

Management of Syphilis Infections

STAGE	INCUBATION PERIOD	DISEASE MANIFESTATIONS	TREATMENT ^{1,2,3} Contact the Sexual Health Clinic to order free Penicillin G Benzathine-Long Acting (LA)	SEROLOGICAL/CSF MONITORING ⁵		PARTNER NOTIFICATION ¹ Contact Trace Back Period	CONTACT FOLLOW-UP ¹	
				Monitoring Schedule	Adequate RPR Response			
INFECTIOUS	PRIMARY	3-90 days (avg. 21 days)	<ul style="list-style-type: none"> Painless lesion (chancre), regional lymphadenopathy Those co-infected with HIV can have more aggressive/atypical signs of infection and/or rapidly progress to neurosyphilis. 	<ul style="list-style-type: none"> Penicillin G Benzathine-LA 2.4 million units IM in a single dose.⁴ To avoid unnecessary retreatment, obtain and document prior history of syphilis treatment and prior serologic results. <p>HIV: Available data suggest that HIV+ individuals with early syphilis will respond appropriately to single dose Penicillin G Benzathine-LA 2.4 million units IM.⁴</p>	<ul style="list-style-type: none"> At time of treatment, 3, 6, 12 months after treatment. <p>HIV: At time of treatment, 3, 6, 12, 24 months after treatment and then yearly.</p> <p>Pregnant: Monthly until delivery if at high risk of re-infection or at time of treatment, 1, 3,6,12 months after treatment.</p>	<ul style="list-style-type: none"> 4-fold drop at 6 months 8-fold drop at 12 months <p>HIV: Variable response.</p>	<ul style="list-style-type: none"> 3 months prior to onset of symptoms or date of specimen collection (if asymptomatic). <p>Pregnant Case: Infant should be assessed at delivery.</p>	<ul style="list-style-type: none"> Syphilis serology monthly based on last exposure, until outside of window period (12 weeks). Strongly consider empirically treating sexual contacts of primary, secondary, and early latent syphilis cases from the previous 90 days, especially if they may be lost to follow-up, unable to test or follow up of the contact is not feasible. <p>Empiric treatment:</p> <ul style="list-style-type: none"> Penicillin G Benzathine-LA 2.4 million units IM as a single dose.
	SECONDARY	2-12 weeks (can occur up to 6 months)	<ul style="list-style-type: none"> Rash, fever, malaise, lymphadenopathy, mucosal lesions, condylomata lata, alopecia, headaches Those co-infected with HIV can have more aggressive/atypical signs of infection and/or rapidly progress to neurosyphilis. 	<ul style="list-style-type: none"> Rash, fever, malaise, lymphadenopathy, mucosal lesions, condylomata lata, alopecia, headaches Those co-infected with HIV can have more aggressive/atypical signs of infection and/or rapidly progress to neurosyphilis. <p>Pregnant/Lactating: A single dose of Penicillin G Benzathine-LA 2.4 million units IM in a single dose is effective in most cases of early syphilis.⁴</p> <p>Some experts recommend Penicillin G Benzathine LA 2.4 million units IM weekly for 2 doses, particularly in the 3rd trimester.⁴</p>	<ul style="list-style-type: none"> At time of treatment, 12, 24 months after treatment. <p>Pregnant: At time of treatment, at delivery, 12, 24 months after treatment.</p>	<ul style="list-style-type: none"> 8-fold drop at 6 months 16-fold drop at 12 months <p>HIV: Variable response.</p>	<ul style="list-style-type: none"> 6 months prior to onset of symptoms or date of specimen collection (if asymptomatic). <p>Pregnant Case: Infant should be assessed at delivery.</p>	
	EARLY LATENT	< 1 year	<ul style="list-style-type: none"> Asymptomatic Those co-infected with HIV can have more aggressive/atypical signs of infection and/or rapidly progress to neurosyphilis. 	<ul style="list-style-type: none"> Asymptomatic Those co-infected with HIV can have more aggressive/atypical signs of infection and/or rapidly progress to neurosyphilis. <p>Some experts recommend Penicillin G Benzathine LA 2.4 million units IM weekly for 2 doses, particularly in the 3rd trimester.⁴</p> <ul style="list-style-type: none"> Consult with obstetric/maternal-fetal specialist. 		<ul style="list-style-type: none"> 4-fold drop at 12 months <p>HIV: Variable response.</p>	<ul style="list-style-type: none"> 1 year prior to date of specimen collection. <p>Pregnant Case: Infant should be assessed at delivery.</p>	
LATE LATENT (Not infectious) or UNKNOWN DURATION	>1 year	Asymptomatic	<p>Penicillin G Benzathine LA 2.4 million units IM weekly for 3 doses.⁴</p>	<ul style="list-style-type: none"> At time of treatment, 12, 24 months after treatment. <p>Pregnant: At time of treatment, at delivery, 12, 24 months after treatment.</p>		<p>Variable response.¹</p>	<p>Long-term partners and children as appropriate.</p>	<p>Decision to test contacts depends on estimated duration of infection in index case.¹</p>

