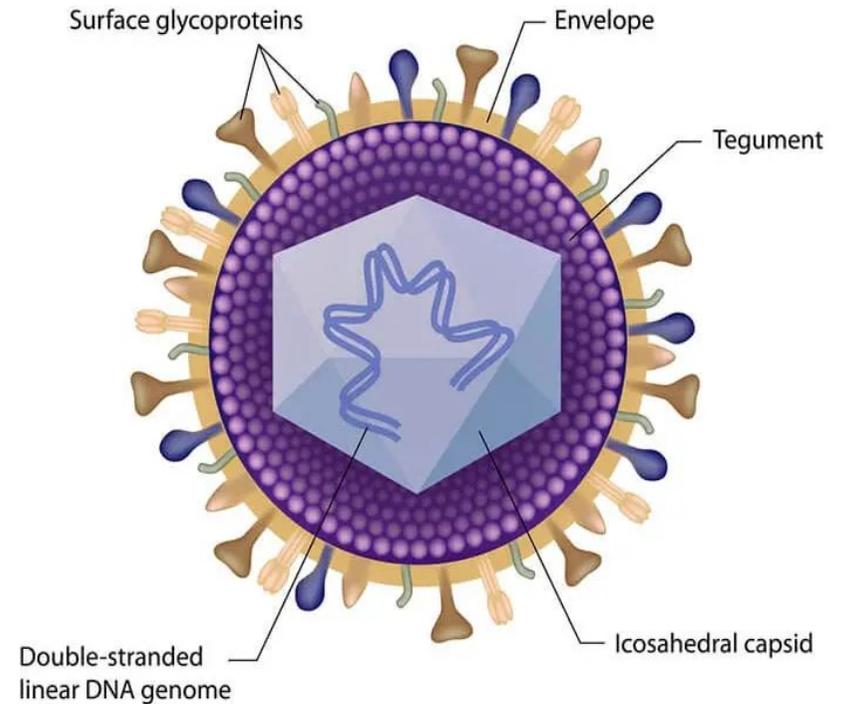
Eight human herpesvirus species are known.

- 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



1:8

Classification of Herpesviruses:

They have been divided into three subfamilies:

	<i>Alpha herpesvirinae</i>	<i>Gamma herpesvirinae</i>	<i>Beta herpesvirinae</i>
1	Herpes simplex virus types 1 (HSV-1 or HHV-1)	Epstein-Barr virus (HHV-4). 4	Cytomegalovirus (HHV-5) 5
2	Herpes simplex virus types 2 (HSV-2 or HHV-2)	Kaposi's sarcoma-associated herpes virus (KSHV) or (HHV-8). 8	Human herpes viruses types 6 (HHV-6) 6
3	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.

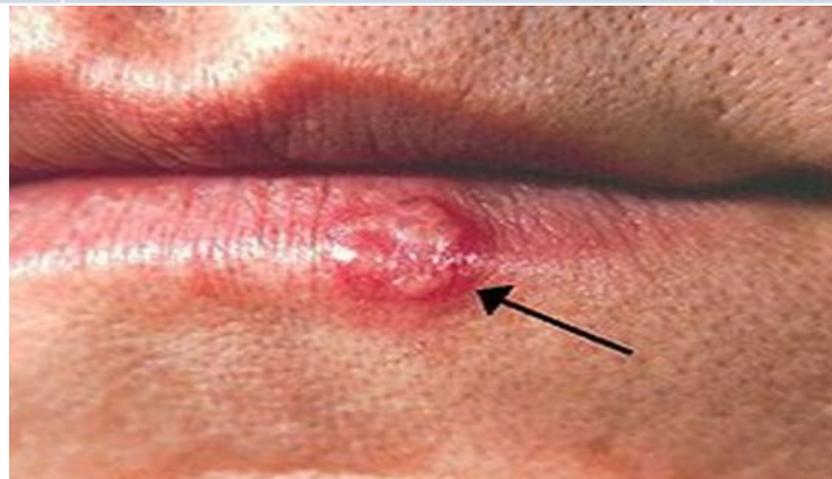
Transmission and pathogenesis:

	HSV-1	HSV-2
Mode of transmission	Primarily in saliva (kissing)	by sexual contact
<ul style="list-style-type: none">• 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

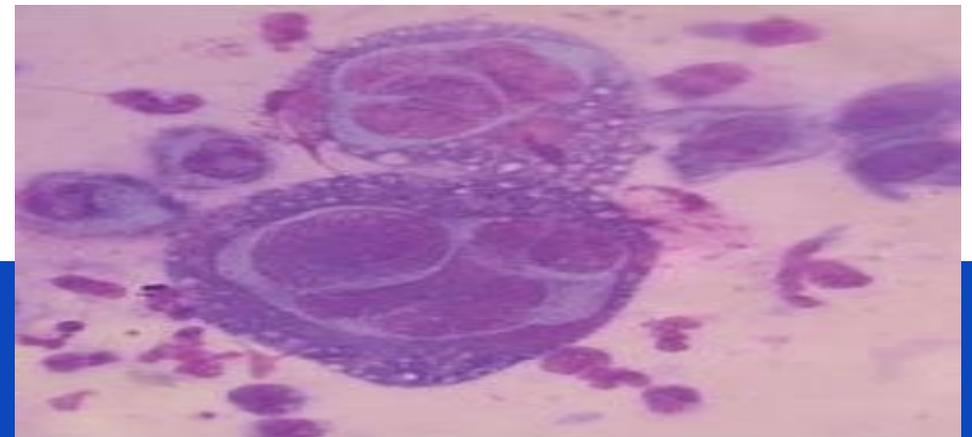
	HSV-1	HSV-2
Primary infection	<ul style="list-style-type: none">- Acute gingivostomatitis .- Herpes labials (cold sores- Herpetic whitlow: is a pustular lesion of the skin of finger or hand of medical personnel.- Keratoconjunctivitis , encephalitis .- Disseminated infections, such as esophagitis and pneumonia in immuno-compromised.	<ul style="list-style-type: none">- 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.

