

Syphilis Infections

STAGE	INCUBATION PERIOD	DISEASE MANIFESTATIONS	TREATMENT	POST TREATMENT SEROLOGICAL MONITORING		PARTNER NOTIFICATION (TIME PERIOD)
				Monitoring Schedule	Adequate Response (2-tube drop = 4 fold drop, e.g. 1:32 to 1:8)	
PRIMARY (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 (mos.) after treatment	2-tube drop at 6 mos. 3-tube drop at 12 mo. 4-tube drop at 24 mo.	3 mos. prior to the onset of symptoms or date of specimen collection (if asymptomatic)
SECONDARY (infectious)	2-12 weeks	Rash, fever, malaise, lymphadenopathy, mucus 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 mos. after treatment	3-tube drop at 6 mos 4-tube drop at 12 mos.	6 mos. prior to the onset of symptoms or date of specimen collection (if asymptomatic)
EARLY LATENT (infectious)	<1 year	Asymptomatic	Benzathine penicillin G 2.4 million units IM as a single dose	3, 6, 12 mos. after treatment	2-tube drop at 12 mos.	1 year prior to the diagnosis
LATE LATENT SYPHILIS or UNKNOWN DURATION (not infectious)	>1 year	Asymptomatic	Benzathine penicillin G 2.4 million units IM weekly for 3 doses	12 and 24 mos. 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
HIV INFECTED (at any stage)			· Treat for stage of diagnosis. Additional doses have not been shown to be more effective for HIV+ individuals. Careful follow-up is essential as there may be increased risk of neurological complications or serologic treatment failure. Refer to STI Guidelines	3, 6, 12 and 24 mos. after treatment and yearly thereafter	· Response will be variable and may take longer to decline · Refer to STI Guidelines	Assess partners based on the stage of diagnosis

- Canadian Guidelines on Sexually Transmitted Infections. Public Health Agency of Canada. Last updated: 2022
<https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections.html>
- PHAC Syphilis Guide – Treatment and follow-up 2022-07-07

STAGE	INCUBATION PERIOD	DISEASE MANIFESTATIONS	TREATMENT	POST TREATMENT SEROLOGICAL MONITORING		PARTNER NOTIFICATION (TIME PERIOD)
				Monitoring Schedule	Adequate Response (2-tube drop = 4 fold drop, e.g. 1:32 to 1:8)	
TERTIARY (not infectious)						
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 mos. after treatment	<ul style="list-style-type: none"> Response will be variable Refer to STI Guidelines 	Assess marital or other long-term partners and children as appropriate
Neurosyphilis (can occur at any stage)	<2-20 years	Cerebrospinal examination to diagnose. Symptoms include headaches, 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 mos. 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 mos. after treatment		
PREGNANT & LACTATING			<ul style="list-style-type: none"> A single dose of benzathine penicillin G-LA 2.4 million units is effective in most cases of early syphilis, but some experts recommend that primary, secondary and early latent cases (due to difficulty in accurately staging cases) should be treated with two doses of benzathine penicillin G-LA 2.4 million units one week apart, particularly in the 3rd trimester. Effectiveness of additional doses to prevent fetal syphilis is not known. Retreatment during pregnancy is not necessary unless there is <ol style="list-style-type: none"> 1) clinical or serologic evidence of new infection (four-fold rise in an NTT titre), 2) serologic evidence of inadequate treatment response, or 3) history of recent sexual contact with a person with infectious syphilis. PHAC 2022 There is no alternative to penicillin for treatment in pregnancy; Refer to STI Guidelines. 	1,3,6,12-mos. post tx 1°, 2° & early latent Monthly until delivery if at high risk of reinfection Late latent at time of delivery and 12 & 24 mo		

