



Net Letter

# Letter in response to “Frequency of asymptomatic neurosyphilis in patients with latent syphilis: A 4-year retrospective study from a tertiary care center”

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Dear Editor,

This is in response to the article titled “Frequency of asymptomatic neurosyphilis in patients with latent syphilis: A 4-year retrospective study from a tertiary care center,” published in the Journal of Skin and Sexually Transmitted Diseases in February 2024.

The article advocates for the routine use of lumbar puncture (LP) for cerebrospinal fluid (CSF) examination to diagnose neurosyphilis in patients with latent syphilis. However, the Centers for Disease Control and Prevention (CDC) guidelines recommend CSF evaluation only in persons exhibiting clinical signs of neurosyphilis, such as cranial nerve dysfunction, meningitis, stroke, acute or chronic altered mental status, or loss of vibration sense.<sup>[1]</sup> It is also recommended in patients with non-neurological tertiary syphilis and those with serofast status, that is, failure of non-treponemal test titers to decrease fourfold within 12 months after therapy.<sup>[2]</sup> In addition, it may be beneficial in patients with ocular symptoms but normal ophthalmologic examination, indicating a primary CNS pathology. CSF evaluation is not recommended in asymptomatic patients, particularly those who have shown adequate treatment response (evidenced by a fall in venereal disease research laboratory (VDRL) titer) and are not immunosuppressed due to human immunodeficiency virus (HIV). Even in HIV-infected patients with syphilis, the major risk factors for asymptomatic neurosyphilis are low CD4 T-cell counts, high HIV viral loads, and a high rapid plasma reagin (RPR) titer.<sup>[3]</sup> The RTI/STI guidelines by the National AIDS Control Organization recommend CSF examination in patients whose non-treponemal test titers do not decrease fourfold within 6–12 months of therapy.<sup>[4]</sup> The 2020 European guidelines similarly advise CSF assessment primarily for patients presenting with neurological, ocular, or auricular symptoms, along with those diagnosed with tertiary syphilis. They recommend conducting non-invasive procedures such as fundoscopy and computed tomography brain scans before opting for LP.<sup>[5]</sup>

LP is a specialized procedure that requires expertise and carries inherent risks. It has complications ranging from headache, backache, and infection to potentially life-threatening conditions such as epidural abscess/hematoma and cerebral herniation. Performing such an invasive procedure in patients who have no signs to suggest neurological or ocular involvement raises ethical concerns and poses unnecessary risks and discomfort to the patient.

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Furthermore, biochemical abnormalities in CSF, such as elevated glucose and protein, can be seen in patients with early syphilis and are of unknown medical significance in the absence of neurologic signs and symptoms.<sup>[1]</sup> Asymptomatic treponemal invasion of CNS occurs in up to 30% of individuals with early syphilis. It is often not associated with other CSF abnormalities and responds to standard, non-neurosyphilis treatment regimens for early syphilis.<sup>[6]</sup> In the pre-antibiotic era, routine LP for all patients with syphilis was the norm, as abnormal CSF findings were associated with a greater risk of developing symptomatic neurosyphilis. However, in the modern antibiotic era, the incidence of neurosyphilis has declined, possibly because antibiotic treatment for other diseases inadvertently treats unsuspected syphilis. In such a situation, doing routine LP is an artifact of the past, and its supposed benefits do not outweigh the risks associated with the procedure.

The significance of identifying asymptomatic neurosyphilis remains a topic of debate, with CDC guidelines stating that CSF examination in neurologically asymptomatic patients does not impact treatment outcomes. Beyond the primary aim of the authors of determining the frequency of asymptomatic neurosyphilis in latent syphilis, it is crucial to consider the best course of action for these patients with abnormal CSF findings and compare the outcomes with those treated with the non-neurosyphilis protocol. This important information, however, is lacking in the study, preventing us from concluding about the advantages of this risky procedure and warranting a subsequent comparative trial.

Given these considerations, the routine use of LP in patients with latent syphilis with no signs suggestive of neurosyphilis is not justified. Advocating for LP in asymptomatic patients may lead to unnecessary healthcare stress and potential harm to patients. Therefore, in alignment with the recommendations of leading world authorities, we do

not support the endorsement of this invasive and risky procedure. Without clearly defined benefits, the routine use of LP in asymptomatic patients with latent syphilis does not stand scientific scrutiny.

#### **Use of artificial intelligence (AI)-assisted technology for manuscript preparation**

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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