	HSV-1	HSV-2
Latency	<ul style="list-style-type: none">• Trigeminal ganglia.	<ul style="list-style-type: none">• Sacral ganglia.
Reactivation:	<ul style="list-style-type: none">• In response to stimuli as common colds, hormonal changes and sunlight.	
	<ul style="list-style-type: none">• Cold sores.• Keratitis	<ul style="list-style-type: none">• 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.



Varicella-Zoster virus

A. Primary infection: Varicella or chicken

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

- **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 zoster 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.

Treatment:

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

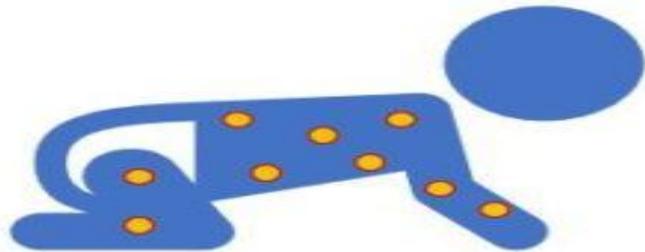
Prevention:

- 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.

*Varicella-zoster
immune globulin
(VZIG)*



Chicken pox



- First exposure to *Varicella zoster virus*
- Full body rash
- Highly contagious
- Common in children
- Live virus vaccine

Shingles



- Reactivation of *Varicella zoster virus*
- Localized rash
- Post herpetic neuralgia
- Common >50 years old
- Recombinant vaccine

Cytomegalovirus (CMV)

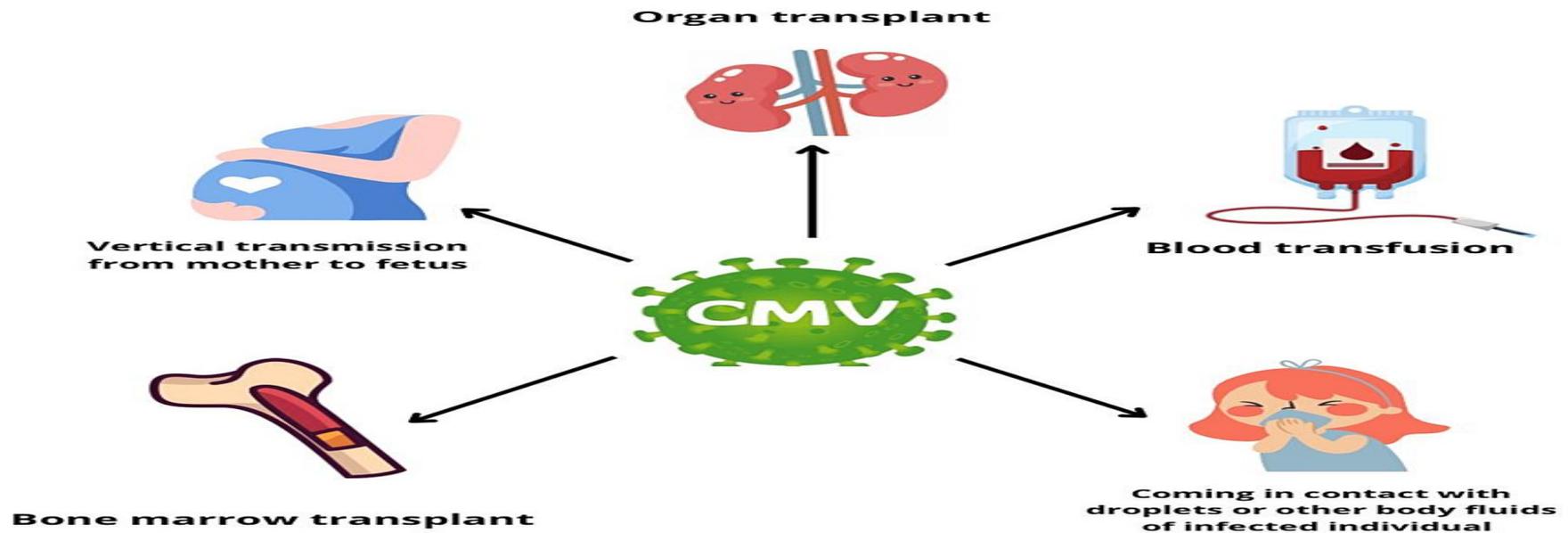
Transmission and pathogenesis:

Early in life:

- Transplacental
- within birth canal
- Via breast milk.

Later in life:

- Saliva (most common route),
- Sexually,
- Blood transfusion
- Organs transplant.



