**INTRODUCTION**

Syphilis is one of a group of diseases caused by spirochaete organisms of the genus *Treponema*. Sexually acquired syphilis occurs worldwide and is caused by *T. pallidum* subspecies *pallidum*. Serology remains the mainstay of laboratory testing for syphilis, except during the very early stage of infection when direct detection of treponemes in material from lesions by dark-field or fluorescent microscopy is necessary.

**NATURAL HISTORY**

The course of the infection spans many years and may lead to various clinical presentations, which are classified into early (infectious) and late (non-infectious) stages. Early syphilis may be further divided into primary, secondary, and early latent syphilis; late syphilis includes late latent and the various forms of tertiary syphilis.

**IMMUNE RESPONSE**

The immune response to syphilis involves production of antibodies to a broad range of antigens, including non-specific antibodies (cardiolipin or lipoidal antibody) and specific treponemal antibodies. The first demonstrable response to infection is the production of specific antitreponemal IgM, which may be detected towards the end of the second week of infection; antitreponemal IgG appears later, at about four weeks. By the time symptoms develop, most patients have detectable IgG and IgM.

**SEROLOGICAL TESTS**

**Non-treponemal tests** detect non-specific treponemal antibodies. These include the Venereal Diseases Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests.

**Treponemal tests** detect specific treponemal antibodies. These include the *Treponema pallidum* haemagglutination assay (TPHA), the fluorescent treponemal antibody-absorbed test (FTA-abs), and most enzyme immunoassay (EIA) tests.

An important principle of syphilis serology is the detection of treponemal antibodies by a screening test, followed by confirmation of a reactive screening test result by further testing. The confirmatory test, or tests, should ideally have equivalent sensitivity and greater specificity than the screening test and be an alternative methodology, so as to reduce the chance of coincident false positive reactions.

A quantitative non-treponemal test and/or detection of specific antitreponemal IgM may be useful for assessment of the stage of infection and to monitor the effect of treatment.

**CONFIRMATORY TESTS**

Although the FTA-abs is still generally regarded as the ‘gold standard’, TPHA is the most appropriate test for confirming reactive EIA results at present. Treponemal IgG can also be used for confirmation.

Currently there are two schools for the testing algorithm of syphilis. One uses RPR screening while the other prefers newer ELISA based methods.
**ASSESSMENT OF STAGE OF INFECTION AND MONITORING OF TREATMENT**

A quantitative non-treponemal test and/or a test for specific antitreponemal IgM helps to assess the stage of infection, and provides a baseline for monitoring the effect of treatment. In general, IgM becomes undetectable within three to nine months after adequate treatment of early syphilis, but it may persist for 12 to 18 months after treatment of late disease.

Detection of specific antitreponemal IgM in patients with no history of recent treatment suggests active disease and the need for treatment. Quantitative nontreponemal tests such as the VDRL/RPR remain the method of choice for follow up testing, the object being to demonstrate a decline in titre, depending on a range of factors including the initial titre, stage of infection when treated, treatment regimen, and HIV status.

Detection of specific antitreponemal IgM may also be useful in the diagnosis of congenital infection but, because a negative result around the time of delivery does not exclude congenital infection, serological follow up is necessary. This should include repeat IgM testing, together with repeat quantitative nontreponemal and treponemal testing to demonstrate loss of passive maternal antibodies.

**SUMMARY**

Syphilis is a disease whose diagnosis is primarily limited to serologic testing. Even in the minority of cases where a lesion can be tested, the dwindling use of dark-field microscopy, the difficulty in obtaining reagents for direct fluorescent testing, and the lack of molecular/PCR-based assays necessitate the continued use of antibody detection assays for the diagnosis of syphilis. The presence of detectable antibodies is dependent on the individual’s immune competency, the infectious dose, and the length of time between exposure/infection and screening.

Defining one specific testing algorithm that will address the needs of screening both high- and low-risk populations, detecting antibodies at all the various clinical stages of syphilis and meeting the laboratory needs for efficiency and accuracy will continue to be problematic.

**References**


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