PUBLIC HEALTH AGENCY OF CANADA

Clinical Syphilis Case Studies

A resource for health professionals involved in syphilis screening, diagnosis and management in Canada

Fabricated clinical case studies for education and training purposes

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Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

Clinical Syphilis Case Studies

Intended audience

Health professionals and public health professionals involved in syphilis screening, diagnosis and management in Canada, including: pharmacists, midwives, public health nurses, nurse practitioners, family physicians, emergency medicine physicians, obstetricians and gynaecologists, general internal medicine specialists and infectious diseases specialists.

Objectives

After reviewing these fabricated clinical case studies, health professionals will be able to:

- Recall, refer to and implement the Public Health Agency of Canada (PHAC) screening recommendations for syphilis, including prenatal screening recommendations
- As relevant to their role, integrate epidemiologic information, clinical exam findings and laboratory test results to diagnose syphilis infections
- As relevant to their role, follow PHAC recommendations for the treatment and follow-up of individuals diagnosed with syphilis infections, including syphilis during pregnancy

> **Note:** PHAC's recommendations for the screening, diagnosis and management of syphilis do not supersede provincial/territorial legislative, regulatory, policy and practice requirements or any professional guidelines that govern the practice of health professionals in their respective jurisdictions, whose recommendations may differ due to local epidemiology or context.

Additional resources

PHAC's STBBI Guides for Health Professionals: Syphilis guide: Key information and resources – Canada.ca

PHAC syphilis awareness resources: Syphilis: Awareness resources – Canada.ca

Background

Etiology

Syphilis is a complex systemic disease caused by infection with the spirochete bacterium Treponema pallidum, subspecies pallidum (TP). It is a disease found only in humans. Other non-venereal treponemal infections [bejel (dry, arid regions of Africa and the Middle East), yaws (tropical regions of Africa, Southeast Asia and Oceania) and pinta (tropical regions of the Americas)] cause distinct clinical syndromes.

Epidemiology

Cases of infectious syphilis, neurosyphilis and tertiary syphilis are nationally notifiable in Canada and are reported to the Canadian Notifiable Disease Surveillance System (CNDSS).

In Canada, rates of syphilis declined dramatically in the latter half of the twentieth century, reaching a nadir of 1.64 cases per 100,000 in 1999 before beginning to increase (PHAC, 2025b). Rates of infectious syphilis increased nearly 5-fold between 2014 and 2023 (6.5 cases per 100,000 in 2014; 30.5 cases per 100,000 in 2023), with 12,135 cases reported in 2023 (PHAC, 2025b). In recent years, rates of infectious syphilis have been rising more rapidly among females compared to males (PHAC, 2025b). Increasing rates among reproductive-age females has coincided with increases in reported congenital syphilis cases. From 1993 until 2017, annual rates of confirmed congenital syphilis ranged from 0.26 to 2.6 per 100,000 live births. Increases have been observed since 2018, reaching a recent peak of 31.7 cases per 100,000 live births in 2022.

Social and structural determinants of health and health inequities contribute to differences in rates of syphilis across different geographic regions and populations. Key populations disproportionately impacted by syphilis infections include gay, bisexual and other men who have sex with men (GBMSM), some Indigenous communities and people experiencing homelessness.

Transmission

TP is primarily spread through direct contact with an infectious lesion during vaginal, anal or oral sexual contact. Vertical transmission also occurs, via transplacental spread or contact with a genital lesion at the time of delivery.

Screening and diagnostic tests

Screening is a process aimed at detecting a condition in an asymptomatic person. Screening and diagnostic tests for syphilis include conventional serologic tests, point-of-care tests and molecular tests.

Syphilis screening and diagnostic testing involve conventional serologic testing of blood samples. For such testing, laboratories in Canada may follow a sequence termed the “traditional algorithm” or the “reverse algorithm”. In the traditional algorithm, a (preferably quantitative) non-treponemal test (NTT) is followed by a confirmatory treponemal test (TT). In the reverse algorithm, a treponemal test (TT) is initially used, and, if reactive, is followed by a quantitative non-treponemal test (NTT). Additional TTs may also be performed to increase the specificity of reported results. Consult your local laboratory for details about testing protocols used in your clinical setting.

See **Case 2** for more information about conventional serologic tests for syphilis.

Syphilis point-of-care testing is currently available in some settings in Canada. As of February 2026, four syphilis POCT that can use fingerstick specimens have been approved for use in Canada. Two are dual HIV/syphilis POCTs, and two are syphilis-only POCTs.All are treponemal antibody tests. Other syphilis POCT that include both treponemal and non-treponemal assays have been developed, but none are yet approved for use in Canada.

Molecular diagnostic tests are a definitive method for diagnosing syphilis. They can be performed on swab specimens from anatomical sites or lesions, blood, tissue or cerebrospinal fluid (CSF). See **Case 3** for more information about polymerase chain reaction testing to detect *Treponema pallidum* in lesions.

Clinical manifestations

Untreated sexually-acquired syphilis infections progress through primary, secondary and latent phases. If left untreated, tertiary syphilis can develop.

The stage of infection has implications for transmission, treatment and follow-up. Primary, secondary and early latent syphilis are considered infectious. Importantly, neurosyphilis can occur at any stage, and is categorized as early neurosyphilis (occurring in the first year following infection) and late neurosyphilis (occurring more than one year following infection).

Staging a syphilis infection involves integrating clinical history (including past syphilis infections, known or potential syphilis exposures and signs or symptoms consistent with syphilis), physical exam findings and test results. See **Case 1** for more details about the clinical manifestations of syphilis by stage.

Treatment and follow-up

Recommended treatment for syphilis depends on the stage of infection. According to PHAC, the preferred treatment for infectious syphilis is intramuscular long-acting benzathine penicillin G 2.4 million units in a single dose. The preferred treatment for late latent and tertiary syphilis is parenteral benzathine penicillin G 2.4 million units administered weekly for three doses.

Syphilis in pregnancy, congenital syphilis and neurosyphilis should be managed in consultation with an expert.

See **Case 3** for more details about syphilis treatment.

Serial quantitative NTT testing is used as a proxy for treatment response. The recommended timing for follow-up testing and the expected decline in NTT titres vary by stage. See **Case 3** for more details about post-treatment serologic monitoring.

Public health reporting and management of sexual partners

Infectious syphilis, neurosyphilis and tertiary syphilis are nationally notifiable to the Public Health Agency of Canada.

Partner notification, assessment and management are critical to controlling the spread and impact of syphilis. See **Case 1** for more information about the management of sexual partners of individuals diagnosed with syphilis.

CASE 1

This is a fabricated case. Any similarities that you may notice between this case and a real person are coincidental.

A 25-year-old cisgender man[1] presents to a sexual health booth at a pride festival for point-of-care testing for human immunodeficiency virus (HIV) and syphilis. He tells the public health nurse working at the booth that he has noticed a skin rash in the last week. His sexual partners are cisgender men, and he has had 15 partners in the past 3 months. He engages in oral, and insertive and receptive anal sex, using condoms sometimes for anal sex. He occasionally uses poppers. He travels around Canada and around the world to attend pride festivals and has recently returned from New Zealand.

He has not been diagnosed with syphilis in the past nor with HIV. He previously took oral pre-exposure prophylaxis for HIV (HIV PrEP), but discontinued this when his last prescription ran out 3 months ago.

