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Cryptococcal Meningitis: Intracranial Pressure and Antifungal Drug Penetration.

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Introduction

Cryptococcal meningitis (CM) is a life-threatening fungal infection of the central nervous system (CNS), primarily caused by *Cryptococcus neoformans* and *Cryptococcus gattii*. It disproportionately affects immunocompromised individuals, especially those with advanced HIV/AIDS. Despite the availability of antifungal therapies, CM remains associated with high morbidity and mortality, largely due to complications such as elevated intracranial pressure (ICP) and challenges in drug delivery across the blood-brain barrier (BBB) [1, 2].

Cryptococcus species enter the body through inhalation and initially infect the lungs. In susceptible hosts, the fungus disseminates hematogenously to the CNS, where it causes meningoencephalitis. The hallmark symptoms include headache, fever, neck stiffness, altered mental status, and visual disturbances [3, 4].

Elevated ICP is a common and dangerous complication, often resulting from obstruction of cerebrospinal fluid (CSF) flow due to fungal proliferation in the subarachnoid space [5, 6].

Elevated ICP is observed in up to 60–70% of CM cases and is a major contributor to neurological deterioration and death. Pressures exceeding 250 mm H_2O are considered pathological and require urgent intervention. Management of ICP is essential for improving survival. Serial lumbar punctures are the standard approach to relieve pressure, though they are invasive and resource-intensive2 [7, 8].

Amphotericin B is fungicidal but has poor CSF penetration and significant nephrotoxicity. Flucytosine enhances efficacy but is often unavailable in low-resource settings. Fluconazole, though fungistatic, penetrates the CSF well and is widely used2.Effective treatment of CM depends on antifungal drug concentrations in the CSF. **Amphotericin B**: Detectable in CSF only in trace amounts; its efficacy relies on high plasma levels and prolonged exposure [9, 10].

Conclusion

Cryptococcus neoformans is the predominant species in HIV-associated CM, while *C. gattii* affects immunocompetent individuals. Resistance to fluconazole and flucytosine is emerging, particularly in regions with widespread monotherapy use. Genotypic characterization helps tailor therapy and monitor resistance trends.CM causes over 220,000 infections and 181,000 deaths annually, with the highest burden in sub-Saharan Africa and Southeast Asia. Resource limitations hinder access to:Efforts to improve access to diagnostics and essential medicines are critical for reducing CM mortality.Research into non-invasive ICP monitoring and pharmacologic ICP control could revolutionize CM care, especially in low-resource settings.

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