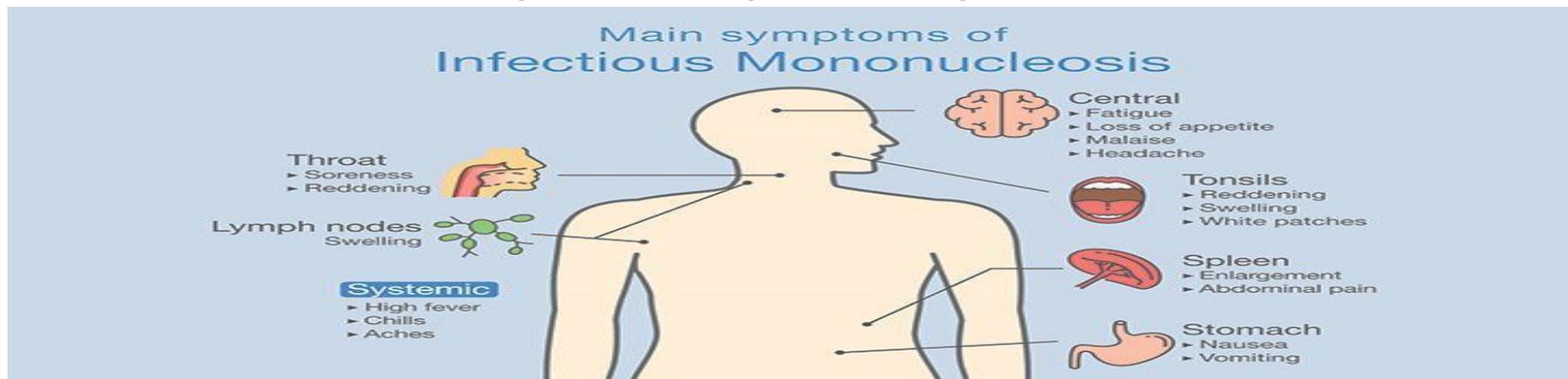
Cytomegalovirus (CMV)

Clinical Significance:

A. Primary infection:

In healthy individuals may cause:

- **Asymptomatic** infection with intermittent shedding in saliva and urine.
- **Infectious mononucleosis –like syndrome:** similar to EBV infection but heterophil antibodies negative.
- **Infection of immunodeficient patients.** Hepatitis and pneumonia are common,



- **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.

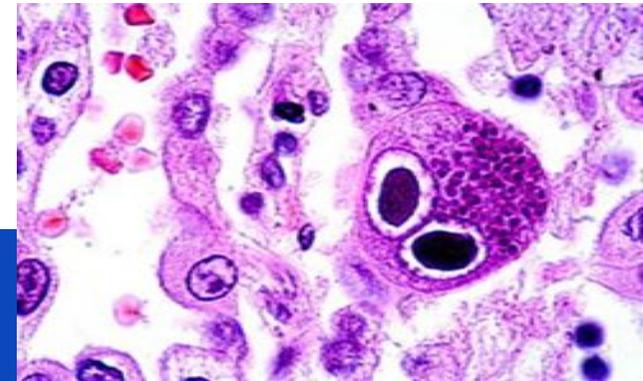
B- Latency and reactivation:

- 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: **Ganciclovir**

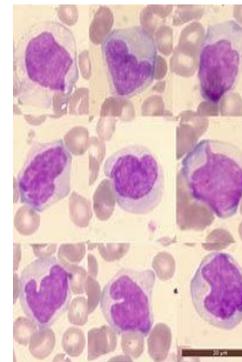


Epstein Barr virus (EBV)

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



2. Latency and reactivation: in B lymphocytes,

- reactivation, results in lytic cycle

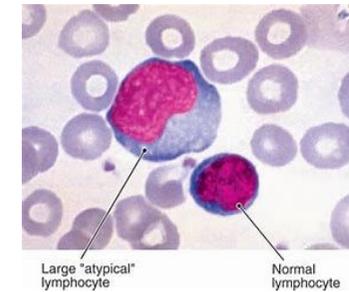
Mononucleosis causes:

- Fever
- Fatigue
- Sore throat
- Swollen lymph glands



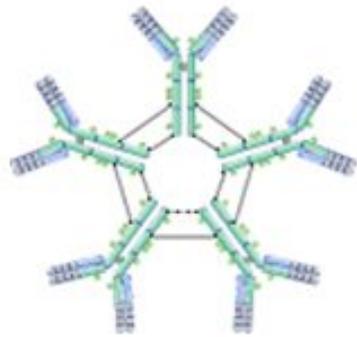
Laboratory diagnosis:

- Blood smear to detect lymphocytosis.
- Detection of EBV in patient's peripheral lymphocytes by DNA hybridization.
- Detection of heterophile antibodies.
- Detection of EBV specific antibodies.
- Virus isolation from saliva.



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

Heterophile Antibody (Monospot)



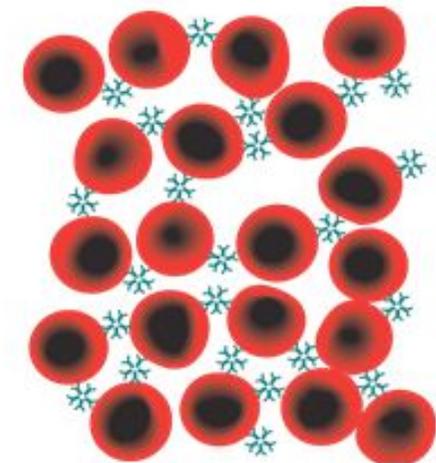
Patient's blood: IgM
against viral antigens

+



Sheep or horse
RBCs

X-reactivity
→



Agglutination

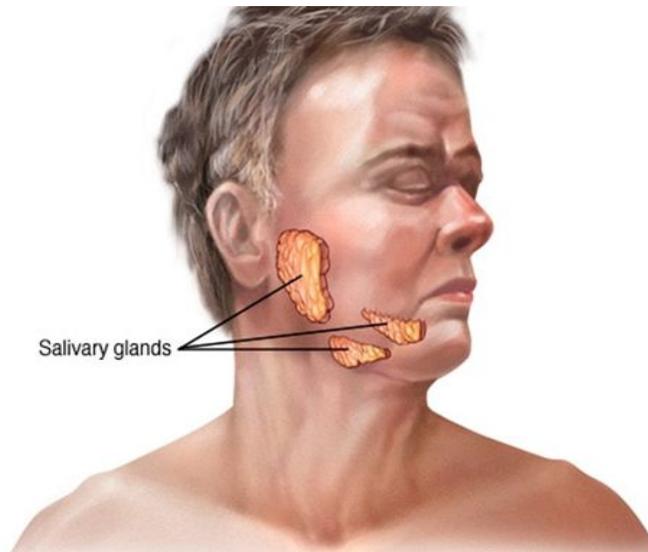
Mumps Virus

- **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

- **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.**

Laboratory 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: 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 picture:

- **Prodromal** phase is characterized by fever, dry cough, sore throat, conjunctivitis, and **Koplik's** spots (raised red spots with white centers in the mouth).



