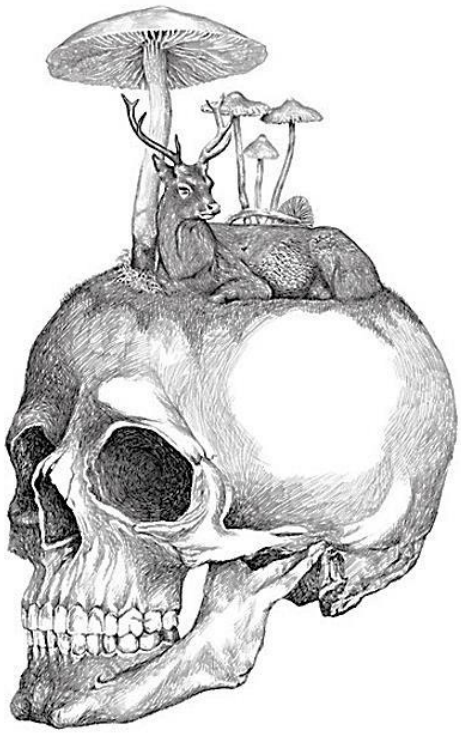
Fungal CNS Infection

microBiology 434



- **Important**
- Extra explanation

- **CNS infections:**
  - **diagnostic challenge**: can be mistaken with TB or Tumors and it has non-specific symptoms
  - **medical emergency:** rapidly progressive
- **Delay** in diagnosis + initiation of appropriate therapy → high mortality rate or in permanent, severe neurological damage.
- Fungal infections of the CNS are **not common** However, they are being increasingly diagnosed. Why?
  Because of the growing population of immunocompromised individuals, resulting from changes in medical practice such as the use of intensive chemotherapy and immunosuppressive drugs.

- **Risk factors:**

HIV/AIDS - Hematopoietic stem cell transplant (HSCT) - Solid organs transplantation - Malignancies - Neutropenia - Hereditary immune defects - Immunosuppressive medications [Steroids] - Diabetes mellitus - Surgery or trauma - Indwelling catheters (e.g. **candidemia** → CNS seeding)

- **Mechanisms: How fungi reach the CNS?**

  - Hematogenous spread [Most common]
  - Local extension from the paranasal sinuses, the ear, or the orbits. [Spreads from adjacent places to the CNS]
  - Traumatic introduction. Ex: Surgical procedures, Head trauma, Injections, lumbar punctures , instrumentation in the ICU

- **Clinical Syndromes [they can happen alone or together - Certain clinical syndromes are specific for certain fungi]**

  - Meningitis. [sub- acute or chronic] → not acute
  - Brain Abscess ↑IOP [with or without vascular invasion]

- **Etiology**

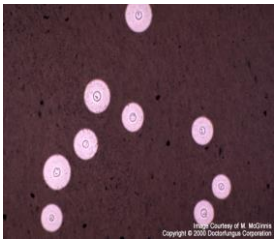
  - **Yeast:** Candida spp - Cryptococcus spp
  - **Mold:** Aspergillus spp - Zygomycetes - Exophiala spp - Cladophialophora bantiana - Rhinocladiella Mackenzie.
  - **Dimorphic:** Histoplasma spp - Blastomyces spp - Coccidioides spp - Paracoccidioides spp

