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NEVADA DIVISION of PUBLIC and BEHAVIORAL HEALTH

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TECHNICAL BULLETIN

DATE: February 20, 2024
TOPIC: CDC Provides New Laboratory Recommendations for Syphilis Testing
CONTACT: Ghasi Phillips-Bell, ScD, MS, Maternal and Child Health Epidemiologist
TO: All Health Care Providers and Facilities; Laboratories; Local Health Authorities

INTRODUCTION

Currently, no available nucleic acid amplification tests (NAATs) are cleared by Food and Drug Administration (FDA) for marketing in the United States to screen or diagnose syphilis, and culture for T. pallidum is cumbersome and is available only in selected research laboratories. Nontreponemal (lipoidal antigen) tests are most suitable for screening or diagnosis in conjunction with a medical history and physical examination when antibody titers are important to determine recent exposure to infection; a presumptive diagnosis in persons with signs or symptoms suggestive of syphilis; or to determine response to treatment.

Nontreponemal tests typically have been used as a screening test for syphilis; as a diagnostic test when patients have signs or symptoms suggestive of syphilis or have a known sexual contact when assessing possible reinfections; and when monitoring treatment outcomes.

When performed by an experienced laboratory technician and used in conjunction with treponemal tests, clinical history, physical examination and contact history, the nontreponemal (lipoidal antigen) tests are a highly reliable testing method for screening and determining the endpoint titer for subsequent serologic monitoring post-treatment.

The traditional algorithm for syphilis serologic screening begins with a nontreponemal test, and any reactive specimens are tested for confirmation by a treponemal test.

On Feb. 8, 2024, the Centers for Disease Control and Prevention (CDC) provided new evidence-based recommendations (see Table 1) for tests and methods that support a diagnosis of syphilis, including laboratory-based tests, point-of-care (POC) tests, processing of samples, and reporting of test results to aid laboratorians and clinicians in the detection of *Treponema pallidum*, the causative agent of syphilis. These recommendations are intended for use by clinical laboratory directors, laboratory staff, clinicians, and disease-control personnel who must choose among multiple available testing methods; establish standard operating procedures for collecting and processing specimens; interpret test results for laboratory reporting; and counsel and treat patients.

The primary recommendations fall under seven topics:

1. Endpoint titers
2. Syphilis serologic testing algorithm
3. Serologic syphilis testing

4. Syphilis serologic testing in pregnant persons
5. Syphilis serologic testing in persons living with HIV/AIDS
6. Direct detection of *Treponema pallidum* by darkfield microscopy
7. Direct detection of *Treponema pallidum* by immunohistochemistry and silver staining

Table 1. Summary of CDC laboratory recommendations for syphilis testing, United States, 2024

Topic	Recommendation
Endpoint titers	Endpoint titers (the highest dilution yielding a reactive result) should be determined and clearly reported when testing serum with nontreponemal (lipoidal antigen) assays that detect antibodies to lipoidal antigens (i.e. rapid plasma reagin and Venereal Disease Research Laboratory). Reports should not contain mathematical symbols such as > or < signs.
Syphilis serologic testing algorithm	Serologic tests that measure antibodies to both nontreponemal (lipoidal) and treponemal antigens related to syphilitic infections should be used in combination, when the primary test is reactive, to aid in the diagnosis of syphilis. Sole reliance on one reactive serologic test result can misclassify a patient's syphilis status. Both the traditional syphilis screening algorithm (initial screening with nontreponemal [lipoidal antigen] assays) and the reverse syphilis screening algorithm (initial screening with treponemal immunoassays) are acceptable. The preferred algorithm should be based on laboratory resources, including staff, space and costs, test volume, and patient populations served.
Serologic syphilis testing	Nontreponemal (lipoidal antigen) tests (e.g., rapid plasma reagin or Venereal Disease Research Laboratory) are not interchangeable when used to determine antibody titers; testing on follow-up samples must be performed with the same type of test. The *Treponema pallidum* particle agglutination test is the preferred manual treponemal test.
Syphilis serologic testing in pregnant persons	Nontreponemal (lipoidal antigen) and treponemal tests should be interpreted in the same manner regardless of pregnancy status.
Syphilis serologic testing in persons living with HIV/AIDS	Nontreponemal (lipoidal antigen) and treponemal tests should be interpreted in the same manner regardless of HIV status.
Direct detection of *Treponema pallidum* by darkfield microscopy	Darkfield microscopy should be maintained if already in use or established in sexually transmitted diseases clinics where a point-of-care test for primary or secondary syphilis diagnosis would be beneficial for timely patient treatment.
Direct detection of *Treponema pallidum* by immunohistochemistry and silver staining	Immunohistochemistry is preferred over silver staining for formalin-fixed, paraffin-embedded tissue sections regardless of anatomic site.

Detailed CDC recommendations can be found here.

Reporting

All positive syphilis direct detection tests, along with specimen site and positive syphilis serologic tests, must be reported to the appropriate state or local public health authority (see table below). Laboratories should list all tests used, report each result with an interpretation, and document the syphilis algorithm applied to render the interpretation to both the ordering provider and the appropriate public health authority.

4150 Technology Way, Suite 300 ● Carson City, NV 89706 ● (775) 684-4200 ● Fax (775) 687-7570 ● dpbh.nv.gov

Health Department	County	Phone Number to Report
Southern Nevada Health District (SNHD)	Clark	(702) 759-1300 (24 hours)
Washoe County Health District (WCHD)	Washoe	(775) 328-2447 (24 hours)
Carson City Health and Human Services (CCHHS)	Carson City, Douglas, and Lyon	(775) 887-2190 (24 hours)
Nevada Division of Public and Behavioral Health (DPBH)	All other counties	(775) 684-5911 (M-F 8am to 5pm) (775) 400-0333 (after hours)

Reporting to health care providers

When reporting results to health care providers, laboratories should list all tests used, report each result with an interpretation, and document the syphilis algorithm applied to render the interpretation, when appropriate.

Questions

For updated guidance, review the Division of Public and Behavioral Health Technical Bulletin web page regularly. Email stateepi@health.nv.gov for other questions regarding the CDC laboratory recommendations for syphilis testing.

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