- After few days, the characteristic red, **maculopapular rash** starts on the head and then spreads to body.

complications

- **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: Trivalent live attenuated vaccine (MMR) is usually given by subcutaneous 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.

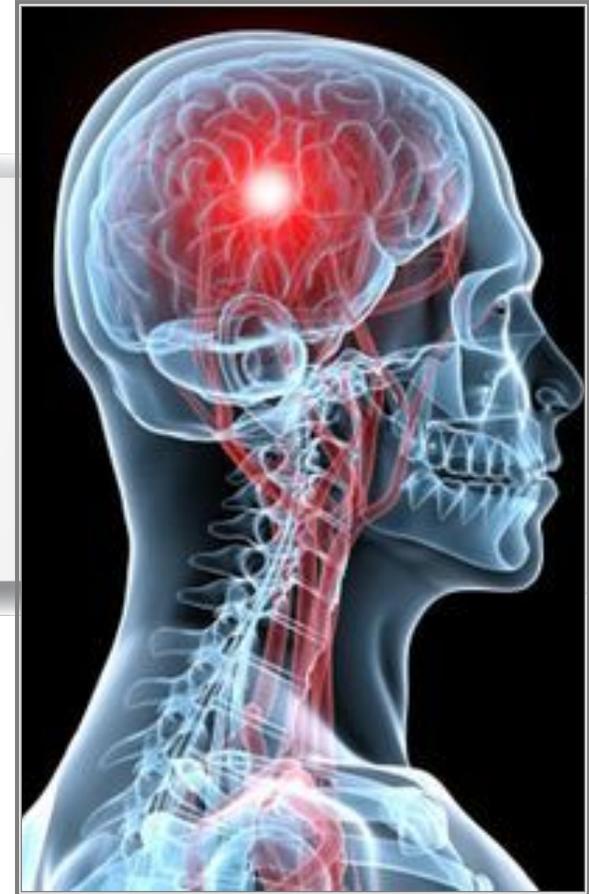




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Faculty Of Medicine - MANSOURA NATIONAL UNIVERSITY



Viral Encephalitis



Causes of Encephalitis

Viral

Arboviruses, Poliovirus, Measles, Mumps, Rabies, Varicella-zoster virus, Herpes simplex virus, Enteroviruses, HIV

Fungal

Candida, Mucor, *Aspergillus*, Cryptococcus.

Bacterial

N. Meningitidis, *Pneumococcus*, *Mycoplasma*, *Treponema pallidum*.



Arboviruses Causing Encephalitis

Togaviridae

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

Flaviviridae

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

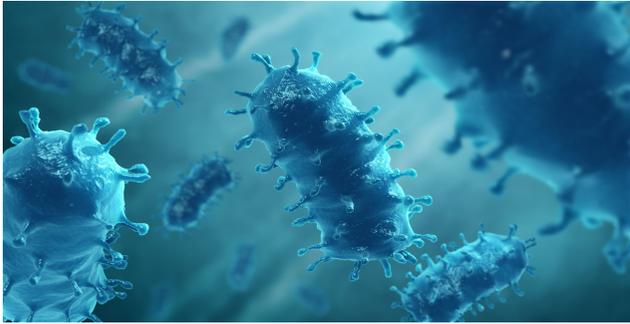
Bunyaviridae

- La crosse encephalitis

Viral Encephalitis

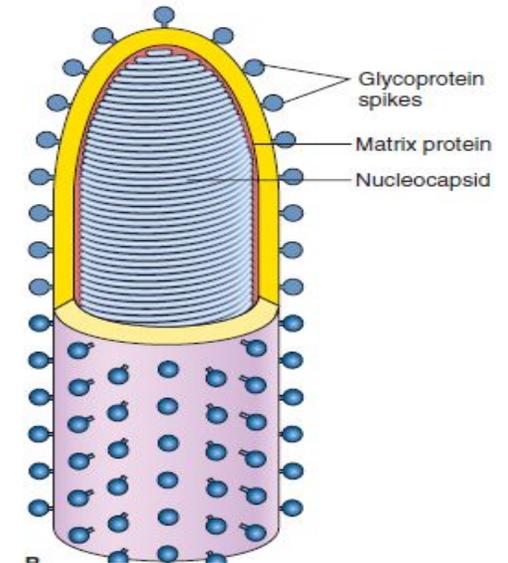
- Primary Encephalitis
- Secondary encephalitis

PRIMARY	SECONDARY
1- Eastern equine encephalitis virus (EEE) =Togaviridae	1-measles virus
2- Western equine encephalitis virus (WEE)= Togaviridae (Rare in Egypt due to cross immunity with West Nile Fever Virus)	2-Rubella virus
La crosse encephalitis (Bunyaviridae)	3- Varicella zoster virus.
Rabies virus.	



Rhabdoviruses

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



Rabies Pathogenesis

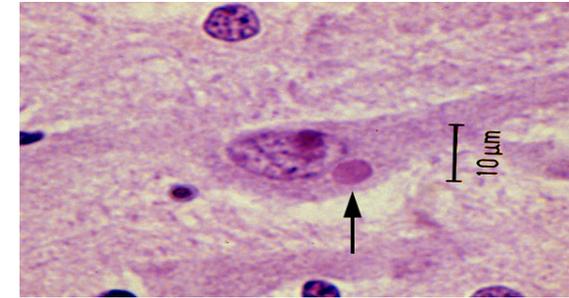
I.P: varies from 3-8 weeks to 1 year depending on size & site of inoculation (**head/face/neck vs. hands or feet**).