Question 1: Which of the following is NOT an advantage of treponemal antibody point-of-care tests (POCT) for syphilis?

a) Can be performed using fingerstick specimens
b) Can be performed in outreach settings
c) Can distinguish between a current and prior syphilis infection
d) Results are available within minutes

Correct answer: c)

Explanation

Health Canada approves medical devices, including syphilis point-of-care tests (POCT), for use in Canada. The intended users and settings for approved devices are specified in the Instructions for Use. As of February 16, 2026, 2 dual HIV/syphilis POCT and 2 syphilis POCT have been approved for use in Canada: bioLytical's INSTI® MULTIPLEX HIV-1/2 Syphilis Ab test (MDL# 116586) and iStatis Syphilis Antibody Test (MDL# 113685), and MedMira's Multiplo® Rapid TP/HIV test (MDL# 112461) and Reveal® Rapid TP antibody test (MDL# 113872). All four approved tests are treponemal tests (TT).

[1]This individual was assigned male sex at birth and his gender identity is man.

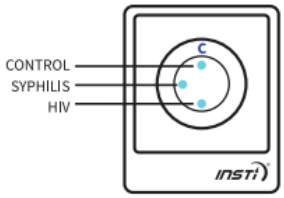
Syphilis POCTs can use fingerstick specimens. They may be conducted outside of laboratory settings, including outreach settings. Syphilis POCTs give results in minutes, and so can be used to inform immediate clinical care.

TTs, including treponemal POCT, generally remain reactive for life. In individuals without a prior diagnosis of syphilis, reactive TT results can indicate a syphilis infection (or infection with another treponeme). In individuals who are known to have had syphilis previously, the presence of treponemal antibodies is expected, and additional information is required to diagnose syphilis. Refer to **Case 2** for more details about serologic tests for syphilis.

Case 1 continued

The POCT available at the festival booth is the bioLytical INSTI® Multiplex HIV-1/2 Syphilis Antibody Test, which was the first syphilis POCT licensed for use in Canada. The patient's POCT result is reactive for syphilis and non-reactive for HIV (see Figure 1):

Figure 1: Reactive syphilis POCT result, bioLytical INSTI Multiplex HIV-1/2 Syphilis Antibody Test

Test result	Interpreting INSTI® Multiplex HIV-1/2 Syphilis Antibody Test
	**NON-REACTIVE** One blue dot that is clearly discernible above any background tint should appear on the membrane. This is the procedural Control Dot and shows that the test has been performed correctly. No reaction should be visible at either of the two test spots. A non-reactive result indicates that antibodies to HIV-1/HIV-2 and syphilis were not detected in the specimen. **REACTIVE** Two or three blue dots that are discernible above any background tint indicate that the specimen contains HIV-1 and/or HIV-2 and/or syphilis antibodies, depending on the position of the dots. One dot may be darker than the other. A sample giving these patterns is considered a preliminary reactive. Following a reactive rapid test result, a venous blood sample must be drawn and forwarded to a laboratory for HIV and/or syphilis confirmatory testing.

Source: bioLytical Laboratories, Inc. INSTI® MULTIPLEX HIV-1/2 Syphilis Ab test. 90-1110. 2025a Oct 21. Accessed 2026 Feb 10. https://cdn.prod.website-files.com/6626d03f56b08d1dc8b66b3b/6913c45a29ae1694c71cccb2_IFU%20INSTI%20Multiplex%20AB%20CA%20en.pdf

Question 2: What should the next steps in the management of this individual be?

a) Obtain a blood sample for conventional syphilis serologic testing, including treponemal and non-treponemal testing

b) Administer treatment with long-acting benzathine penicillin G 2.4 million units as a single dose
c) Advise abstinence until seven days after the individual and their partners have completed treatment
d) All of the above

Correct answer: d) All of the above

Explanation

In the presence of a reactive treponemal POCT result and symptoms that could be consistent with a syphilis infection, conventional serologic testing as well as treatment for syphilis are indicated. Individuals with syphilis should be advised to abstain until seven days after they and their sexual partner(s) have completed treatment.

Case 1 continued

The festival booth only has the capacity to perform point-of-care testing and connect individuals with reactive results to clinical care. An appointment with a public health sexual health clinic is coordinated for the next business day for further assessment, testing and treatment. He is advised to abstain from sexual contact.

When he is seen in clinic, he tells the clinician that the rash seems to be spreading, and denies any associated pain or pruritus. He has not noticed any oral, genital or anal lesions, or hair loss. He has not experienced any fevers, sore throat or swollen glands. He has not had any new headaches, vision or hearing problems, or balance impairment.

He has not been informed that he is a sexual contact of anyone diagnosed with a sexually transmitted or blood-borne infection (STBBI). He was last tested for STBBI (including syphilis) 6 months ago, and no infections were identified at that time. He has been previously treated for pharyngeal and rectal chlamydia on 2 occasions. He confirms that he has no prior history of syphilis. He denies using any injection drugs. He inhales poppers on occasion. He has previously used cocaine and has shared inhalation equipment. He has not received any tattoos or piercings from unlicensed facilities.

He reports a history of a severe allergic reaction to penicillin requiring hospitalization when he was a teenager. There is no other notable past health history. He is not taking any regular medications.

He was born in Canada and received a combination hepatitis A virus (HAV) and hepatitis B virus (HBV) vaccine series before travelling with his family as a child. He has received all recommended doses of vaccine against monkeypox virus (MPXV). He has not been vaccinated against human papillomavirus (HPV).

A physical examination reveals hyperpigmented, ovoid macules on his neck, trunk, arms, buttocks and legs and involving his palms and soles. His scalp and nails are unaffected.

There are no oral mucosal lesions, and no cervical or axillary lymphadenopathy is detected.

There are no abnormalities on cranial nerve exam. Tandem gait is normal, Romberg testing is negative, and there is no dysdiadochokinesia. Patellar reflexes are normal and symmetrical bilaterally.

Heart sounds are normal, with no extra sounds and no murmurs.

There are no anal or genital lesions, and no inguinal lymphadenopathy.

Question 3: What is the clinical syphilis stage?

a) Primary syphilis
b) Secondary syphilis
c) Early latent syphilis
d) Late latent syphilis
e) Early neurosyphilis

Correct answer: b) Secondary syphilis

Explanation

Staging a syphilis infection involves integrating epidemiological information with clinical history, exam findings and results of investigations. The stage of a syphilis infection informs treatment and follow-up decisions.

Clinical manifestations of syphilis by stage

Untreated sexually-acquired syphilis infections progress through primary, secondary and latent phases. If left untreated, tertiary syphilis can develop.

Primary syphilis: The hallmark of primary syphilis is the chancre. Classically, the chancre is a singular, painless ulcer that develops about 3 weeks after infection at the site of inoculation. Multiple and painful lesions can develop. There may also be regional lymphadenopathy.

Secondary syphilis: Heralded by the appearance of a skin rash 2 to 12 weeks after infection. The rash is extremely variable, may be subtle and may involve the palms and soles. It may be indistinguishable from other dermatological conditions, drug reactions and other infectious exanthemas. Secondary syphilis can also present with fever, malaise, lymphadenopathy, mucosal lesions, condylomata lata and patchy or diffuse alopecia.

Latent syphilis: Characterized by reactive syphilis serologic tests in the absence of signs and symptoms. Early latent syphilis refers to an asymptomatic infection acquired in the prior year. It is considered infectious because of the 25% chance of relapse to the secondary stage. Late latent syphilis is an asymptomatic infection acquired more than one year ago.