Syphilis Laboratory Interpretation

TEST			INTERPRETATION		
Syphilis Screen (Treponemal) e.g. EIA, CMIA, CLIA	RPR (Non Treponemal) Note: RPR ≥ 8 are more likely to be infectious syphilis	TP-PA (Treponemal)	Most Likely Interpretation (results should be interpreted in conjunction with history and clinical findings)	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 (dilutions may vary)	Reactive OR Indeterminate	<p>Consistent with recent or prior syphilis infection. Results may indicate the following:</p> <p>(a) Infectious syphilis (primary, secondary, early latent), especially if titre > 1:8 & history of symptom(s), contact with an infected partner, other risk factors</p> <p>OR</p> <p>(b) Late latent syphilis or latent syphilis of unknown duration, especially if titre < 1:8 & no history of treatment</p> <p>OR</p> <p>(c) Old treated syphilis</p> <p>OR</p> <p>(d) In persons from endemic countries, yaws (e.g. Caribbean), pinta (e.g. Central America), or bejel</p> <p>PLAN: repeat blood work in 2-4 weeks to observe rise in titre or TPPA seroconversion</p>	<p>INFECTIOUS</p> <ul style="list-style-type: none"> • bacterial endocarditis (e.g. rheumatic heart disease) • chancroid • chickenpox • infectious mononucleosis (e.g. EBV) • leprosy (e.g. Hansen's disease) • lymphogranuloma venereum (LGV) • malaria • mumps • mycoplasma pneumonia • pneumococcal pneumonia • rickettsial disease • tuberculosis • viral hepatitis • viral pneumonia • other treponemal infections: yaws, pinta, or bejel 	<p>INFECTIOUS</p> <ul style="list-style-type: none"> • brucellosis • genital herpes • infectious mononucleosis (e.g. EBV) • leprosy • leptospirosis • lyme disease • malaria • other treponemal infections: yaws, pinta, or bejel
Reactive	Non Reactive	Reactive	<p>Consistent with recent or prior syphilis infection. Results may indicate the following:</p> <p>(a) Usually late latent syphilis or latent syphilis of unknown duration, with no history of treatment</p> <p>OR</p> <p>(b) Old treated syphilis</p> <p>OR</p> <p>(c) Incubating infectious syphilis (primary), especially if history of symptom(s), contact with an infected partner, or other risk factors</p> <p>OR</p> <p>(d) In persons from endemic countries, yaws (e.g. Caribbean), pinta (e.g. Central America), or bejel</p> <p>PLAN: repeat blood work in 2-4 weeks to observe rise in titre</p> <ul style="list-style-type: none"> • if results change, reinterpret 		
Reactive	Non Reactive	Indeterminate	<p>Inconclusive syphilis serology results. Possible interpretations include:</p> <p>(a) Incubating infectious syphilis (primary), especially if history of symptom(s), contact with an infected partner, or other risk factors</p> <p>OR</p> <p>(b) Old treated or untreated syphilis</p> <p>OR</p> <p>(c) Biological false positive</p> <p>PLAN: repeat blood work in 2-4 weeks to observe rise in titre or TPPA seroconversion</p> <ul style="list-style-type: none"> • if results change, reinterpret 		

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Syphilis Screen (Treponemal) e.g. EIA, CMIA, CLIA	RPR (Non Treponemal)	TP-PA (Treponemal)	Most Likely Interpretation (results should be interpreted in conjunction with history and clinical findings)	Alternative Causes for Reactive Serological Tests	
				False Positive Results for Non Treponemal Tests (RPR)	False Positive Results for Treponemal Tests (SCREEN & TP-PA)
Reactive	Non Reactive	Non Reactive	Usually biological false positive. Alternate interpretations include incubating infectious syphilis, previously treated syphilis, or rarely, late latent syphilis PLAN: repeat blood work in 2-4 weeks to observe rise in titre or TPPA seroconversion • if results change, reinterpret	NON INFECTIOUS <ul style="list-style-type: none"> • advancing age • chronic liver disease (e.g. hepatitis) • connective tissue disease (e.g. rheumatoid arthritis) • immunizations • injection drug use • malignancy • multiple myeloma • pregnancy • ulcerative colitis 	NON INFECTIOUS <ul style="list-style-type: none"> • advancing age • chronic liver disease (e.g. hepatitis) • drug addiction • hyperglobulinemia • scleroderma • systemic lupus erythematosus • thyroiditis
Reactive	Reactive (dilutions may vary)	Non Reactive	Inconclusive syphilis serology results. Possible interpretations include: (a) Incubating infectious syphilis (primary), especially if history of symptom(s), contact with an infected partner, or other risk factors OR (b) Old treated or untreated syphilis OR (c) Biological false positive PLAN: repeat blood work in 2-4 weeks to observe rise in titre or TPPA seroconversion • if results change, reinterpret		
Non Reactive	Test not done	Test not done	• No confirmatory testing performed when screen is non-reactive • Early incubating syphilis can be non-reactive before antibodies develop PLAN: If clinical suspicion of early syphilis, repeat blood work in 2-4 weeks to observe rise in titre or TPPA seroconversion		

Adapted from: TPH STI Syphilis Treatment Guide (2018), Toronto Public Health

Last updated: March 2023

- Canadian Guidelines on Sexually Transmitted Infections. Public Health Agency of Canada. Last updated: 2022 <https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections.html>
- Public Health Ontario. (2023). Syphilis <https://www.publichealthontario.ca/en/diseases-and-conditions/infectious-diseases/sexually-transmitted-infections/syphilis>
- Public Health Ontario. (2020). Syphilis Serologic Testing Update https://www.publichealthontario.ca/-/media/Documents/Lab/lab-sd-057-syphilis-treponema-pallidum-serology-testing.pdf?la=en&rev=742325e9cd1645f893f5fb240623ff9f&sc_lang=en&hash=DF41311F059835C304EE502F29F75723

Hastings Prince Edward Sexual Health Program
613-966-5500 ext. 243 hpePublicHealth.ca



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