- **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.



Diagnosis

CNS, Neuronal cytoplasmic
eosinophilic inclusion
bodies, H&E

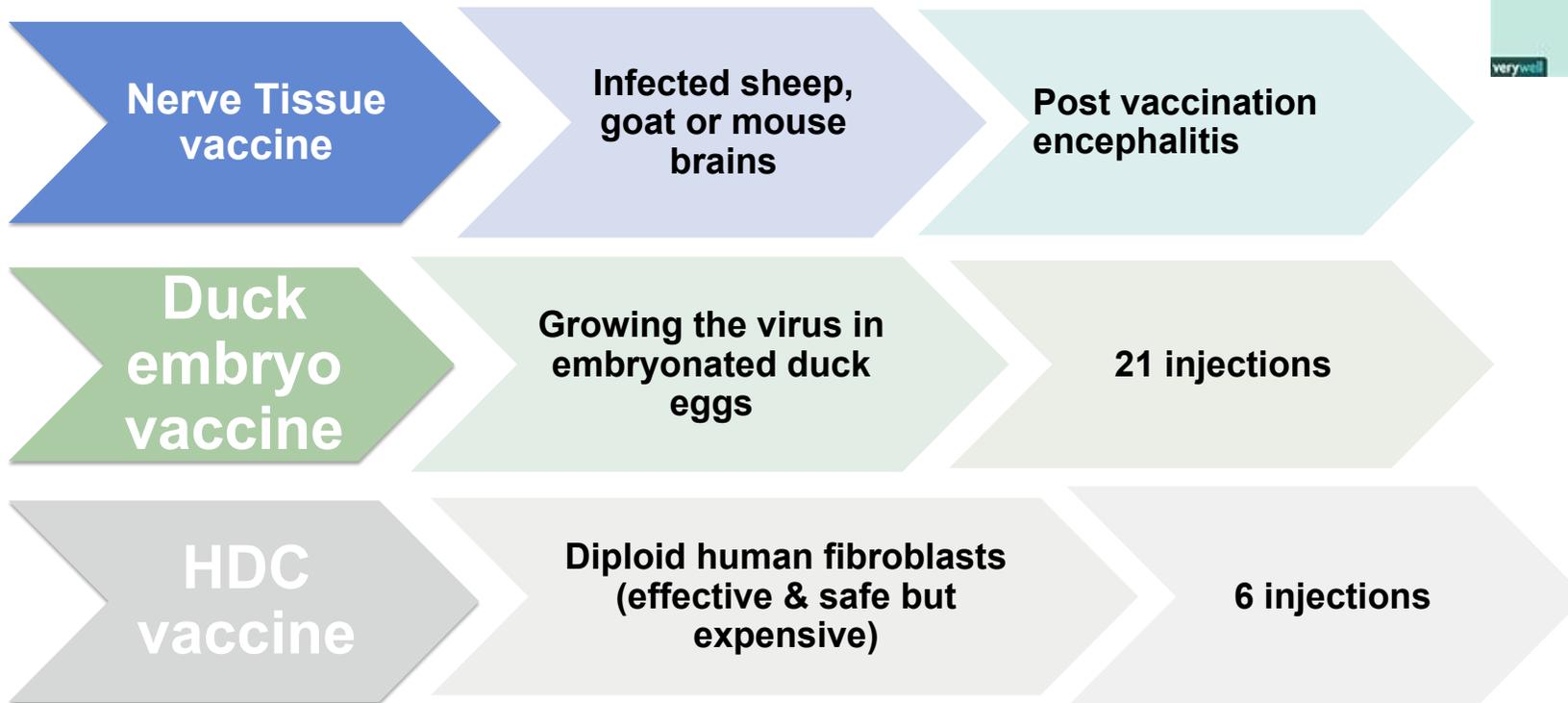


- **Specimen:** saliva, serum, spinal fluid, and skin biopsies and infected brain (postmortum and in animals).
- 1) **Detection of viral antigens or nucleic acid: IF & PCR.**
- **2) Histopathological diagnosis by detection of Negri bodies** in the brain or spinal cord.
- **3) Isolation of the virus:** infected tissue is inoculated into a suckling mice result in encephalitis & death.

Vaccination & Treatment

- **In veterinary medicine:** rabies vaccines are used as a preventive measure.
- **Vaccination of humans** 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).

Human Vaccines

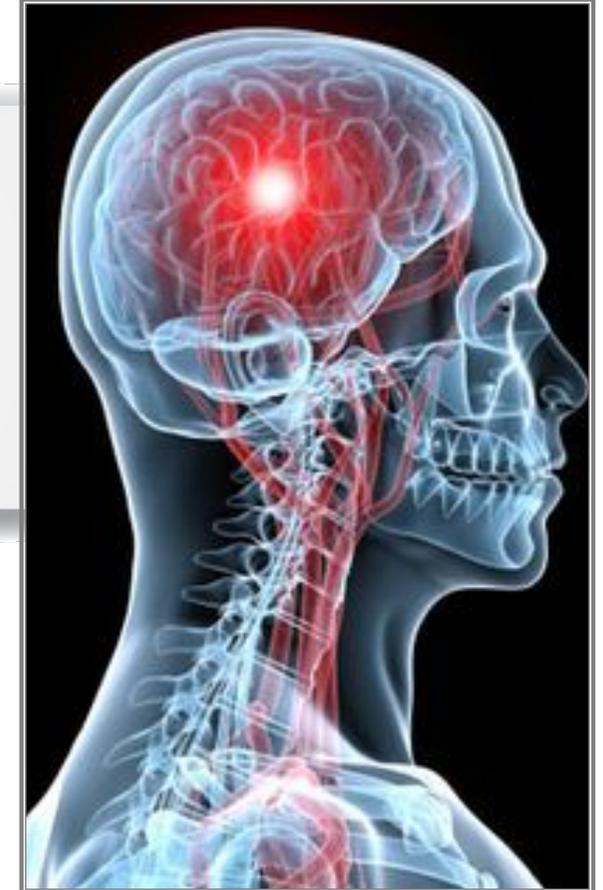




كلية الطب - جامعة المنصورة الأهلية
Faculty Of Medicine - MANSOURA NATIONAL UNIVERSITY