When test results indicate a new syphilis infection but the patient does not have any signs or symptoms, it can be challenging to determine whether the patient has an early or late latent infection. Laboratory evidence of seroconversion can support clinicians in definitively staging an infection as early latent. If a patient who does not have signs or symptoms of syphilis had serologic testing within the prior year and their treponemal test result is newly positive or their non-treponemal titre has increased at least four-fold, equivalent to an increase of at least two dilutions, a clinical diagnosis of early latent syphilis can be made. In the absence of such historical results, asymptomatic infections may be clinically staged as 'latent syphilis of unknown duration'. 'Latent syphilis of unknown duration' is generally treated as late latent syphilis, to ensure adequate treatment and prevent long-term sequelae.

Refer to **Case 3** for more information about syphilis treatment. Contact tracing in such cases may be conducted as for early latent syphilis, especially if the patient had a high non-treponemal titre (often defined as 1:8 dilutions or greater), as a higher titre is more suggestive of infectious syphilis. More details about the management of sexual partners are below.

Early neurosyphilis: Occurs in the first year following infection. It can present as meningitis, uveitis/retinitis, otic signs and symptoms (e.g., hearing loss, tinnitus) and cerebrovascular involvement. Co-infection with HIV alters the natural course of syphilis and may result in more rapid progression of neurosyphilis with more aggressive or atypical signs of infection.

Tertiary syphilis: Untreated, syphilis can progress to tertiary syphilis, including late neurosyphilis, cardiovascular syphilis or gumma. Late neurosyphilis occurs more than one year following infection. It can present with general paresis (e.g., personality and cognitive changes), tabes dorsalis (e.g., Argyll Robertson pupils, ataxia, sensory changes, abnormal reflexes). Cardiovascular involvement may present with aortic aneurysm, aortic regurgitation or coronary artery ostial stenosis. Syphilis can cause tissue destruction, leading to gummatous lesions.

Case 1 continued

A preliminary diagnosis of secondary syphilis can be made for this case. This diagnosis is based on: no previous history of syphilis infection; a positive treponemal POCT result; the clinical finding of a rash involving the palms and soles; and the absence of neurological signs and symptoms.

The clinician therefore advises collecting blood for conventional serologic syphilis testing to confirm the diagnosis and document the baseline non-treponemal titre. Treatment for secondary syphilis is initiated without waiting for confirmatory test results. Following jurisdictional protocols, the clinician notifies public health of the preliminary infectious syphilis diagnosis.

The clinician also recommends testing for other STBBI. This includes collecting specimens for gonorrhea and chlamydia at 3 anatomical sites (throat, urethra, rectum) and collecting blood for HIV testing, hepatitis C testing and confirmation of hepatitis B immunity. The clinician encourages HPV vaccination, and the patient indicates that they would prefer to initiate that vaccine series at a future visit.

Question 4: In the context of severe penicillin allergy in a non-pregnant person, what alternative treatment(s) are recommended for secondary syphilis?

a) Doxycycline 100 mg PO BID for 14 days
b) Doxycycline 100 mg PO BID for 28 days
c) Azithromycin 1 g PO as a single dose
d) Azithromycin 1 g PO weekly for 3 doses
e) Ceftriaxone 500 mg IM as a single dose

Correct answer: a) Doxycycline 100 mg PO BID for 14 days

Explanation

The recommended treatment for syphilis varies by stage. See **Case 3** for more details about syphilis treatment. Considering effectiveness evidence, the preferred treatment for infectious syphilis (i.e., primary, secondary and early latent syphilis) is benzathine penicillin G long-acting (LA) 2.4 million units as a single dose. For non-pregnant individuals with penicillin allergies, the alternative treatment is doxycycline 100 mg PO BID for 14 days. In exceptional circumstances (e.g., hospitalization for another indication), ceftriaxone 1 g IV or IM daily for 10 days can be used. Azithromycin is not a recommended alternative treatment for syphilis, as rates of macrolide resistance in TP are very high. Per consensus recommendations, individuals diagnosed with syphilis should abstain from condomless sex (including oral, vaginal and anal sex) until seven days after the patient and their partners have completed treatment.

Public health reporting and management of sexual partners

In all provinces and territories in Canada, cases of infectious syphilis must be reported to relevant public health authorities.

To control the spread and impact of syphilis and to prevent re-infections, individuals who had oral, vaginal or anal sex with the person diagnosed with syphilis should also be notified, clinically assessed and tested for syphilis. The trace-back period for sexual contacts depends on the stage of the syphilis infection in the person diagnosed with syphilis (Table 1):

Table 1: Trace-back period for sexual contacts of individuals diagnosed with venereal syphilis

Stage of infection in case	Trace-back period for sexual contacts
Primary syphilis	3 months from symptom onset or specimen collection, if no symptoms*
Secondary syphilis	6 months from symptom onset or specimen collection, if no symptoms*

Stage of infection in case	Trace-back period for sexual contacts
Early latent syphilis	1 year from symptom onset or specimen collection, if no symptoms*
Late latent syphilis Tertiary syphilis	Assess long-term partners as appropriate. The decision to test these contacts depends on estimated duration of infection in the index case.

* If the individual diagnosed with syphilis indicates that they did not have any sexual partners during the trace-back period, notify their most recent sexual partner.

Source: Public Health Agency of Canada. Syphilis Guide. In: Sexually Transmitted and Blood-Borne Infections: Guides for Health Professionals. 2025. Accessed 2026 Feb 4. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html

PHAC recommends considering empiric treatment with a single dose of benzathine penicillin G-LA 2.4 million IU IM for individuals who have had sexual contact in the prior 3 months with an individual diagnosed with primary, secondary or early latent syphilis, especially if there are concerns about loss-to-follow-up. In some instances, test results and clinical staging may lead to a determination that additional doses of benzathine penicillin G-LA are indicated.

> **Note:** If contacts are tested with POCT, standard serologic testing should be collected to validate any negative POCT results and to obtain non-treponemal titre results for those with positive POCTs. NTT titres at baseline are important for follow-up and detecting re-infection.

Case 1 continued

As the patient history indicates a severe allergy to penicillin, the patient is treated for presumptive secondary syphilis with doxycycline 100 mg PO BID for 14 days without waiting for his confirmatory test results. He is advised to abstain from condomless sex until 7 days after his antibiotic course is complete.

In addition, given the patient's history of penicillin allergy with severe features, referral to an allergist is initiated, to confirm the diagnosis and future management decisions.

CASE 2

This is a fabricated case. Any similarities that you may notice between this case and a real person are coincidental.

A 29-year-old transgender woman[2] presents to an urban walk-in clinic requesting testing for sexually transmitted and blood-borne infections (STBBI). She has not experienced any symptoms of concern and has not been notified that she is a contact of anyone diagnosed with a STBBI. She reports that she has had approximately 10 sexual partners in the past 3 months. Her partners are cisgender men[3] and she engages in oral and receptive anal sex. She shares that she uses methamphetamines regularly and sometimes shares inhalation equipment. She has not received any tattoos or piercings at unlicensed facilities. She was born in Canada and completed a hepatitis B virus (HBV) vaccine series in middle school. She has not been vaccinated against hepatitis A virus (HAV), human papillomavirus (HPV) or monkeypox virus (MPXV).

She had primary syphilis when she was 19 years old and was treated with Benzathine penicillin G-LA 2.4 million units by intramuscular injection. When she was diagnosed, her non-treponemal RPR titre was reactive at 1:64 dilutions. She last had syphilis testing 3 years ago, and the non-treponemal test (RPR) titre at that time was reactive at 1:1 dilution.

She has also been previously treated for rectal chlamydia and pharyngeal gonorrhea infections. She takes cyproterone acetate 12.5 mg PO daily and estradiol 4 mg PO daily, and does not have any known drug allergies.