Type	Yeast [in ↓ immunity]		Mold[in ↓ immunity]		
SPP	Candidiasis	Cryptococcus Meningitis	Asperigellosis	Zygomycosis [mucoromycosis]	Pheohyphomycosis
Etiology	Candida albicans [Most common] **C**. glabrata **C**. tropicalis **C**. parapsilosis **C**. krusei	Cryptococcus neoformans [Most common]	Aspergillus fumigatus [Most common] **A**. flavus **A**. terrus	• Rhizopus, • Absidia, • Mucor **[Fast growing fungi]**	Caused by **Dematiaceous** [Dark] **Neurotropic** fungi: • Rhinocladiella mackenziei **[Mainly Middle East]** • Cladophialophora • Exophiala
Risk factor	• Surgery • Catheters	**AIDS**	• Malignancies • Transplantation • Chemotherapy	**Diabetics with ketoacidosis**	--
Acquired by	Hematogenous	**Inhalation**	• Hematogenous • from adjacent sinuses	Sinusitis → progress → involve the orbit → eye → optic nerve → brain **[rhinocerebral form → most common]**	--
Notes	4th most common cause of hospital acquired blood stream infections	• **Capsulated** yeast cells [easily diagnosed] • Naturally in **Pigeon** habitats + soil	Mortality rate is high	• Mortality is high (80-100%) • Progression is **rapid** • **For better outcome:** ○ Rapid diagnosis ○ Control the underlying disease ○ Early surgical debridement ○ Appropriate antifungal therapy	• In immunocompetent hosts
Clinical representation	Cerebral abscesses Meningitis	Meningitis	brain abscesses [single or multiple]	Facial edema - pain - necrosis - loss of vision - black discharge due to necrosis **Angiotropism:** As **angio-invasion** is very frequent	brain abscesses Chronic → takes long time to develop

Type	Dimorphic [appears in normal people]
SPP	Histoplasmosis - Blastomycosis - Coccidiodomycosis - Paracoccidiodomycosis
Etiology	• By primary pathogen [not 2ry to decreased immunity] • Can be 2ry to respiratory infection
Clinical representation	• Cerebral abscesses • Meningitis [sub-acute - chronic]

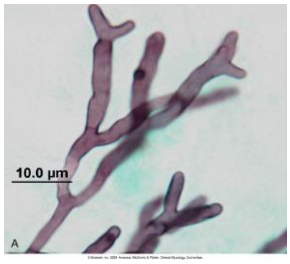
- **Diagnosis:**
  - Clinical features (history [travel] , **risk factors**, occupation , etc) → Not Specific
  - Neuro-imaging → Good value in diagnosis and therapy monitoring [MRI – CT]
  - Lab Investigations
    - **Histopathology**
    - **Microbiology:**
      - Direct microscopy: Fungal stains: Giemsa, GMS, PAS, KOH **India ink (Cryptococcus neoformans)**
      - Culture: Fungal media: SDA, BHI, other media if needed.
    - **Clinical samples:**
      - Biopsy
      - Pus, aspirate
      - Blood (for serology)
      - CSF → [cell count - **↓ Glucose - ↑ Protien**] → Not specific for fungal infection
    - **Serology:**
      - Candida - Aspergillus - Cryptococcus
      - Histoplasma - Blastomyces - Coccidioides - Paracoccidioides
    - **PCR**

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



Yeast showing a capsule around it [india ink]

Budding yeast → elongating → appear as psuduhyphae



Asperigellosis showing septated hyphze

Zygomycetes showing non-septated hyphae

- **Management:**
  - Control of the **underlying** disease
  - **Reduce immunosuppresion**, restore immunity if possible
  - Start **antifungal** therapy promptly
    - **Polyenes**
    - **Azoles**
    - **Echinocandins**
  - Consider surgery in certain situations

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

MCQ's :

1.Which one of the following fungal infections is common in diabetes:

a) Aspergillosis b) Pheohyphomycosis c) Zygomycosis

2.Which one of the following has no treatment:

a) Candidiasis b) Phehyphomycosis c) Cryptococcal meningitis

3.Which one of the following is the drug of choice of Aspergillosis:
]
a) Voriconazole b) Flucytosine c) Amphotericin B

4.An HIV patient came to the clinic with meningitis. Direct microscopy shows yeast capsulated cells by the use of india ink. What is the most common causative organism :

a) Candida albicans b) Rhinocladiella Mackenziei c) Cryptococcus neoformans

5.An immunocompestent host came to the clinic with chronic brain abscess. Direct microscopy showed brown septate hyphae. Which one of the following is the most common causative organism:

a) Rhinocladiella mackenziei b) Zygomycetes c) Rhizopus

ANSWERS :

1-C 2-B 3-A 4-C 5-A