Fungal Encephalitis



Causes of fungal encephalitis

- 1. Cryptococcus neoformans:** This **encapsulated** yeast is a leading cause of fungal meningitis and **encephalitis**.
- 2. Candida species:** **Candida albicans** and other Candida species, especially in **neonates**, **elderly** individuals, **diabetics** or prolonged **antibiotic** use.
- 3. Aspergillus species:** Aspergillus **fumigatus** and other Aspergillus particularly those with **hematological malignancies** or recipients of solid organ **transplants**.
- 4. Histoplasma capsulatum:** particularly in **immunocompromised** individuals or those residing in **endemic** areas.
- 5. Blastomyces dermatitidis:**
- 6. Coccidioides immitis:**
- 7. Mucormycetes:**

Diagnosis of fungal infections

- **Sample:**
- According to the site of infection * skin, hair & nail, sputum, blood, CSF, biopsy.....

1. Direct Microscopic Preparation:

- a) **Unstained** preparation: KOH (10 – 30%).
- b) **Stained** preparation: Lactophenol cotton blue stain.

2. Culture for isolation of fungi

Media: Sabouraud's dextrose agar (SDA)

3-Histopathology

detect Fungi in tissue

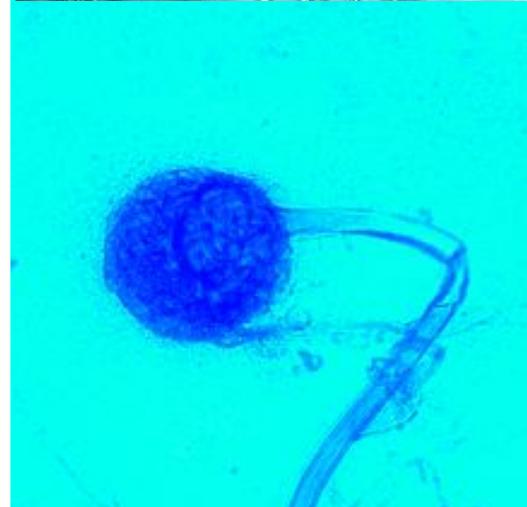
4- Woods light

- **clinical** diagnosis.
- **Ultraviolet** rays which when come in contact produce **fluorescent** colours.



Infectious organisms glowing under Wood's lamp illumination

#ADAM



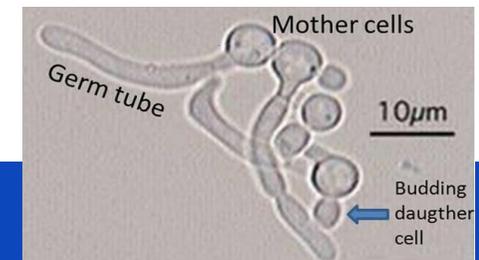
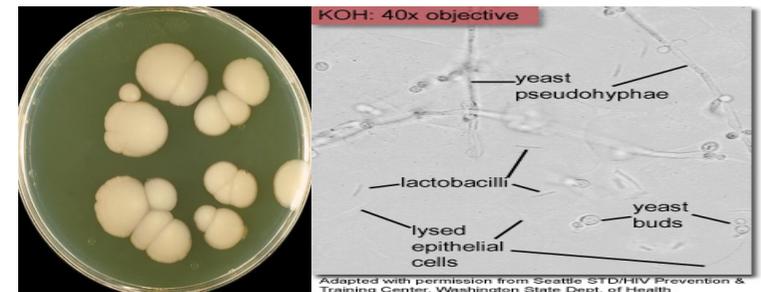
Candida albicans in SDA
Source: Wikipedia

Trichophyton terrestris in SDA
Source: Wikipedia

produce

Candida Infection

- **Source of infection**
- **Endogenous:** (autoinfection): Present as normal flora in oral cavity, GIT, female genital tract and skin which is the **major** source of infection.
- **Exogenous: contact**
- Candidiasis caused by the **yeast like** *Candida albicans*, and other candida species
- There is more than 200 species of Candida
 1. **Microscopic examination:**
 - Unstained preparation (**KOH**)
 - Stained preparation **lactophenol-cotton blue** stains.
 - For detection of yeast cells and **Pseudohyphae**
 2. **Culture** on Sabouraud`s dextrose agar (SDA) White creamy colonies
 3. **Germ tube formation:** Filamentation in the serum (Germ tube formation): When Candida is grown on human serum at 37°C for 4 hours, show **pseudohyphae**.