The assessing clinician collects a urine specimen for gonorrhea and chlamydia nucleic acid amplification testing (NAAT), instructs the patient on self-collection of pharyngeal and rectal gonorrhea and chlamydia NAAT specimens and provides the patient with a requisition for screening blood tests for syphilis, HIV, HCV and immunity to HBV.

Her test results are summarized below:

Test	Result
Chlamydia trachomatis NAAT – pharynx	Not detected
Neisseria gonorrhoeae NAAT – pharynx	Not detected
Chlamydia trachomatis NAAT – urine	Not detected
Neisseria gonorrhoeae NAAT – urine	Not detected
Chlamydia trachomatis NAAT – rectum	Not detected
Neisseria gonorrhoeae NAAT – rectum	Not detected

[2]This individual was assigned male sex at birth and her gender identity is woman.

[3]Her partners are individuals who were assigned male sex at birth and whose gender identity is man.

Test	Result
HIV-1,2 antibody – serum	Non-reactive
Treponema pallidum chemiluminescent microparticle immunoassay (CMIA) – serum	Reactive
Rapid plasma reagin (RPR) – serum	Reactive, 1:2
Hepatitis B surface antibody – serum	60.00 IU/L
Hepatitis C antibody – serum	Non-reactive

Question 1: What do her syphilis test results most likely indicate?

a) Syphilis reinfection – a clinical examination is required for staging
b) Previously treated syphilis with no serologic evidence of re-infection
c) False positive RPR result
d) Infection with an endemic treponeme

Correct answer: b) Previously treated syphilis with no serologic evidence of re-infection

Explanation

See the "Conventional serologic tests for syphilis" section below for a detailed explanation of the test interpretation.

Conventional serologic tests for syphilis

In Canada, the workflow termed the "reverse algorithm" is most commonly used for serologic syphilis testing. In the reverse algorithm, a treponemal test (TT) is initially performed. TTs detect antibodies to Treponema pallidum (T. pallidum), and the screening TT is typically an enzyme immunoassay (EIA) or chemiluminescent microparticle immunoassay (CMIA). If the screening TT is reactive, a quantitative non-treponemal test (NTT) is performed. NTTs detect antibodies to lipoidal antigens. Examples of NTTs are the Venereal Disease Research Laboratory test (VDRL) and the rapid plasma reagin test (RPR). NTT results are reported as titres, and titre results can vary by laboratory and assay. In some instances, and following laboratory-specific protocols, additional TTs may be performed, e.g., Treponema pallidum particle agglutination assay (TP-PA), or Innogenetics line immunoassay (INNO-LIA).

TT may be non-reactive when a syphilis infection was acquired 2 to 4 weeks prior to testing, while antibodies are developing. In general, TTs remain reactive for life following a venereal or non-venereal T. pallidum infection. In some cases of early primary syphilis, TTs may revert to non-reactive following treatment.

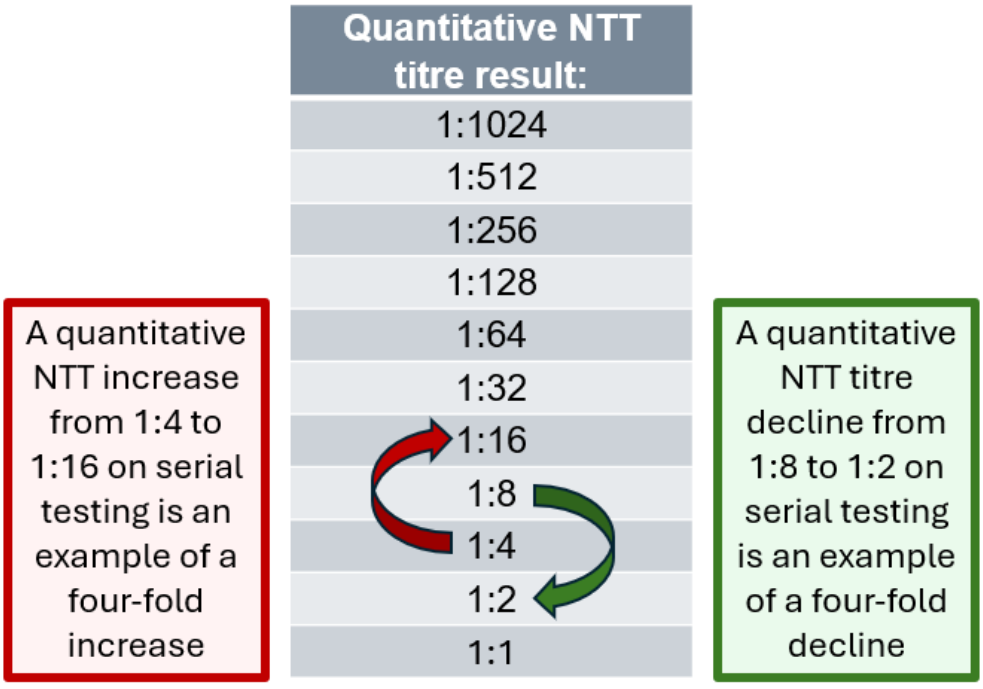
NTTs are not specific to syphilis, and reactive NTT results can be due to infections with T. pallidum, other infections, pregnancy and rheumatologic conditions. In individuals with syphilis, quantitative NTT titres generally rise and then decline over time following infection. A titre of 1:8 dilutions or greater is considered to be relatively high, and is suggestive of infectious syphilis. Notably, NTTs can be non-reactive when a syphilis infection has been recently acquired and in individuals with late latent and late presentations of tertiary syphilis. NTT titres decline following treatment and frequently revert to non-reactive. NTT are more likely to remain reactive in individuals with early and late latent infections and those with reinfections. NTTs are clinically useful as a proxy for treatment response. See **Case 3** for more details about post-treatment syphilis serology.

In addition, quantitative NTTs are used to detect reinfections. A two dilution, or four-fold, increase in NTT titre is concerning for syphilis reinfection. For example, if an individual had RPR titres of 1:1 and 1:4 on serial testing, these results would be considered to be clinically significantly different and could indicate re-infection. Figure 2 depicts possible NTT titre results and examples of a four-fold increase and a four-fold decline in titre.

When interpreting NTT titre results, it is important to be aware that a one dilution, or two-fold, change in NTT titre can be explained by within-laboratory test variability. Additional variability can be introduced with different laboratories and when different assays are used. For example, if an individual had RPR titres of 1:1 dilutions and 1:2 dilutions on serial testing using the same assay and laboratory, these results would not be considered to be different.

Refer to Table 2 for examples of common syphilis serologic test results using the reverse algorithm along with possible interpretations.

Figure 2: Depiction of quantitative non-treponemal test (NTT) titre dilutions and examples of a four-fold (or two dilution) change



Adapted from: New South Wales Health. Syphilis control guideline. 2025 May 1. Accessed 2026 Feb 16. https://www.health.nsw.gov.au/Infectious/controlguideline/Pages/syphilis.aspx

Table 2: Interpreting common syphilis serologic test results in adolescents and adults – Reverse algorithm

Screening treponemal test result (e.g., EIA, CMIA)	Confirmatory non-treponemal test result (e.g., RPR, VDRL)	Additional treponemal test result (e.g., TP-PA, INNO-LIA)	Possible interpretation
Non-reactive	Not tested	Not tested	No recent or prior syphilis. Could also represent early syphilis; repeat serology in 4 weeks if at risk.
Reactive†	Reactive† 1:x‡	Not tested	Recent or prior syphilis
Reactive†	Non-reactive	Reactive†	Recent or prior syphilis
Reactive†	Non-reactive	Non-reactive	False-positive TT. Could also represent early syphilis, previously treated syphilis or late latent syphilis; repeat serology in 4 weeks if at risk.

