

FACT SHEET FOR HEALTHCARE PROVIDERS

Multiplo® Complete Syphilis (TP/nTP) Antibody Test

MedMira Inc.



This fact sheet is intended for healthcare professionals and informs them of the significant known and potential benefits and risks associated with the use of Multiplo® Complete Syphilis (TP/nTP) Antibody Test.

Intended use: Multiplo® Complete Syphilis (TP/nTP) Antibody Test (Multiplo® TP/nTP) is a single use, manually performed, visually interpreted, qualitative immunoassay based on Rapid Vertical Flow Technology®, to detect antibodies to *Treponema pallidum* (TP), the causative agent of syphilis, and nontreponemal (nTP) antigens in human serum, plasma, or fingerstick whole blood specimens. Multiplo® TP/nTP is intended for use by healthcare professionals as an aid in the diagnosis of active syphilis infection.

What is syphilis? Syphilis is among most common sexually transmitted diseases (STDs) worldwide and is caused by the *Treponema pallidum* (TP) bacterium that spreads through direct contact with active lesions during vaginal, oral, or anal sexual contact with someone who has the infection. It can also be transmitted vertically when the infection is passed on from a pregnant person to their baby.

Syphilis is an easily treatable and preventable STD when diagnosed during early infections, however, when left untreated it can result in serious complications for the patient such as severe heart disease, brain damage, spinal cord damage, blindness, and death. It is referred to as “the great imitator” since many of the early signs and symptoms are indistinguishable from those of other diseases.

What are the symptoms of syphilis? Typical symptoms of syphilis generally vary over time and are dependent on the stage of infection.

Primary Syphilis: Early infection (between 10 - 90 days post infection) is characterized by the formation of sores (Chancer), which are usually painless, at the infection site. The sores usually heal without treatment in a few weeks (3-6 weeks). Infected individuals are highly contagious at this stage.

Secondary Syphilis: 2 - 8 weeks after from the formation of sores, the infection continues to spread throughout the body in the form of diffused rashes. Other symptoms observed during this stage include fever, sore throat, fatigue, headaches, etc. Infected individuals are still considered as highly contagious at this stage.

Latent (hidden) Syphilis: When left untreated, the infected person progresses into the latent stage. This stage can last between a few months to several years. Clinical manifestations observed during the secondary stage subside and infection is only apparent on serologic testing. A small proportion of patients exhibit relapse/s of symptoms that are characteristic of the secondary stage. Infected individuals are only contagious (through contact) during the relapse of secondary stage symptoms.

Tertiary (late) Syphilis: While most people with untreated syphilis do not progress to the tertiary stage, it is considered the most destructive stage (between 10 - 30 years after the first infection) affecting multiple organs and systems including the heart, blood vessels, eyes (ocular syphilis), ears (otosyphilis), and the nervous system (neurosyphilis) and can result in death.

What are syphilis tests and why are they important? Syphilis tests are used for screening and diagnosis of infection with TP. Since syphilis is easy to cure during the early stages of infection, early detection and treatment of syphilis are necessary to prevent its progression to tertiary stage. Early diagnosis and intervention can also prevent the spread to others.

The urgency for testing is further aggravated by the fact that syphilis can be transmitted from a pregnant person to their child during pregnancy, so a rapid diagnostic tool that can determine the current infection status is essential to public health worldwide as we develop strategies aimed to prevent the spread of syphilis. According to the Center for Diseases Control and Prevention (CDC), syphilis is the third most common STD in North America. Even though it is so common and easily preventable, due to the low prevalence of diagnostic testing, syphilis is one of the three STDs that required nearly 1.1 billion dollars in direct medical costs towards treatments in 2019 alone. The European Center of Disease Prevention and Control (ecdc) reported a steady increase of syphilis rate across Europe of approximately 50% each year. Taking just the congenital cases into consideration, the WHO estimated that nearly 1 million pregnant women are infected with syphilis annually, a number supported by the CDC, which reported an increase in congenital syphilis cases of around 291% between 2015 and 2019.

What do the test measure? Most syphilis tests target various types of antibodies generated against the TP bacterium. Generally these tests fall into two major types: Treponemal antibody tests and Nontreponemal antibody tests.

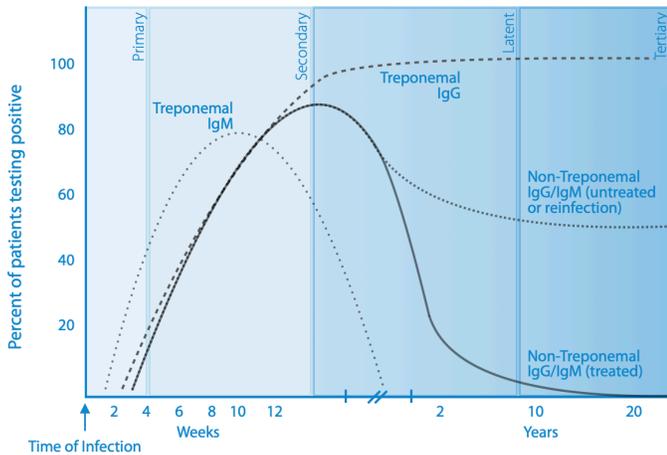
Treponemal antibody tests (TP) detect antibodies that are produced after syphilis infections. These antibodies are detectable earlier than nontreponemal antibodies and typically remain indefinitely after the initial infection. Since these antibodies remain even after treatment, they cannot be used to distinguish between current or past syphilis infection.