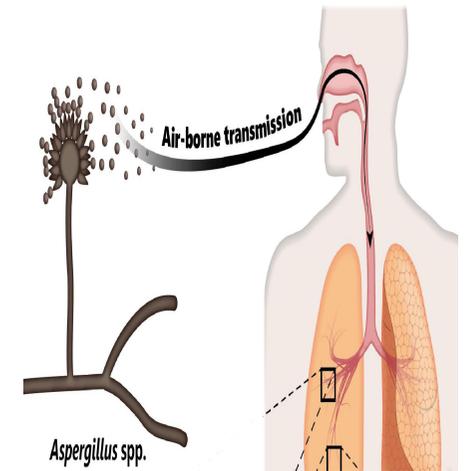


Question

- **A female complains of a white vaginal discharge & itching. Laboratory examination of the discharge reveals yeasts & pseudohyphae, what is the most likely diagnosis?**
 - a) Aspergillosis.
 - b) Candidiasis.
 - c) Cryptococcosis.
 - d) Histoplasmosis

Aspergillosis

- Fungal infection by *Aspergillus* spp.
- **Mode of transmission:** Environmentally by **inhalation** of spores.
- Fungal ball in old TB cavity (Aspregilloma).
- Allergic type: Asthma.
- Acute pneumonia and Disseminated encephalitis.



Diagnosis

- **Film stained by lactophenol blue:**
septated mycelium and Aspergillus **head**.
- **Culture:**
 - On SDA incubated at room temperature for 24-48 hr.
 - **Hairy** colonies different in color according to the species(niger, fumigatous, flavus)



Mucormycosis

Reproduction

A) Asexual :

1-primarily through the production of spores

2-The fragmentation of hyphae.

B) Sexual reproduction:

Zygospore.

Habitat: The fungal species belonging to the **order Mucorales**

They are **saprophytes** commonly found in **soil**, decaying **organic** matter, and various **environmental** substrates.

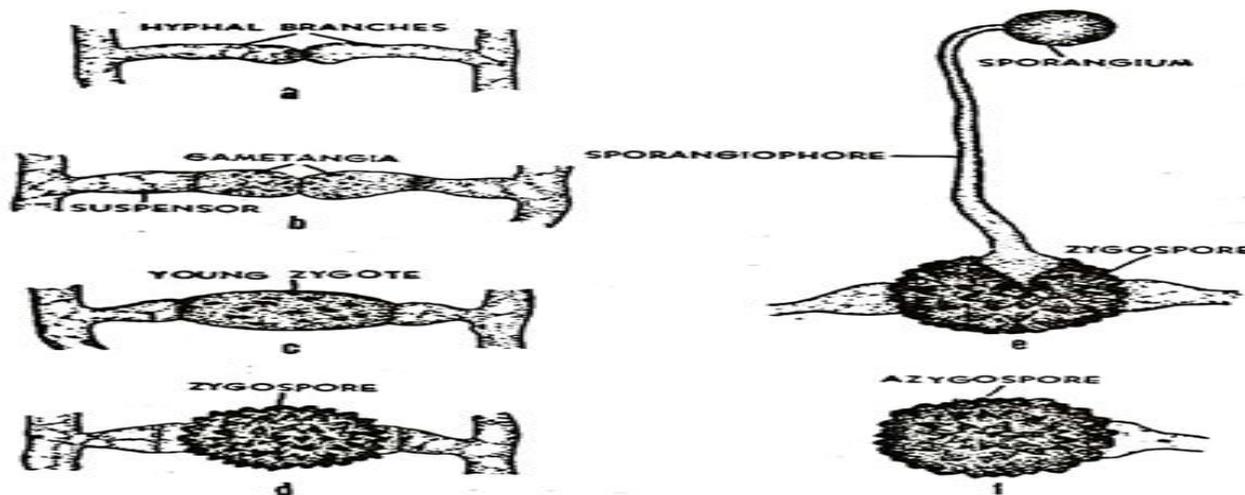
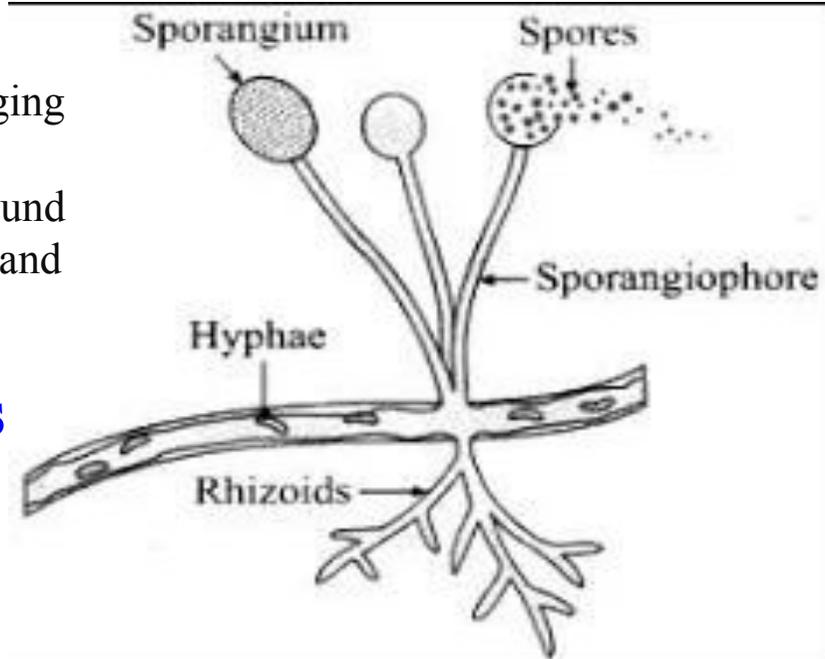
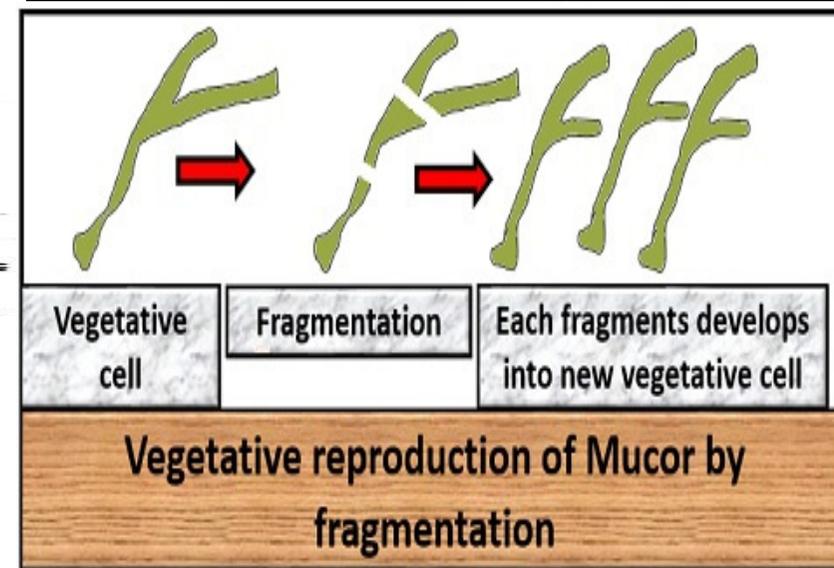