Abbreviations: EIA: enzyme immunoassay; CMIA: chemiluminescent microparticle immunoassay; RPR: rapid plasma reagin; VDRL: Venereal Disease Research Laboratory; TP-PA: Treponema pallidum particle agglutination assay; INNO-LIA: Innogenetics line immunoassay

† Non-venereal treponemal infections (i.e., bejel, yaws, pinta) can cause reactive treponemal test results. Other infections, rheumatologic conditions and pregnancy can cause reactive non-treponemal test (NTT) results.

‡ An NTT titre of 1:8 dilutions or greater is considered to be relatively high, and is suggestive of infectious syphilis. A two dilution, or four-fold, increase in NTT titre is concerning for syphilis reinfection.

Adapted from: Public Health Agency of Canada. Syphilis Guide. 2025. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html; Public Health Ontario. Syphilis – Serology. 2026. https://www.publichealthontario.ca/en/laboratory-services/test-information-index/syphilis-serology

Case 2 continued

The patient in this case is known to have been treated for a previous primary syphilis infection. After treatment, her TT and NTT results remained reactive, and so her reactive CMIA and RPR results are expected. Her current results are most consistent with a previously treated syphilis infection. This is because: her current RPR result is within the margin of error (or laboratory variation) of the test; she is not a recent sexual contact of someone with a syphilis infection; and she did not endorse any symptoms of early syphilis

at the clinic visit. If her NTT titre had increased at least four-fold, this would be concerning for possible re-infection.

Question 2: What should the next steps in management of this patient be?

a) Recall the patient for a syphilis staging exam
b) Treat for infectious syphilis with a single dose of Benzathine penicillin G-LA 2.5 million units by intramuscular injection
c) Treat for late latent syphilis with Benzathine penicillin G-LA 2.5 million units by intramuscular injection weekly for 3 doses
d) Encourage the patient to return for regular syphilis screening as frequently as every 3 months

Correct answer: d) Encourage the patient to return for regular syphilis screening as frequently as every 3 months

Explanation

Neither a staging exam nor syphilis treatment is indicated at this time. This is based on: patient report of appropriate treatment for a previous syphilis infection; no serologic evidence of reinfection; no known recent syphilis exposures; and no reported symptoms of early syphilis at the clinic visit.

It is important to note that NTT titres can take at least two to four weeks to increase after infection. Thus, if the patient was known to have been recently exposed to syphilis or reported recently experiencing symptoms that could be consistent with primary syphilis (i.e., a chancre), repeating the NTT two to four weeks after the initial test would confirm or refute that there is no reinfection.

If there was any uncertainty about the past treatment, it would be prudent to treat for syphilis. The recommended treatment for syphilis varies by stage. See **Case 1** for more details about the clinical manifestations of syphilis by stage.

Screening for syphilis among non-pregnant adults and adolescents

Regular syphilis screening using conventional serologic testing (including TT and NTT) is recommended for people at ongoing risk of acquiring syphilis. PHAC recommends syphilis screening for all sexually active persons with a new partner or multiple partners , or who request to be screened. Individuals with multiple partners can be screened every three to six months. PHAC suggests targeted “opt-out” screening as frequently as every 3 months when serving population groups and/or communities experiencing a high prevalence of syphilis (and other STBBI). Population groups and/or communities experiencing high prevalence of syphilis include: gay, bisexual and other men who have sex with men; people living with HIV; people who are or have been incarcerated; people who use substances or addiction services; and some

Indigenous communities. When determining which groups/communities to prioritize, consider local epidemiology. For specific individuals, consider travel history and patient risk factors.

Case 2 continued

Considering the patient's report of multiple sexual partners and previous history of STBBI, the patient is advised to return for repeat syphilis screening as often as every 3 months.

A clinical encounter for STBBI screening is an opportunity to discuss the range of effective STBBI prevention options. In addition to regular screening, the clinician encourages the use of other strategies that are relevant to this patient. These includes the consistent and correct use of barriers and safer substance use (i.e., not sharing substance use equipment). They also include vaccines and therapeutics used for pre- and post-exposure prophylaxis against STBBI. Such interventions are referred to as "biomedical prevention strategies". For this case, it would be appropriate to discuss vaccination against hepatitis A, human papillomavirus (HPV) and mpox. It would also be appropriate to discuss HIV pre- and post-exposure prophylaxis (HIV PrEP and HIV PEP) and the use of prophylactic doxycycline to prevent chlamydia, gonorrhea and syphilis. As of February 16, 2026, there were published recommendations from the National Advisory Committee on Sexually Transmitted and Blood-Borne Infections (NAC-STBBI) to inform consideration of doxycycline post-exposure prophylaxis (Doxy-PEP) for cisgender gay, bisexual and other men who have sex with men and transgender women. There were no recommendations for the use of doxycycline pre-exposure prophylaxis.

CASE 3

This is a fabricated case. Any similarities that you may notice between this case and a real person are coincidental.

A 23-year-old cisgender woman[4] presents to an urban emergency department for STBBI testing, indicating that she was a sexual contact of someone with a confirmed syphilis infection. She is pregnant, and the emergency department visit is her first presentation to care in this pregnancy. Using her last menstrual period for pregnancy dating, the gestational age is 14 weeks. While it was not planned, she intends to continue the pregnancy.

She has not previously been diagnosed with syphilis, and her most recent testing was in her prior pregnancy, approximately 2 years ago. She has not noticed any signs or symptoms of syphilis, including no signs or symptoms of neurosyphilis. Her sexual partners are cisgender men[5] and she has had 1 partner in the last 3 months and 3 in the last 6 months. She has never used inhaled or injection drugs.

She has had 1 previous uncomplicated pregnancy and 1 spontaneous vaginal delivery at term, 15 months ago. She had her tonsils and adenoids removed as a child, and has pollen and dust allergies. She was taking an oral contraceptive pill, but discontinued that when she learned that she was pregnant. She takes cetirizine as needed for allergic rhinitis.

She was born in Canada and received hepatitis B virus (HBV) and human papillomavirus (HPV) vaccine series through school-based programs. She does not use non-prescribed substances, and has not received any tattoos or piercings at unlicensed facilities.

The emergency department clinician examines her. There are no findings of note on head and neck exam, including no oral mucosal lesions, and no cervical or axillary lymphadenopathy. Cranial nerves examination reveals no abnormalities. Tandem gait is normal, Romberg testing is negative, and there is no dysdiadochokinesia. Patellar reflexes are normal and symmetrical bilaterally. Heart sounds are normal, with no extra sounds and no murmurs.

On genital exam, a solitary, round, approximately 8 mm diameter, well-demarcated ulceration with a flat, dry base and heaped-up edges is noted on the inner aspect of the left labia minora. It is non-tender. A swab of the lesion is collected for syphilis polymerase chain reaction (PCR) testing. There is left-sided non-tender inguinal lymphadenopathy. On vaginal speculum exam, there are no vaginal or cervical lesions, and no cervicitis. A small amount of clear mucoid cervical discharge is present. On bimanual exam, the uterine fundus is palpable just below the mid-point of the pubic symphysis and umbilicus. Fetal heart sounds are detected by Doppler at a rate of 140 beats per minute.

[4]This individual was assigned female sex at birth and her gender identity is woman.

[5]Her partners are individuals who were assigned male sex at birth and whose gender identity is man.

