

## **Resource-Limited ENLS Meningitis and Encephalitis**

<u>Clinical recognition and initial stabilization</u>: CNS infection should be suspected in any patient with fever and altered mental status, with a higher index of suspicion in patients with human immunodeficiency virus (HIV) infection or other causes of suppressed immunity. As in any setting, the first priorities for managing patients with a suspected central nervous system (CNS) infection are to assess the patient's circulation, airway, and breathing, and to promptly initiate antimicrobial therapy that empirically targets epidemiologically relevant organisms.

**Diagnostic workup:** Evaluation should begin with a basic neurologic assessment including mental status, Glasgow Coma Scale (GCS) score, pupillary response, motor exam, and examination for meningismus. A standard infectious workup, including comprehensive metabolic panel, complete blood count, liver function tests, urinalysis, chest X-ray, and blood cultures should be obtained to assess for reversible metabolic derangements and alternative sources of infection. Neuroimaging should be obtained in all patients, ideally before lumbar puncture (LP) is performed, to assess for structural evidence of infection, space-occupying lesions, and hydrocephalus. When CT is unavailable for acute early decision-making, the safety of LP should be determined with available clinical evidence, mindful of the risk of downward herniation in patients with increased intracranial pressure (ICP). LP is likely safe in awake patients with no focal neurologic deficits. In patients with depressed level of alertness, nausea/vomiting, papilledema, abnormal pupillary exam, severe headache, seizure, or focal motor deficit, LP should be deferred until neuroimaging can be performed. LP may be particularly informative in patients with a known or possible diagnosis of HIV to assess for evidence of opportunistic CNS infection. CSF should be tested for cell counts, protein, glucose, culture, and gram stain. Viral PCR tests are unavailable in many LMICs but should be sent if available.

**Management:** As above, empiric antimicrobial therapy should be promptly initiated for all patients with suspected CNS infection and should not be delayed for neuroimaging or lumbar puncture. The selection of antibacterial, antiviral, and anti-tuberculous agents should be determined by local infectious disease epidemiology and medication availability. All regimens should target a broad spectrum of gram positive and gram negative bacteria. Intravenous acyclovir should be administered if there is clinical suspicion herpes simplex virus (HSV) or varicella zoster virus (VZV) encephalitis, though antiviral medication and confirmatory PCRs may be unavailable in many resource-limited settings. There should be a low threshold to initiate anti-tuberculous therapy if tuberculous meningitis is suspected or locally endemic. Patients with tuberculous meningitis may be at increased risk of hydrocephalus. Those with radiographic or clinical manifestations of increased ICP should be evaluated for CSF diversion.

For patients with suspected bacterial meningitis, consideration should be given to administering dexamethasone before the first dose of antibiotics to minimize neurologic sequelae from *Streptococcus pneumoniae* infection. However this intervention has not been shown to improve outcomes in sub-Saharan Africa and other regions with high rates of HIV infection, malnutrition, or delayed hospital presentation.<sup>1</sup> For patients with confirmed or suspected tuberculous meningitis, the World Health Organization recommends a 6–8-week course of adjunctive corticosteroids to be administered with anti-tuberculous therapy given its demonstrated mortality benefit in both adult and pediatric populations.<sup>2</sup>



<u>**Triage:**</u> Patients with suspected CNS infection should be transferred to the highest available level of care after all feasible measures are taken to stabilize the patient for transport, and after antibiotics are administered if they are available at the referring center. Patients with an abnormal neurologic examination should be monitored in an intensive care unit if available to facilitate timely response to neurologic or medical deterioration.

*Supportive care:* Patients with CNS infections are at increased risk of secondary brain injury and hospital-acquired complications. Vital signs should be monitored at least every four hours to detect physiologic derangements. Aggressive fever control should be pursued with antipyretics and chilled saline. Patients requiring intubation for airway protection should be supported on mechanical ventilation. Septic shock commonly complicates bacterial meningitis, and hemodynamic support with IV fluid resuscitation and vasopressors should be provided to maintain mean arterial pressure above 65 mmHg. The medication record should be reviewed daily to ensure active medication orders and appropriate administration of antimicrobials. Comatose or immobilized patients should be turned regularly to prevent pressure ulcers and treated with pharmacologic prophylaxis for deep venous thrombosis if there are no contraindications. Dysphagia screening should be performed for all patients with changes in mental status to minimize risk of aspiration pneumonia, and non-oral tube feeding should be maintained at 30 degrees to minimize risk of ICP elevation and aspiration pneumonia. Finally, a comprehensive neurologic assessment should be performed at least daily to monitor clinical response to treatment and determine the need to broaden the therapeutic regimen for patients who fail to improve.

## References

1. Brouwer MC, Mcintyre P, Prasad K, van de Beek D. Corticosteroids for acute bacterial meningitis. *The Cochrane database of systematic reviews*. 2015;2015(9).

2. World Health Organization. WHO consolidated guidelines on tuberculosis: Module 4: Treatment - Drugsusceptible tuberculosis treatment. Geneva: World Health Organization; 2022. PMID: 35727905. 2022.