Fig. 194. *Mucor* : a-d—stages in the formation of Zygospore; e—zygospore germinating; f—an Azygospore.



Virulence factors of Mucorales fungi

1. **Thermotolerance:** thrive in a wide range of temperatures.
2. **Rapid growth:** allowing them to quickly colonize and invade host tissues.
3. **Ability to penetrate tissues:** rhizoids and sporangiophores, which aid in the penetration and invasion of host tissues.
4. **Iron acquisition:** have high affinity for iron and can acquire iron from host tissues, allowing them to grow and proliferate within the host.
5. **Production of proteolytic enzymes:** degrade host tissues, facilitating tissue invasion and damage.

Mucormycosis (Zygomycosis)

Patients: with acidosis associated with diabetes mellitus, corticosteroids treatment, severe burn & other debilitating diseases

Etiology: *Rhizopus* (*R. oryzae*), *Rhizomucor* & *Mucor*.

Clinical Diseases

1. Rhinocerebral mucormycosis:

Results from **germination** of the spores in nose & invasion of the **hyphae** into blood vessels (angiotrophic), causing thrombosis & infarction.

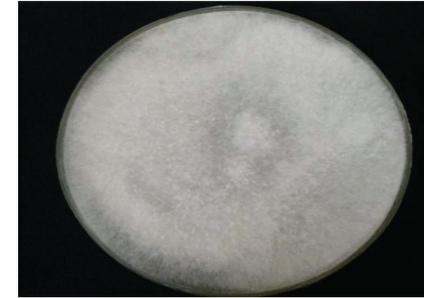
The disease progresses rapidly with invasion of **sinuses, eye, cranial bone & brain**.

Blood vessels & nerves are damaged.

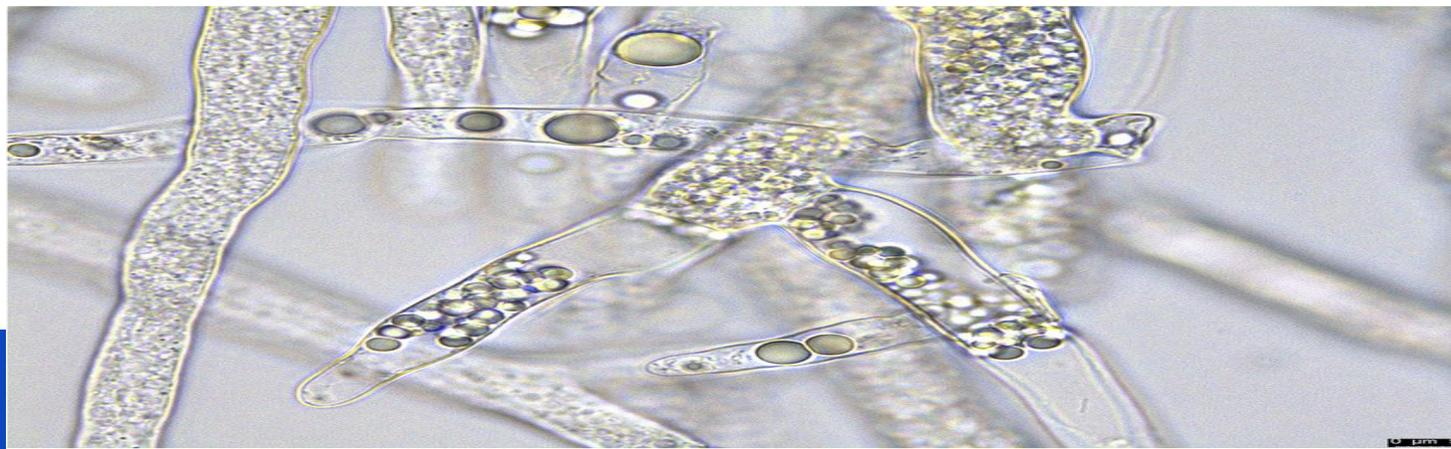
2. Thoracic mucormycosis:

Follows **inhalation** of the spores with invasion of lung **parenchyma & vasculature** causing ischemic necrosis & massive tissue destruction.

Laboratory Diagnosis



- **Specimen:** nasal discharge, tissue or sputum.
- **Direct examination:** 10% KOH mount of sample: **irregular branching broad hyphae** & **non-septated** or **sparse** septations, hyphae are **hyaline** (the translucent or colorless appearance. they lack pigmentation) with **sporangia** containing **sporangiospores**.
- **Culture on SDA without cyclohexamide to show:**
Rapidly growing **cottony white-to-gray or black** colonies



Hyaline hyphae with sporangia containing sporangiospores.



Thank You!