An obstetrical ultrasound is conducted. The ultrasound reveals a singleton pregnancy, and fetal measurements correspond with a gestational age of 14 weeks and 6 days. There are no abnormalities on ultrasound.

Polymerase chain reaction testing to detect Treponema pallidum in lesions

Polymerase chain reaction (PCR) is a type of nucleic acid amplification test (NAAT). PCR testing can be used to detect *Treponema pallidum* in skin and mucosal lesions that are clinically concerning for primary or secondary syphilis. Such tests can be very sensitive (depending on the specimen type and, for swabs of skin or mucosal lesions, depending on the type and location of the lesion) and are highly specific. The availability of syphilis PCR testing and instructions for specimen collection are laboratory-specific.

Question 1: What is the clinical syphilis stage?

a) Primary syphilis
b) Secondary syphilis
c) Early latent syphilis
d) Late latent syphilis
e) Early neurosyphilis

Correct answer: a) Primary syphilis

Explanation

For this case, given known exposure to syphilis, the clinical findings of a painless, solitary vulvar ulcer and inguinal lymphadenopathy, and the absence of neurological signs and symptoms, a clinical diagnosis of primary syphilis can be made while results are pending.

Refer to **Case 1**: Clinical manifestations of syphilis by stage for more information about signs and symptoms of the different stages of syphilis.

Question 2: What treatment is recommended?

a) Long-acting benzathine penicillin G 2.4 million units IM in a single dose
b) Long-acting benzathine penicillin G 2.4 million units IM weekly for 2 doses
c) Long-acting benzathine penicillin G 2.4 million units IM weekly for 3 doses
d) Doxycycline 100 mg PO BID x 14 days
e) Either (a) or (b), as per the guidance of local experts

Correct answer: e) Either (a) or (b), as per the guidance of local experts

Explanation

While a single dose of intramuscular long-acting benzathine penicillin G is effective in most cases of infectious syphilis in pregnancy, some experts recommend treating primary, secondary and early latent syphilis in pregnancy with 2 doses of intramuscular benzathine penicillin G administered one week apart, particularly in the third trimester. Individuals diagnosed with infectious syphilis during pregnancy should be managed in consultation with an expert.

For pregnant individuals, the Jarisch-Herxheimer reaction is of particular relevance and should be considered when providing treatment (see details below).

Syphilis treatment

Recommended options for syphilis treatment vary by stage and pregnancy status (see Table 3 and Table 4). Preferred treatment for syphilis is with penicillin G. Optimal patient care can be supported by penicillin allergy delabelling, oral challenges for individuals at low risk of a serious reaction and allergist referral for those with severity criteria on history.

Note: It is critical to record and communicate detailed information regarding prenatal test results, clinical staging and the treatment given, including timing with the medical team present at delivery and to the specialist(s) who will assess the newborn.

Table 3: Recommended treatment of syphilis in non-pregnant adults

Syphilis stage	Preferred treatment	Alternative treatment for people with penicillin allergies
Primary Secondary Early latent	Long-acting benzathine penicillin G 2.4 million units IM as a single dose	Doxycycline 100 mg PO BID for 14 days *In exceptional circumstances and when close follow-up is assured: Ceftriaxone 1 g IV/IM daily for 10 days*
Latent of unknown duration Late latent Tertiary: Cardiovascular Tertiary: Gumma	Long-acting benzathine penicillin G 2.4 million units IM weekly for 3 doses	Consider penicillin desensitization and treatment with penicillin Doxycycline 100 mg PO BID x 28 days *In exceptional circumstances: Ceftriaxone 1 g IV/IM daily for 10 days*
Neurosyphilis	*Manage in consultation with an expert*	

Adapted from: Public Health Agency of Canada. Syphilis Guide. 2025. Accessed 2026 Feb 4. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html

Table 4: Recommended treatment of syphilis in pregnant adults

> **Manage syphilis in pregnancy in consultation with an expert.**

Syphilis stage	Preferred treatment	Alternative treatment for people with penicillin allergies
Primary Secondary Early latent	Long-acting benzathine penicillin G 2.4 million units IM as a single dose OR Benzathine penicillin G-LA 2.4 million units IM once weekly for two (2) doses†	There is no satisfactory alternative to penicillin for the treatment of syphilis in pregnancy Strongly consider penicillin desensitization followed by treatment with penicillin *Insufficient data exist to recommend ceftriaxone*
Latent of unknown duration Late latent Tertiary: Cardiovascular Tertiary: Gumma	Long-acting benzathine penicillin G 2.4 million units IM weekly for 3 doses	
Neurosyphilis	*Manage in consultation with an expert*	

† Some experts recommend that primary, secondary and early latent cases be treated with two (2) doses of benzathine penicillin G-LA 2.4 million units one (1) week apart, particularly in the third trimester. This is because of: the difficulty in accurately staging cases of syphilis and physiological changes in pregnancy that may alter the pharmacokinetics of penicillin and reduce plasma penicillin levels. The effectiveness of additional doses to prevent fetal syphilis is not known.

Adapted from: Public Health Agency of Canada. Syphilis Guide. 2025. Accessed 2026 Feb 4. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html

The Jarisch-Herxheimer reaction

People treated for syphilis with penicillin should be advised about the Jarisch-Herxheimer reaction. It is an acute inflammatory reaction that may occur as early as 2 hours after administration of penicillin for the treatment of syphilis. It most commonly occurs in individuals with secondary syphilis but can occur at any stage. Individuals may experience fever, chills,

myalgia, headache and intensification of the skin rash of secondary syphilis. Signs and symptoms generally resolve within 24 hours. Over-the-counter antipyretics can be used as needed. No other interventions are recommended.

For pregnant individuals, the Jarisch-Herxheimer reaction can be more consequential. While Canadian data indicate that significant Jarisch-Herxheimer reactions in pregnancy are relatively uncommon, such reactions have been associated with fetal distress and premature labour. Local or institutional protocols (when applicable and available) should be used to guide decisions about treatment of syphilis in pregnancy. Such protocols may consider: gestational age; ultrasound findings; proximity to higher-level obstetrical and paediatric care facilities. Pregnant individuals treated as outpatients should be instructed to seek prompt medical attention if they experience fever, decreased fetal movement or the onset of regular uterine contractions in the 24 hours after treatment.

Case 3 continued

Considering normal ultrasound findings and the early gestational age, the patient was advised about the Jarisch-Herxheimer reaction and treated for primary syphilis with 1 dose of intramuscular long-acting benzathine penicillin G 2.4 million units. She was referred to an obstetrician for prenatal care. The treating clinician recommended that her regular sexual partner be assessed as soon as possible at a local sexual health public health clinic and instructed the patient to abstain from any intimate contact until after his assessment and appropriate management (see **Case 1** for more information about the management of sexual partners of individuals diagnosed with syphilis).

Results of the tests collected in the emergency department are summarized below:

Test	Result
Treponema pallidum PCR – vulvar ulcer	Detected
Chlamydia trachomatis NAAT – urine	Not detected
Neisseria gonorrhoeae NAAT – urine	Not detected
HIV-1,2 antibody – serum	Non-reactive
Treponema pallidum chemiluminescent microparticle immunoassay (CMIA) – serum	Reactive
Rapid plasma reagin (RPR) – serum	Reactive, 1:64
Hepatitis B surface antigen – serum	Non-reactive
Hepatitis C antibody – serum	Non-reactive

Treponema pallidum detected in the lesion specimen confirms that the lesion was a syphilitic chancre. This supports the clinical staging as a primary syphilis infection. Serologic test results of reactive treponemal CMIA antibody test and reactive and high non-treponemal test (RPR) titre are consistent with this diagnosis.