Nontreponemal antibody tests (nTP) detect nonspecific antibodies against lipoidal biomarkers (cardiolipin, lecithin, etc) that are released during the cellular damage caused by a syphilis infection. Since these biomarkers can also be produced in response to other conditions and infections (i.e., not specific to TP), they are regarded as screening tests.

When and how are syphilis tests performed? Syphilis testing should be performed on all symptomatic patients that exhibit signs or symptoms of infection, as well as any asymptomatic patients who are at high risk for infection or transmitting the infection to others. Diagnosis of syphilis should not be made on the basis of a single test result. Clinical history, symptoms, and risk factors must be considered when diagnosing and staging individuals.

Historical testing algorithms for syphilis employed a two-stage approach, by first screening with a non-treponemal test for primary evaluation, followed by a treponemal test for confirmation.

Contemporary “reverse” screening algorithms, currently recommended by most health authorities, screen with a treponemal test first; if positive, a follow up non-treponemal test is performed. Occasionally an additional treponemal test (e.g. EIA) is recommended for further confirmation. Because non-treponemal tests take longer to turn positive in early infection and decline over time even in untreated individuals, screening with treponemal tests first is a more sensitive approach.



Based on Peeling RW, Ye H. Diagnostic tools for preventing and managing maternal and congenital syphilis: an overview. Bull World Health Organ. 2004 & Soreng K, Levy R, Fakile Y. Serologic Testing for Syphilis: Benefits and Challenges of a Reverse Algorithm. Clin Microbiol News. 2014

Why Multiplo® TP/nTP? Rising syphilis rates call for an urgent scale-up of global testing strategies. Our Multiplo® Complete Syphilis (TP/nTP) Antibody Test is a rapid test that combines both the screening (nTP) and the confirmation (TP) tests into a single device. It is ideally suited for point of patient care settings that require a portable and all-in-one testing solution.

On the Multiplo® TP/nTP test, a reactive TP result indicates previous exposure to the TP bacteria, while a reactive nTP result indicates the presence of antibodies produced during an active infection. Thus, the innovative dual detection offered by Multiplo® TP/nTP not only identifies exposure to TP but can determine the current infection status.

TP	nTP	Possible interpretation
-	-	<ul style="list-style-type: none"> Negative Repeat if at risk for syphilis
+	-	<ul style="list-style-type: none"> Repeat after 2-4 weeks May be currently in the incubation period Prior treated syphilis
+	+	<ul style="list-style-type: none"> Active syphilis Recently treated syphilis *
-	+	<ul style="list-style-type: none"> False positive Repeat testing

Note: For more recommendations on possible interpretation please refer to the references section. * Recently treated for syphilis but nontreponemal (nTP) titers have not reduced yet

Technology and Performance: Multiplo® TP/nTP is built on MedMira’s patented Rapid Vertical Flow Technology®, which has offered quick and reliable results for over 28 years.

The easy-to-use characteristics of all MedMira’s tests allow them to be used in the most diverse environments, including and particularly in resource limited areas, since they do not require specialized instruments, trained operators, nor cold chain to be used or stored. Multiplo® TP/nTP can therefore be applied in prenatal screening, public health STD prevention programs, occupational exposures, point-of-care (POC) settings, counselling centers, and mobile clinics. Importantly, Multiplo® TP/nTP can act as a key tool to accelerate the detection and potential elimination of syphilis in all possible settings. With a simple and rapid test you will get an easy-to-read answer, going from sample collection to results in minutes - helping people know...® instantly.

In a recent evaluation, Multiplo® TP/nTP displayed excellent performance, showing 100.00% sensitivity and specificity for the detection of active syphilis infections.

Important information and references:

- <https://www.cdc.gov/std/syphilis/stdfact-syphilis.htm>
- <https://www.ecdc.europa.eu/en/syphilis>
- <https://www.who.int/health-topics/syphilis>
- <https://www.who.int/data/gho/data/themes/topics/topic-details/GHO/data-on-syphilis>
- <https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html>

About MedMira: MedMira’s patented Rapid Vertical Flow Technology® delivers fast, accurate results in a range of applications. Our products help care providers and their patients know more, instantly. MedMira rapid tests are manufactured in a cGMP facility with a quality management system registered to ISO 9001 and ISO 13485. In addition, MedMira’s facility is MDSAP and CE certified. For more information about our products visit medmira.com. For support contact us at +1 902 450 1588 or support@medmira.com.



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