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				Monitoring Schedule	Adequate RPR Response			
	NEURO-SYPHILIS	Can occur at any stage	<ul style="list-style-type: none"> CSF examination to diagnose. Asymptomatic or ataxia, vertigo, dementia, headaches, personality changes, Otic symptoms (e.g., tinnitus, hearing loss) Ocular symptoms (e.g., blurred vision, flashing lights, floaters, eye redness, Argyll Robertson pupil). 	Refer to neurologist/ID specialist	<ul style="list-style-type: none"> 6, 12, 24 months after treatment. CSF monitoring based on ID specialist recommendations. 	Variable response. ¹	According to stage at diagnosis.	According to stage at diagnosis.
TERTIARY NON-INFECTIOUS	CARDIO-VASCULAR	10-20 years	Aortic aneurysm, aortic regurgitation, coronary artery ostial stenosis.	Penicillin G Benzathine LA 2.4 million units IM weekly for 3 doses. ⁴	<ul style="list-style-type: none"> 12, 24 months after treatment. 		Long-term partners and children as appropriate. ¹	Decision to test contacts depends on estimated duration of infection in index case. ¹
	SYPHILITIC GUMMA	1-46 years (Most cases within 15 years).	Gummatous lesions can cause tissue destruction of any organ; manifestations depend on site involved.					
CONGENITAL	EARLY CONGENITAL⁶	Within 2 years of birth	<ul style="list-style-type: none"> Asymptomatic or Neurosyphilis, rhinitis, osteochondritis, hepatosplenomegaly, mucocutaneous lesions, fulminant disseminated infection. Spontaneous abortion/stillbirth/hydrops fetalis.⁶ 	<ul style="list-style-type: none"> All neonates potentially exposed to syphilis should be assessed at delivery by an ID specialist. See Canadian Pediatric Society (CPS) resource for additional information.⁶ 	<ul style="list-style-type: none"> See CPS resource for detailed monitoring and follow-up guidance.⁶ Test infant if signs of congenital syphilis even if mother was seronegative as they may have become infected near term. 	See CPS resource for detailed monitoring and follow-up guidance. ⁶	Biological mother if syphilis not previously identified (e.g., no prenatal screening, mother seronegative at birth may have become infected near term).	
	LATE CONGENITAL⁶	2 years+ after birth	Anemia, neurosyphilis, bone involvement, interstitial keratitis (age 2-20 years), lymphadenopathy, hepatosplenomegaly, dental abnormalities, deafness (age 10-40 years).	Refer to ID specialist.	See CPS resource for detailed monitoring and follow-up guidance. ⁶			

¹For additional information refer to Canadian STI Guidelines (2021): <https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html>

²Advise those treated with Penicillin G to abstain from sexual contact for 7 days after completion of treatment.

