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# Questions

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## Q1 Treatment of Early Syphilis

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Persons with early syphilis, including persons with HIV infection, can be effectively treated on a single occasion with benzathine penicillin G administered in a single dose of 2.4 million units.

- True
- False

**Educational Point:** Syphilis is a chronic human bacterial (*Treponema pallidum*), sexually transmitted infection that has been recognized as a threat to human health for centuries. The disease remains a public health priority owing to its transmissibility, potential for neurologic and cardiovascular complications, association with an increased risk of human immunodeficiency virus (HIV) acquisition, and role in adverse pregnancy outcomes. Throughout the 21st century, syphilis rates have increased. Rates of HIV coinfection are higher among persons with syphilis.

Long-acting penicillin has been the preferred therapy for syphilis treatment since the early 1950s. Although a single dose of benzathine penicillin G has been the accepted standard for treatment of early (i.e., primary, secondary, and early latent) syphilis for decades, concerns about the adequacy of a single dose of benzathine penicillin G for treatment of early syphilis in persons with HIV infection are of long standing. Despite recommendations from the Centers for Disease Control and Prevention for single-dose benzathine penicillin G therapy, many clinicians treat persons who have HIV infection with multiple doses.

To address the continuing controversy regarding the appropriate duration of treatment with benzathine penicillin G for early syphilis, the authors conducted an open-label, multi center, noninferiority, randomized, controlled trial comparing single-dose therapy with 2.4 million units of benzathine penicillin G to therapy with three 2.4-million-unit doses of benzathine penicillin G administered at three successive weekly intervals.

**Reference:** Hook EW 3rd, Dionne JA, Workowski K, McNeil CJ, Taylor SN, Batteiger TA, et al. One dose versus three doses of benzathine penicillin g in early syphilis. *N Engl J Med.* 2025;393(9):869-878.

**Link:** <https://www.nejm.org/doi/pdf/10.1056/NEJMoa2401802>

**PMID:** 40902161

The percentage of participants with a serologic response at 6 months was 76% (95% confidence interval [CI], 68 to 82) in the single-dose group and 70% (95% CI, 61 to 77) in the three-dose group (difference, -6 percentage points; 90% CI, -15 to 3, indicating noninferiority). No clinical relapse or treatment failure occurred in either group. In the one-dose group, a serologic response at 6 months was observed in 76% of participants who had HIV infection and 76% of those who did not, and in the three-dose group, a serologic response at 6 months was observed in 71% of participants who had HIV infection and 70% of those who did not.

**This trial provides data that indicate that persons with early syphilis, including persons with HIV infection, can be effectively treated on a single occasion with benzathine penicillin G administered in a single dose of 2.4 million units.** The elimination of unnecessary doses of benzathine penicillin G reduces the cost of treatment, aligns with the principles of antimicrobial stewardship, and is more convenient for patients in that the numbers of clinic visits and painful intramuscular injections are decreased.

*The correct answer is true.*