Question 3: How soon after treatment should this patient have repeat syphilis serologic testing done?

a) 1 week after treatment
b) 2 weeks after treatment
c) 3 weeks after treatment
d) 4 weeks after treatment
e) 12 weeks after treatment

Correct answer: d) 4 weeks after treatment

Explanation

For people treated for syphilis in pregnancy, PHAC recommends repeating syphilis serologic testing one month after treatment was administered.

Post-treatment syphilis serology

Changes in non-treponemal test (NTT) titre are used to evaluate treatment response. Serial testing, ideally conducted by the same laboratory and using the same NTT assay, should be done at intervals until NTT titres revert to negative or reach a stable low level (e.g., stable titres ≤ 1:4 dilutions) (see Table 5). Variability in NTT results may be introduced if different NTTs, different test manufacturers or different laboratories are used. In early syphilis, NTT titres can rise rapidly. If there is a delay between initial testing and treatment, repeating serologic testing prior to treatment can ensure that an accurate baseline NTT titre is captured and support assessments of treatment response.

Table 5: Recommended timing for follow-up syphilis serology for infectious and late latent syphilis

Syphilis stage	Follow-up serologic testing
Primary Secondary Early latent	**Non-pregnant:** At 1*, 3, 6 and 12 months after treatment **Pregnant:** Monthly for duration of pregnancy if at risk of re-infection, otherwise at 1, 3, 6 and 12 months after treatment
Late latent	**Non-pregnant and not living with HIV:** At 12 and 24 months after treatment **Non-pregnant and living with HIV:** At 1*, 3, 6, 12 and 24 months after treatment, then yearly **Pregnant and living with HIV:** Monthly for duration of pregnancy if at risk of re-infection, otherwise at 1, 3, 6 and 12 months after treatment

* To ensure that the NTT titre is not rising, some experts recommend follow-up testing start one (1) month after treatment for those with primary, secondary, early latent syphilis and for those co-infected with HIV.

Adapted from: Public Health Agency of Canada. Syphilis Guide. 2025. Accessed 2026 Feb 4. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html

The expected rate and extent of NTT titre decline can vary following treatment depending on: the stage of infection at the time of treatment; baseline NTT titre; and history of previous infections (Table 6). Individuals with more recently acquired infections and those with higher baseline NTT titres are more likely to experience at least a four-fold decline in NTT titre within 6 months. In individuals with syphilis re-infections, NTT titres may decline more slowly and are less likely to revert to non-reactive compared to individuals with a first infection. The rate of NTT decline may be attenuated in pregnancy, and a four-fold or greater decline might not be observed during the pregnancy in those with infections acquired more remotely, whose baseline NTT titres are lower and when infections were treated later in pregnancy.

If an adequate decline in NTT titres is not observed, consider: inadequate treatment; re-infection; and neurosyphilis. Review the care of patients who do not experience an adequate NTT titre decline with an expert.

Table 6: Adequate decline in NTT titre by infectious syphilis stage

Stage	Adequate NTT titre decline
Primary	≥ 4-fold drop at 6 months ≥ 8-fold drop at 12 months
Secondary	≥ 8-fold drop at 6 months ≥ 16-fold drop at 12 months
Early latent	≥ 4-fold drop at 6 months

* Note: expected rate and extent of NTT decline can vary; NTT may decline more slowly when baseline NTT titres are lower, in the context of reinfection and in pregnancy.

Adapted from: Public Health Agency of Canada. Syphilis Guide. 2025. Accessed 2026 Feb 4. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis.html

Case 3 continued

The patient is advised that her PCR swab and bloodwork results confirm the diagnosis of primary syphilis, and informed that repeat syphilis testing should be conducted regularly during pregnancy, starting 1 month after treatment. Test results are highlighted in the prenatal record and shared with the hospital where the patient plans to deliver, so that they can be available to the obstetrical and paediatric teams.

Question 4: Which details regarding prenatal syphilis investigations and care will be considered by the neonatal care team when they determine whether syphilis treatment was adequate?

a) The clinical syphilis stage of the mother/birthing parent
b) The antibiotic regimen administered and date of treatment completion
c) Baseline and follow-up maternal/birthing parent NTT titres
d) Obstetrical ultrasound findings suggestive of congenital syphilis
e) All of the above

Correct answer: e) All of the above

Explanation

Neonates whose mothers/birthing parents were treated for syphilis in pregnancy require assessment for congenital syphilis. Details regarding prenatal syphilis investigations and care are necessary to assess the likelihood of congenital syphilis infection in the newborn. Diagnosing congenital syphilis is complex, because the placental transfer of antibodies makes serologic tests challenging to interpret and because a substantial proportion of infected infants do not show any clinical signs or symptoms at birth. Information about the clinical syphilis stage of the mother/birthing parent (including whether genital lesions are present at delivery), the antibiotic regimen administered, interval between treatment completion and delivery and maternal/birthing parent NTT titre decline, as well as consideration of the risk of re-infection, enable assessment of treatment adequacy. Abnormal findings on obstetrical ultrasound and clinical and laboratory findings in the newborn are also considered as part of risk-based decision-making about the need for full work-up and newborn treatment for congenital syphilis. Engaging with the appropriate specialists (high-risk obstetrician / paediatric infectious diseases specialist) will ensure appropriate assessment and follow-up.

CASE 4

This is a fabricated case. Any similarities that you may notice between this case and a real person are coincidental.

A 25 year-old cisgender woman[6] attends her first prenatal visit at an urban primary-care-run prenatal clinic. This is her first pregnancy, and the pregnancy was planned. By last menstrual period, the gestational age of the pregnancy is 10 weeks and 2 days.

She was born in the Democratic Republic of Congo. She and her spouse arrived in Canada 2 years ago as refugee claimants, and she and her spouse currently have permanent resident status. She indicates that, during the medical examination that was conducted in Canada 18 months ago as part of the immigration process, she was advised that her syphilis test results were positive, and she indicates that she received antibiotics by injection at that time. She has moved provinces since that testing was conducted, and has not had any subsequent syphilis testing.

She otherwise has no medical or surgical history. She takes daily multivitamins, and no prescription medications. She has no known drug allergies. She has never used any injection or inhaled substances. She is not sure what vaccines she has previously received.

She has been in a closed monogamous relationship with her spouse, a cisgender man[7], for the last 4 years. She does not recall whether her spouse had positive test results or was treated during his immigration medical examination, or as her sexual contact.

Question 1: According to PHAC's STBBI Guides for health professionals, when should pregnant individuals be screened for syphilis?

a) During the first trimester or at the first prenatal visit
b) At 28–32 weeks if at ongoing risk and in areas experiencing outbreaks
c) At the time of delivery if at ongoing risk and in areas experiencing outbreaks
d) More frequently for those at increased risk of syphilis
e) All of the above

Correct answer: e) All of the above

Explanation

[6]This individual was assigned female sex at birth and her gender identity is woman.
[7]This individual was assigned male sex at birth and his gender identity is man.

> See the “Screening for syphilis in pregnancy” section below.

Screening for syphilis in pregnancy

The national recommendations for syphilis screening in pregnancy have been prioritized for review, and that work has started. As of February 16, 2026, PHAC recommends screening pregnant individuals for syphilis in the first trimester or at the first prenatal visit. In areas with outbreaks and for people at ongoing risk of infection, screening should be repeated between 28 and 32 weeks’ gestation and again during labour. More frequent screening can be considered for pregnant individuals assessed to be at increased risk of syphilis. PHAC also recommends syphilis screening for individuals who experience a stillbirth after 20 weeks’ gestation.

