

**Lecture Title:**

**Fungal Infections of Central Nervous System**



(CNS Block, Microbiology)

# Lecture Objectives..



1. To know the main fungi that affect the central nervous system and the clinical settings of such infections.
2. To acquire the basic knowledge about fungal meningitis and brain abscess: clinical features, etiology, diagnosis, and treatment.



# Fungal infections of central nervous system (CNS)

- CNS infections are both diagnostic challenge and medical emergency
- Delay in diagnosis and initiation of appropriate therapy will lead to high mortality rate or in permanent, severe neurological damage
- Fungal infections of the CNS are not common  
However, they are being increasingly diagnosed

Why?



# Risk factors

HIV/AIDS

Hematopoietic stem cell transplant (HSCT)

Solid organs transplantation

Malignancies

Neutropenia

Hereditary immune defects

Immunosuppressive medications

Diabetes mellitus

Surgery or trauma

Indwelling catheters (e.g. candidemia  CNS seeding)

# How fungi reach the central nervous system



Fungi reach the central nervous system by different mechanisms:

- Hematogenous spread
- Local extension from the paranasal sinuses, the ear, or the orbits.
- Traumatic introduction
  - Surgical procedures
  - Head trauma
  - Injections
  - lumbar punctures

# Clinical syndromes



## ➤ Meningitis

Sub acute

Chronic

## ➤ Brain abscess

With or without vascular invasion

- These clinical syndromes can occur either alone or in combination.
- Certain clinical syndromes are specific for certain fungi

# Etiology



- Several fungal agents can cause CNS infections.

## Yeast:

*Candida* spp

*Cryptococcus* spp

## Dimorphic

*Histoplasma* spp

*Blastomyces* spp

*Coccidioides* spp

*Paracoccidioides* spp

## Mould

*Aspergillus* spp

*Zygomycetes*

*Exophiala* spp

*Cladophialophora bantiana*

*Rhinocladiella mackinziei*

and Others



# Cryptococcal meningitis

AIDS is the leading predisposing factor

## Etiology:

*Cryptococcus neoformans* is the most common etiology

- Capsulated yeast cells
- Naturally in Pigeon habitats
  
- Acquired by inhalation

Mainly meningitis





# Candidiasis

Candida species are the fourth most common cause of hospital acquired blood stream infections

## ➤ Candida can reach the CNS:

- Hematogenously,
- Surgery, Catheters

## Clinical syndromes

Cerebral abscesses

Meningitis

## Etiology:

*Candida albicans*, and other species including *C. glabrata*, *C. tropicalis*, *C. parapsilosis*, and *C. krusei*.

# ➤ CNS Aspergillosis

Usually brain abscesses (single or multiple)

➤ Common risk factors include:

- Malignancies
- Transplantation
- Chemotherapy

➤ Spread Hematogenously

➤ May also occur via direct spread from the anatomically adjacent sinuses,

➤ Mortality rate is high

**Etiology:**

*Aspergillus fumigatus*, but also *A. flavus*, and *A. terreus*

# CNS Zygomycosis (mucoromycosis)

➤ The rhinocerebral form is the most frequent presenting clinical syndrome in CNS zygomycosis.

Diabetics with ketoacidosis, in addition to other risk factors

➤ The clinical manifestations of the rhinocerebral form start as sinusitis, rapidly progress and involve the orbit, eye and optic nerve and extend to the brain

Facial edema, pain, necrosis, loss of vision, black discharge  
Angiotropism; As angio-invasion is very frequent

**Etiology:** Zygomycetes e.g. *Rhizopus*, *Absidia*, *Mucor*  
Fast growing fungi

➤ **Mortality is high (80- 100%)**  
Progression is rapid,

**To improve the outcome:**

Rapid diagnosis  
Control the underlying disease  
Early surgical debridement  
Appropriate antifungal therapy

# Pheohyphomycosis

- Fungal infections caused by dematiaceous fungi
  - Neurotropic fungi
- CNS infections: Usually brain abscess, and chronic
- Reported in immunocompetent hosts

## Etiology:

*Rhinocladiella mackenziei* ( Mainly reported from Middle East)

*Cladophialophora*,

*Exophiala* , many others

# Other Infections

- Histoplasmosis
  - Blastomycosis
  - Coccidioidomycosis
  - Paracoccidioidomycosis
- 
- Caused by primary pathogens
  - Sub acute or chronic Meningitis (common), and brain abscess
  - Following a primary infection, mainly respiratory