³Those being treated for syphilis should also be screened for Chlamydia, Gonorrhoea and HIV.

⁴One dose of Penicillin G Benzathine-LA is divided into two syringes of 1.2 million units each, administered in the right and left ventrogluteal sites.

⁵Additional testing may be warranted if the stage of diagnosis is uncertain or there are concerns about re-infection.

⁶Canadian Pediatric Society (CPS). 2018. Congenital syphilis: No longer just of historical interest: <https://cps.ca/en/documents/position/congenital-syphilis>

SYPHILIS TITRES				
TITRE Rapid Plasma Reagin (RPR)	DECREASE (DROP)			
	1-tube, 2-fold	2-tube, 4-fold	3-tube, 8-fold	4-tube, 16-fold
Non-Reactive	Non-Reactive	Non-Reactive	Non-Reactive	Non-Reactive
1:1	1:1			
1:2				
1:4	1:2	1:1		
1:8	1:4	1:2	1:1	
1:16	1:8	1:4	1:2	1:1
1:32	1:16	1:8	1:4	1:2
1:64	1:32	1:16	1:8	1:4
1:128	1:64	1:32	1:16	1:8
1:256	1:128	1:64	1:32	1:16

Alternative Treatments for those with Penicillin Allergies		
	For non-pregnant adults	For pregnant adults
Primary, Secondary, Early Latent Syphilis	<ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 14 days. In exceptional circumstances and when close follow-up is assured: <ul style="list-style-type: none"> • Ceftriaxone 1 g IV or IM daily for 10 days. 	<ul style="list-style-type: none"> • For infectious syphilis strongly consider Penicillin desensitization followed by treatment with Penicillin. • There is no satisfactory alternative to Penicillin for the treatment of syphilis in pregnancy. Insufficient data exist to recommend ceftriaxone in pregnancy.
Latent, Late Latent or Unknown, Cardiovascular, Gumma	Consider penicillin desensitization. <ul style="list-style-type: none"> • Doxycycline 100 mg PO BID for 28 days In exceptional circumstances and when close follow-up is assured: <ul style="list-style-type: none"> • Ceftriaxone 1 g IV or IM daily for 10 days. 	<ul style="list-style-type: none"> • There is no satisfactory alternative to Penicillin for the treatment of syphilis in pregnancy. Insufficient data exist to recommend ceftriaxone in pregnancy.

Public Health Agency of Canada. (2023). Canadian STI Guidelines: Treatment and follow-up: <https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/treatment-follow-up.html>

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Syphilis Laboratory Interpretation			
Test			Possible Interpretations
Syphilis Screen Screening Test (e.g., EIA, CMIA)	RPR (Non-Treponemal)	TPPA (Treponemal)	Results should be interpreted in conjunction with history and clinical findings
Non-reactive	Not tested	Not tested	Early incubating syphilis can be non-reactive before antibodies develop. If suspicious of early syphilis repeat serology in 4 weeks.
Reactive	Reactive	Indeterminate or Not Tested	Consistent with recent or prior syphilis infection
Reactive	Non-Reactive	Reactive	
Reactive	Non-Reactive	Non-Reactive	Results consistent with false positive or Rare alternate interpretations: Early Syphilis or Old treated or Late latent Repeat serology in 4 weeks.
Reactive	Non-Reactive	Indeterminate	Inconclusive syphilis serology result: False positive or Early Syphilis or Old treated or Untreated syphilis Repeat serology in 4 weeks.
Reactive	Invalid	Not tested	Inconclusive syphilis serology result Repeat serology

Public Health Ontario. (2020) Syphilis Serology: <lab-sd-057-syphilis-treponema-pallidum-serology-testing.pdf> (publichealthontario.ca)

Contact the Sexual Health Clinic with questions or to order free STI medication

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**Sexual Health
Santé sexuelle**
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