STANDARD OPERATING PROCEDURE

Diagnosis and Management of Cryptococcal Meningitis

Special Region (1)

Union of Myanmar

VERSION:1.0

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APPROVED BY:Internal Medicine

1. Purpose

To provide a standardized protocol for diagnosis and management of cryptococcal meningitis, including antifungal therapy and prevention of complications.

2. Definition

Cryptococcal meningitis is a fungal infection of the CNS caused by *Cryptococcus neoformans* and *Cryptococcus gattii*.

3. Risk Groups

- HIV/AIDS (CD4 <100 cells/µL)
- Immunosuppression (steroids, chemotherapy)
- Malignancy
- Chronic liver or renal disease

4. Clinical Features

Symptoms: headache, fever, vomiting, blurred vision, altered consciousness

Signs: neck stiffness, papilledema, cranial nerve palsies, seizures

5. Diagnosis

- Lumbar puncture mandatory – retinue examination and fungal culture
- Opening pressure >20–25 cm H_2O
- CSF CrAg positive confirms diagnosis

In suspected recurrent cryptococcal meningitis, CSF cryptococcal antigen should NOT be used to diagnose relapses. CSF fungal culture is the gold standard to differentiate relapse from IRIS or raised intracranial pressure.

At the end of induction therapy, CSF microscopy (including India ink) may still demonstrate cryptococcal organisms but cannot differentiate viable from non-viable yeast. Therefore, treatment response must be assessed using CSF fungal culture, which remains the gold standard.

Relapsed cryptococcal meningitis is the reappearance of symptoms + **positive CSF culture** after prior documented sterilization.

6. Treatment Overview

Induction (2 weeks), Consolidation (8 weeks), Maintenance (≥1 year)

7. Antifungal Therapy

- **Induction:** Amphotericin B 1 mg/kg IV daily + Flucytosine 100 mg/kg/day (4 divided doses) for 14 days (first line)

> *Flucytosine-containing regimens remain the gold standard; however, in its absence, Amphotericin B combined with high-dose fluconazole (800–1200 mg/day) is an acceptable alternative for induction therapy.*

- **Consolidation:** Fluconazole 400–800 mg/day for 8 weeks
- **Maintenance:** Fluconazole 200 mg/day ≥12 months

8. Intracranial Pressure Management

Daily LP if pressure >25 cm H_2O

Remove 20–30 mL CSF, target <20 cm H_2O

9. Monitoring

- Potassium alternate day (target >4.0 mmol/L)
- Magnesium 1 time/week (target >2.0 mg/dL)
- Creatinine 2 times/week
- Hemoglobin weekly

10. Empirical Electrolyte Replacement

- Oral KCl 40–60 mmol/day for all patients on Amphotericin
- Adjust based on potassium levels
- Magnesium replacement if low (IV $MgSO_4$ 1–2 g/day)

11. Toxicity

- Amphotericin: nephrotoxicity, hypokalemia, anemia
- Flucytosine: bone marrow suppression

References

1. Panel on Opportunistic Infections in Adults and Adolescents with HIV. **Guidelines for the prevention and treatment of opportunistic infections: cryptococcosis**. National Institutes of Health (NIH); 2024.
2. European Confederation of Medical Mycology (ECMM), International Society for Human and Animal Mycology (ISHAM), American Society of Microbiology (ASM). **Global guideline for the diagnosis and management of cryptococcosis**. 2024.
3. Milsap D, et al. **Induction treatment for HIV-associated cryptococcal meningitis**. 2025.
4. Abassi M, et al. **Cryptococcal meningitis: diagnosis and management update**. Clin Infect Dis. 2015.
5. Musubire AK, et al. **Diagnosis and management of cryptococcal relapse**. J AIDS Clin Res. 2013.
6. Perfect JR, et al. **Clinical practice guidelines for the management of cryptococcal disease**. Clin Infect Dis. 2010;50(3):291–322.
7. Saag MS, et al. **Practice guidelines for the management of cryptococcal disease**. Clin Infect Dis. 2000.
8. Moon S, et al. **Paradoxical cryptococcal IRIS vs relapse differentiation**. J Korean Soc Radiol. 2018.
9. Johns Hopkins ABX Guide. **Cryptococcus infection**.