

# Syphilis Serology Laboratory Interpretation

TEST			INTERPRETATION		
Syphilis Screen (Treponemal e.g. CMIA)	RPR (Non Treponemal)	TP-PA (Treponemal)	Most Likely Interpretation		
			(RESULTS SHOULD BE INTERPRETED IN CONJUNCTION WITH HISTORY AND CLINICAL FINDINGS) (see Public Health Agency of Canada's ~STBBI Guides for Health Professionals; <a href="http://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines.html">www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines.html</a> )		
			Alternative Causes for Reactive Serological Tests		
			False Positive Results for Non Treponemal Tests * (RPR)	False Positive Results for Treponemal Tests * (SCREEN & TP-PA)	
Reactive	Reactive (titre/dilutions may vary)	Not tested	<p>Consistent with recent or prior syphilis infection. Results may indicate the following:</p> <ul style="list-style-type: none"> <li>(a) Infectious syphilis (primary, secondary, early latent), especially if titre <math>\geq</math> 1:8 &amp; history of symptom(s), contact with an infected partner, risks</li> <li>OR</li> <li>(b) Late latent syphilis or latent syphilis of unknown duration, especially if titre &lt;1:8 &amp; no history of treatment</li> <li>OR</li> <li>(c) Old treated syphilis</li> <li>OR</li> <li>(d) ** In persons from endemic countries, yaws (e.g. Caribbean), pinta (e.g. Central America), or bejel</li> </ul> <p><b>PLAN:</b> repeat syphilis blood work in 4 weeks to observe rise in titre for persons suspected of syphilis infection or re-infection</p>	<p><b>INFECTIOUS</b></p> <ul style="list-style-type: none"> <li>• Bacterial endocarditis (e.g., rheumatic heart disease)</li> <li>• chancroid</li> <li>• chickenpox</li> <li>• infectious mononucleosis (e.g., EBV)</li> <li>• leprosy (e.g., Hansen's disease)</li> <li>• lymphogranuloma venereum (LGV)</li> <li>• malaria</li> <li>• mumps</li> <li>• mycoplasma pneumonia</li> <li>• pneumococcal pneumonia</li> <li>• rickettsial disease</li> <li>• tuberculosis</li> <li>• viral hepatitis</li> <li>• viral pneumonia</li> <li>• other treponemal infections: yaws, pinta, or bejel **</li> </ul>	<p><b>INFECTIOUS</b></p> <ul style="list-style-type: none"> <li>• brucellosis</li> <li>• genital herpes</li> <li>• infectious mononucleosis (e.g., EBV)</li> <li>• leprosy</li> <li>• leptospirosis</li> <li>• Lyme disease</li> <li>• malaria</li> <li>• other treponemal infections: yaws, pinta, or bejel **</li> </ul>
Reactive	Non-reactive	Reactive/ Previously Reactive	<p>Consistent with recent or prior syphilis infection. Results may indicate the following:</p> <ul style="list-style-type: none"> <li>(a) Usually late latent syphilis or latent syphilis of unknown duration, with no history of treatment</li> <li>OR</li> <li>(b) Old treated syphilis</li> <li>OR</li> <li>(c) Incubating infectious syphilis (primary), especially if history of symptom(s), contact with an infected partner, or other risk factors</li> <li>OR</li> <li>(d) ** In persons from endemic countries, yaws (e.g. Caribbean), pinta (e.g. Central America), or bejel</li> </ul> <p><b>PLAN:</b> repeat blood work in 4 weeks to observe rise in titre for persons suspected of syphilis infection or re-infection; if results change, reinterpret</p>		
Reactive	Non-reactive	Indeterminate	<p>Inconclusive syphilis serology results. Possible interpretations include:</p> <ul style="list-style-type: none"> <li>(a) Incubating infectious syphilis (primary), especially if history of symptom(s), contact with an infected partner, or other risk factors</li> <li>OR</li> <li>(b) Old treated or untreated syphilis</li> <li>OR</li> <li>(c) Biological false positive</li> </ul> <p><b>PLAN:</b> repeat blood work in 4 weeks to observe rise in titre or TPPA seroconversion for persons suspected of syphilis infection or reinfection; if results change, reinterpret,</p>		
Reactive	Non-reactive	Non-reactive	<p>Usually biological false positive (false reactive screening test). Rare alternate interpretations include incubating infectious syphilis, previously treated syphilis, or, late latent syphilis</p> <p><b>PLAN:</b> repeat blood work in 4 weeks to observe rise in titre or TPPA seroconversion for persons suspected of syphilis infection or reinfection; if results change, reinterpret,</p>		
<b>Infant Serology from venipuncture</b> (for infants $\leq$ 18 months, TPPA tested regardless of RPR)			<b>INTERPRETATION†</b>		
Reactive	Reactive (titre/dilutions may vary)	Reactive/ Non-reactive/ Indeterminate	<ul style="list-style-type: none"> <li>• Suggestive of congenital infection - comparison should be made with maternal titre submitted at delivery.</li> <li>• Patients suspected of congenital syphilis should be referred to an infectious diseases or a paediatric specialist. Consider repeat serology at recommended intervals.</li> </ul>		
Reactive	Non-reactive	Reactive/ Previous Reactive	<ul style="list-style-type: none"> <li>• Does not rule out congenital infection.</li> <li>• Patients suspected of congenital syphilis should be referred to an infectious diseases or a paediatric specialist. Consider repeat serology at recommended intervals.</li> </ul>		
Reactive	Non-reactive	Non-reactive	<ul style="list-style-type: none"> <li>• Inconclusive syphilis serology.</li> <li>• Patients suspected of congenital syphilis should be referred to an infectious diseases or a paediatric specialist. Consider repeat serology at recommended intervals.</li> </ul>	<p><b>NON INFECTIOUS</b></p> <ul style="list-style-type: none"> <li>• advancing age</li> <li>• chronic liver disease (e.g., hepatitis)</li> <li>• connective tissue disease (e.g., rheumatoid arthritis)</li> <li>• immunizations</li> <li>• injection drug use</li> <li>• malignancy</li> <li>• multiple myeloma</li> <li>• pregnancy</li> <li>• ulcerative colitis</li> </ul>	<p><b>NON INFECTIOUS</b></p> <ul style="list-style-type: none"> <li>• advancing age</li> <li>• chronic liver disease (e.g., hepatitis)</li> <li>• drug addiction</li> <li>• hyperglobulinemia</li> <li>• scleroderma</li> <li>• systemic lupus erythematosus</li> <li>• thyroiditis</li> </ul>