# Diagnosis

## Clinical features (history, risk factors, etc)

Not Specific

## Neuro-imaging

Good value in diagnosis and therapy monitoring

## Lab Investigations

CSF examination (cell count, chemistry)

Histopathology

Microbiology



# Lab Diagnosis

## Clinical Samples

CSF

Biopsy

Pus, aspirate

Blood (for serology)

## 1. CSF abnormalities

Cell count

Glucose level (low)

Protein level (high)

**Not specific for Fungal infections**

# Lab Diagnosis



## 2. Direct Microscopy

Fungal stains: Giemsa, GMS, PAS, India ink (*Cryptococcus neoformans*)

## 3. Culture

Fungal media: SDA, BHI, other media if needed.

## 4. Serology

*Candida*

*Aspergillus*

*Cryptococcus*

*Histoplasma*

*Blastomyces*

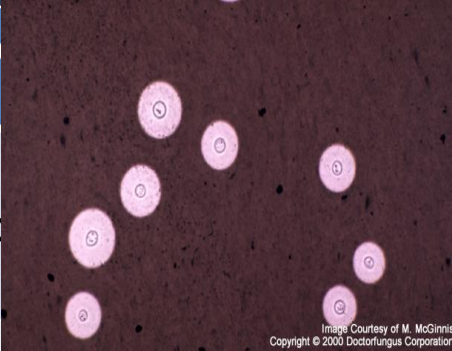

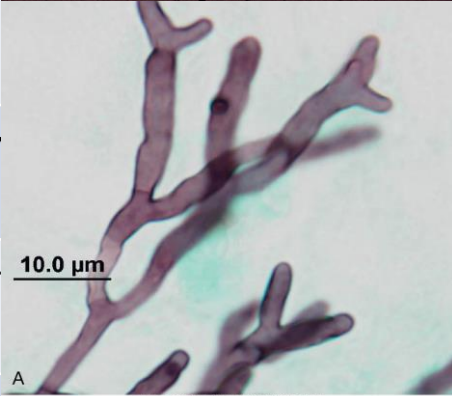
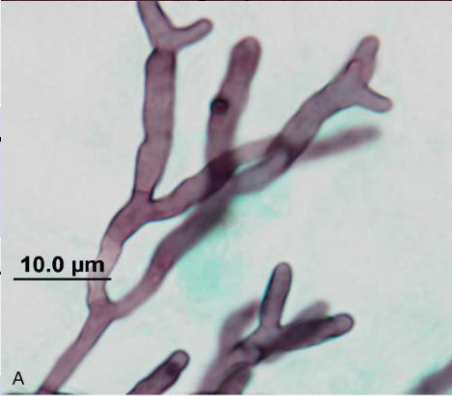
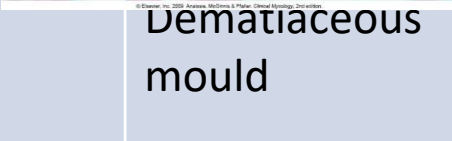

*Coccidioides*

*Paracoccidioides*

## 5. PCR



# Lab. Diagnosis

CNS infection	Direct microsc		
Cryptococcal meningitis	Yeast cells Capsulated (ind ink)		
Candidiasis	Yeast cells and pseudohyphae		ll)
Aspergillosis	Septate branch hyphae		
Zygomycosis	Broad non-sep hyphae		e
Pheohyphomycosis	Brown septate hyphae		Dematiaceous mould
			β-D- Glucan

## \*Serology: β-D- Glucan

For diagnosis of invasive fungal infections except cryptococcosis and zygomycosis

# Management



1. Control of the underlying disease
2. Reduce immunosuppression, restore immunity if possible
3. Start antifungal therapy promptly

Polyenes

Azoles

Echinocandins

Consider surgery in certain situations

# Antifungal therapy



CNS fungal infection	Treatment
Cryptococcal meningitis	Amphotericin B (combination with Flucytosine)
CNS Candidiasis	Caspofungin, Fluconazole, Voriconazole, Amphotericin B
CNS Aspergillosis	Voriconazole
CNS Zygomycosis	Amphotericin B



# Thank You 😊

(CNS Block, Microbiology)