Considering local epidemiology, some public health agencies in Canada recommend screening all pregnant individuals for syphilis at two or three time points: at the first prenatal visit, in the third trimester and again at the time of delivery. Where local/regional/provincial/territorial recommendations differ from PHAC’s recommendations, clinicians should follow local/regional/provincial/territorial recommendations.

Case 4 continued

Routine prenatal screening, including screening for sexually transmitted and blood-borne infections (STBBI) and a dating ultrasound, are ordered by the assessing physician, and a follow-up visit is booked for a prenatal physical.

Results for STBBI tests performed as part of the patient’s routine prenatal testing are summarized below:

Test	Result
Chlamydia trachomatis NAAT – urine	Not detected
Neisseria gonorrhoeae NAAT – urine	Not detected
HIV-1,2 antibody – serum	Non-reactive
Treponema pallidum chemiluminescent microparticle immunoassay (CMIA) – serum	Reactive
Rapid plasma reagin (RPR) – serum	Non-reactive
Treponema pallidum particle agglutination (TP-PA) – serum	Reactive
Hepatitis B surface antigen – serum	Non-reactive
Hepatitis C antibody – serum	Non-reactive

Her obstetrical ultrasound is conducted a week after her visit. The ultrasound reveals a singleton pregnancy. Fetal measurements correspond with a gestational age of 11 weeks and 0 days. There are no abnormalities on ultrasound.

She is recalled for assessment when the syphilis results are received. She affirms that she and her partner are in a closed monogamous relationship. She reiterates that her syphilis test was positive during her immigration medical exam. That testing was performed in another province, and the results are not available. She recalls receiving one injection in each buttock during a single visit. She doesn't recall being advised that she should have any follow-up testing. Her spouse does not recall having a positive syphilis test or receiving treatment at that time.

She has not noticed any signs or symptoms of syphilis, including no signs or symptoms of neurosyphilis. She is examined by the physician. There are no findings of note on head and neck exam, including no oral mucosal lesions and no cervical or axillary lymphadenopathy. Cranial nerves examination reveals no abnormalities. Tandem gait is normal, Romberg testing is negative and there is no dysdiadochokinesia. Patellar reflexes are normal and symmetrical bilaterally. Heart sounds are normal, with no extra sounds and no murmurs.

Anogenital exam is normal, with no external lesions noted. On vaginal speculum exam, there are no vaginal or cervical lesions and no cervicitis. A small amount of white mucoid vaginal discharge is present. On bimanual exam, the uterine fundus is palpable just below the pubic symphysis. Fetal heart sounds are detected by Doppler, at a rate of 150 beats per minute.

Question 2: What is the clinical syphilis stage?

a) Early latent syphilis
b) Latent syphilis of unknown duration
c) Late latent syphilis
d) Non-venereal treponematosis
e) (c) or (d)

Correct answer: e) (c) or (d)

Explanation

Because the patient does not have any signs or symptoms of syphilis, it is not possible to determine whether her syphilis serologic test results are due to a prior infection with a non-venereal treponeme or represent a latent syphilis infection. Non-venereal treponematoses include bejel (caused by *T. pallidum* subsp. *endemicum*), yaws (caused by *T. pallidum* subsp. *pertenue*) and pinta (caused by *T. carateum*). Yaws is the most common of these, and is found in equatorial regions of Africa (including the Democratic Republic of the Congo), Southeast Asia and the Pacific. Yaws is targeted for eradication by 2030.

Previous laboratory test results and exposure history can help distinguish between an early or late latent syphilis infection. In this instance, the history indicates that previous syphilis testing 18 months ago was positive, and, by history, she received treatment appropriate for infectious syphilis. It is not clear that there was sufficient clinical or laboratory evidence to definitively stage a syphilis infection as infectious at that time, raising questions about the adequacy of that treatment.

For an individual who has no signs or symptoms of syphilis and who has been in a closed monogamous sexual relationship for several years, a reactive treponemal test result paired with a non-reactive non-treponemal test result would be most consistent with either non-venereal treponematosis or late latent syphilis. Notably, non-reactive NTT results can also occur in early syphilis infections. Repeating syphilis serology to confirm that the NTT remains non-reactive would help confirm that the individual does not have a recently acquired syphilis infection.

See **Case 1** for more information about the clinical manifestations of syphilis by stage.

Question 3: What treatment is recommended?

a) No treatment is required, as this patient likely had endemic treponematosis AND/OR a previous syphilis infection that was appropriately treated 18 months ago
b) Long-acting benzathine penicillin G 2.4 million units IM in a single dose
c) Long-acting benzathine penicillin G 2.4 million units IM weekly for 2 doses
d) Long-acting benzathine penicillin G 2.4 million units IM weekly for 3 doses
e) Doxycycline 100 mg PO BID for 28 days

Correct answer: d) Long-acting benzathine penicillin G 2.4 million units IM weekly for 3 doses

Explanation

Treatment for possible late latent syphilis is prudent. This is because a diagnosis of late latent syphilis cannot be excluded, and, if such a diagnosis is missed, there are risks of progression of inadequately treated syphilis to tertiary syphilis for the patient and a risk of vertical transmission. In the absence of any findings consistent with neurosyphilis, late latent syphilis in pregnancy is treated with weekly doses of intramuscular long-acting benzathine penicillin G 2.4 million units for 3 doses.

For pregnant individuals, the Jarisch-Herxheimer reaction, an acute inflammatory reaction following treatment of syphilis with penicillin, has been associated with fetal distress and premature labour. Such reactions are rare in individuals with late latent infections. Institutional practices may exist to guide the management of pregnant persons with syphilis. Pregnant individuals treated as outpatients should be instructed to seek prompt medical attention if they experience fever, decreased fetal movement or the onset of regular uterine contractions in the 24 hours after treatment.

Refer to **Case 3** for additional information about recommended treatment for syphilis in pregnancy and the Jarisch-Herxheimer reaction.

Case 4 continued

Blood was drawn for repeat NTT titre before a first dose of intramuscular long-acting benzathine penicillin G 2.4 million IU was administered. The patient was advised about the Jarisch-Herxheimer reaction. The treating clinician recommended that her spouse be assessed as soon as possible at a local sexual health public health clinic and instructed the patient to abstain from any intimate contact with him until after his assessment and appropriate management (see **Case 1** for more information about the management of sexual partners of individuals diagnosed with syphilis).

Her repeat syphilis serologic test results were unchanged, as below:

Test	Result
Treponema pallidum chemiluminescent microparticle immunoassay (CMIA) – serum	Reactive
Rapid plasma reagin (RPR) – serum	Non-reactive
Treponema pallidum particle agglutination (TP-PA) – serum	Reactive

Since her RPR test was not reactive on repeat testing (a result that would have supported restaging her as having early latent syphilis), the regimen of three doses of intramuscular long-acting benzathine penicillin G 2.4 million IU was completed. Her spouse's syphilis screen was non-reactive, indicating that he had no prior syphilis infection.

Out of an abundance of caution, the patient received repeat syphilis testing one month after treatment completion and again in the third trimester. Results remained unchanged throughout her pregnancy, and, since her NTT titre remained non-reactive, no further syphilis follow-up testing was recommended. See **Case 3** for more information about post-treatment syphilis serology.

Detailed information regarding prenatal test results, clinical staging and the treatment dates were shared with the hospital where she planned to deliver so that they would be available for the obstetrical and neonatal care teams at delivery.

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