Adapted from: Public Health Agency of Canada. 2024. ~Sexually transmitted and blood-borne infections: Guides for health professionals (Syphilis guide);

Public Health Ontario Laboratory (2025). Test Information Index - Syphilis - Serology (<https://www.publichealthontario.ca/en/Laboratory-Services/Test-Information-Index/Syphilis-Serology>);

†Canadian Paediatric Society - Diagnosis and management of congenital syphilis – Avoiding missed opportunities (<https://cps.ca/en/documents/position/congenital-syphilis>).

• \*\* for information regarding endemic treponemal infections, please refer to Heymann, David L. (Editor) 2015. Control of Communicable Disease Manual, 20th edition, American Public Health Association. Washington.

# Syphilis Infection

STAGE	INCUBATION PERIOD	DISEASE MANIFESTATIONS	TREATMENT (for alternative treatment for penicillin-allergic patients, refer to STBBI Guides)	POST TREATMENT SEROLOGICAL MONITORING		PARTNER NOTIFICATION (time period)
				Monitoring Schedule	Adequate Response (2-tube drop = 4 fold drop e.g., from 1:32 to 1:8)	
<b>PRIMARY</b> (infectious)	3-90 days (average is 21 days)	Chancre, and/or regional lymphadenopathy	Benzathine penicillin G 2.4 million units IM as a single dose	3, 6, 12 months after treatment	2-tube drop at 6 months 3-tube drop at 12 months 4-tube drop at 24 months	3 months prior to the onset of symptoms
<b>SECONDARY</b> (infectious)	2-12 weeks	Rash, fever, malaise, lymphadenopathy, mucosal lesions, condyloma lata, alopecia, (for meningitis, headaches, uveitis, and/or retinitis, refer to neurosyphilis)	Benzathine penicillin G 2.4 million units IM as a single dose	3, 6, 12 months after treatment	3-tube drop at 6 months 4-tube drop at 12 months	6 months prior to the onset of symptoms
<b>EARLY LATENT</b> (infectious)	< 1 year	Asymptomatic	Benzathine penicillin G 2.4 million units IM as a single dose	3, 6, 12 months after treatment	2-tube drop at 12 months	1 year prior to the diagnosis
<b>LATE LATENT SYPHILIS or SYPHILIS OF UNKNOWN DURATION</b> (not infectious)	≥ 1 year	Asymptomatic	Benzathine penicillin G 2.4 million units IM weekly for 3 doses	12 and 24 months after treatment	Response will be variable	As late latent syphilis is not considered infectious, consider the assessment of marital or other long-term partners and children as appropriate
<b>TERTIARY</b> (not infectious)					<ul style="list-style-type: none"> <li>Response will be variable</li> <li>Refer to STBBI Guides</li> </ul>	Assess marital or other long term partners and children as appropriate
Cardiovascular Syphilis	10-30 years	Aortic aneurysm, aortic regurgitation, and/or coronary artery ostial stenosis	Benzathine penicillin G 2.4 million units IM weekly for 3 doses	12 and 24 months after treatment		
Neurosyphilis (can occur at any stage; infectious when diagnosed in primary, secondary, or early latent stage)	<2-20 years	Cerebrospinal fluid examination to diagnose. Symptoms include headache, vertigo, personality changes, dementia, ataxia, meningitis, auditory symptoms, cranial nerve abnormalities, uveitis, and/or retinitis.	Penicillin G 3 - 4 million units IV q4h (16 - 24 million units/day) for 10 - 14 days	6, 12 and 24 months after treatment		
