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# **Consensus Statement on the Clinical Implications of a Positive Syphilis Serology Test in the Context of a Previous Negative Syphilis Point of Care Test**

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## Introduction

The recent introduction of point-of-care tests for syphilis has raised the issue of the clinical implications of a past negative point-of-care test in the clinical staging, and hence treatment, of a person with a subsequent positive laboratory-based serological syphilis test result. It is also important to note that all currently available syphilis point of care tests cannot reliably distinguish past from active infection and therefore should not be used in people with a previous syphilis infection<sup>1</sup>.

This paper outlines the current view in 2018 of the Australasian Chapter of Sexual Health Medicine (AChSHM) in the context of the northern Australia Syphilis Outbreak.

## Background

The treatment of syphilis differs by the stage of infection. Early or infectious syphilis (also known as primary, secondary and early latent) is treated with a single dose (1.8g) of intramuscular benzathine penicillin; whereas any case lacking evidence consistent with early infectious syphilis otherwise requires weekly intramuscular benzathine penicillin treatment for 3 weeks.

Australian expert opinion, backed by the United States Centers for Disease Control and Prevention Guidelines<sup>2</sup>, requires that early or infectious syphilis is diagnosed where there is either 1) unequivocal symptoms of primary or secondary syphilis or 2) a recent sex partner with early syphilis or 3) serological evidence from a laboratory-based test that the infection has occurred in the past two years as shown by seroconversion or 4-fold rise in non-treponemal test titre.

The expansion of point-of-care testing raises the question as to whether a prior negative syphilis point-of-care test, during the previous two years for an individual who has now received a positive laboratory based syphilis test, result would constitute adequate evidence to treat the patient as having an early stage infection.

## Consensus statement

A prior negative syphilis point-of-care test within two years of a subsequent positive laboratory based syphilis test should generally be considered adequate to clinically stage the person's infection as an early infectious case and, therefore, to treat with a single dose (1.8g) of benzathine penicillin.

However, in situations where the quality of point-of-care testing is in doubt, especially in populations with a high prevalence of past infection, it would be reasonable to offer extended treatment as a possible late latent case.

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<sup>1</sup> Causer, L. M., Kaldor, J. M., Conway, D. P., Leslie, D. E., Denham, I., Karapanagiotidis, T., et al (2015). An evaluation of a novel dual treponemal/nontreponemal point-of-care test for syphilis as a tool to distinguish active from past treated infection. *Clin Infect Dis*, 61(2), 184-191.

<sup>2</sup> MMWR, R. (2014). Sexually Transmitted Diseases Treatment Guidelines, 2015. 64(1).

## Rationale

The Australian Therapeutic Goods Administration has registered the Alere Determine™ Syphilis TP for use as a point of care syphilis test in Australia. An Australian laboratory-based evaluation demonstrated an overall sensitivity of 97.3% and specificity of 96.4%. Sensitivity was slightly better in symptomatic primary and secondary syphilis (100%) compared to early (95.6%) and late/unknown duration (96%) latent syphilis<sup>3</sup>. Further, the negative predictive value of a negative point of care test result would be 99.3% to 98.3%, assuming as shown elsewhere a population prevalence of past syphilis infection of between 20 to 38%<sup>4</sup>.

In the context of clinical decision making, a negative predictive value of 98% is likely to be as accurate as other accepted means of determining early stage infection, such as symptoms and non-treponemal test titre variation.

Furthermore the risks of under treatment stemming from a false negative point-of-care test result is likely to be low as point of care tests are generally used in populations where ongoing testing rates are relatively high. Despite some people with late infection failing to complete a full (3-dose) course of treatment, case reports of either tertiary syphilis or congenital syphilis following a 1-dose course of treatment are rare or non-existent in the penicillin era.

As with any test, real world performance is dependent on the extent to which actual use follows best practice. Inadequate transport, storage, use and interpretation may all lead to decreases in both sensitivity and specificity. The AChSHM affirms the importance of adherence to the Communicable Disease Network of Australia Syphilis Series of National Guidelines recommendations for ensuring adequate syphilis point-of-care test performance.

## References

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2. Causer, L. M., Kaldor, J. M., Fairley, C. K., Donovan, B., Karapanagiotidis, T., Leslie, D. E., et al (2014). A laboratory-based evaluation of four rapid point-of-care tests for syphilis. *PLoS One*, 9(3), e91504.
3. Mak, D. B., & Holman, C. D. A. J. (1998). Age at first episode of venereal syphilis in an Aboriginal population: an application of survival analysis. 22(6), 704-708.
4. MMWR, R. (2014). Sexually Transmitted Diseases Treatment Guidelines, 2015. 64(1).

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<sup>3</sup> Causer, L. M., Kaldor, J. M., Fairley, C. K., Donovan, B., Karapanagiotidis, T., Leslie, D. E., et al (2014). A laboratory-based evaluation of four rapid point-of-care tests for syphilis. *PLoS One*, 9(3), e91504.

<sup>4</sup> Mak, D. B., & Holman, C. D. A. J. (1998). Age at first episode of venereal syphilis in an Aboriginal population: an application of survival analysis. 22(6), 704-708.