Gumma	1-46 years (most cases 15 years)	Tissue destruction of any organ; manifestations depend on site involved	Benzathine penicillin G 2.4 million units IM weekly for 3 doses	12 and 24 months after treatment		
<b>HIV INFECTED</b> (at any stage)		Co-infection with HIV increases risk of developing neurosyphilis. Consider neurosyphilis in persons presenting with neurologic, ocular, and other signs and symptoms.	<ul style="list-style-type: none"> <li>Treat for stage of diagnosis</li> <li>Refer to STBBI Guides</li> </ul>	3, 6, 12 and 24 months after treatment and yearly thereafter	Response may be delayed; consider CSF examination and re-treatment if RPR does not decrease 2-tube within 24 months. See STBBI Guides	Assess partners based on the stage of diagnosis
<b>‡ INFECTION IN PREGNANCY</b>	Incubation period and disease manifestations are as above.	<b>TREATMENT, FOLLOW-UP, AND PARTNER NOTIFICATION IN PREGNANCY</b>				
		<p>There is NO ALTERNATIVE to penicillin for treatment in pregnancy</p> <ul style="list-style-type: none"> <li>Treat, as above, for stage of infection. For infectious syphilis some experts recommend two doses of IM treatment, one week apart.</li> </ul>	<ul style="list-style-type: none"> <li>To determine the adequacy of syphilis treatment in pregnancy consult the Canadian Paediatric Society's position statement - Diagnosis and management of congenital syphilis – Avoiding missed opportunities. (<a href="https://cps.ca/en/documents/position/congenital-syphilis">https://cps.ca/en/documents/position/congenital-syphilis</a>)</li> </ul>	<p>Re-test:</p> <ul style="list-style-type: none"> <li>Monthly until delivery if at high risk of re-infection</li> <li>At delivery and 1, 3, 6 and 12-months post-treatment (infectious)</li> <li>At delivery and 12 and 24 months (late latent)</li> </ul>	<ul style="list-style-type: none"> <li>Assess partners based on stage of maternal diagnosis.</li> <li>Infant should be assessed/tested/treated at delivery‡</li> </ul>	
<b>‡ EXPOSED INFANTS/ CONGENITAL INFECTIONS</b>	<ul style="list-style-type: none"> <li>For best practices on syphilis management in pregnancy and infants consult the Canadian Paediatric Society's position statement - Diagnosis and management of congenital syphilis – Avoiding missed opportunities (<a href="https://cps.ca/en/documents/position/congenital-syphilis">https://cps.ca/en/documents/position/congenital-syphilis</a>).</li> <li>Maternal antibodies can be present in infants for up to 18 months.</li> </ul>					

## Toronto Public Health STI Program 416-338-2373

- Free medication for reportable syphilis, other bacterial STIs, and condoms are available.
- Toronto Public Health STI Program can assist in partner notification.

Adapted from: •Public Health Agency of Canada (2024). STBBI Guides - Syphilis.

•Centers for Disease Control and Prevention. 2021 STI Treatment Guidelines.

•‡Canadian Paediatric Society - Diagnosis and management of congenital syphilis

–Avoiding missed opportunities (<https://cps.ca/en/documents/position/congenital-syphilis>)