Yukon Communicable Disease Control
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Yukon Syphilis Primer and Management Guide

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Background

Despite the availability of effective diagnostics and treatments, syphilis has re-emerged in Yukon and Canada. This re-emergence creates an immediate opportunity for health care providers to improve the health and wellbeing of Yukoners by reviewing safer sex practices, advocating for healthy relationships, and providing high quality, culturally safe, and ethical sexually transmitted infection (STI) services.

Yukon's syphilis response also requires consistent approaches and collaboration between the Office of the Chief Medical Officer of Health, Yukon Communicable Disease Control (YCDC), primary care practitioners, specialists (especially infectious diseases, pediatrics, obstetrics), and other stakeholders.

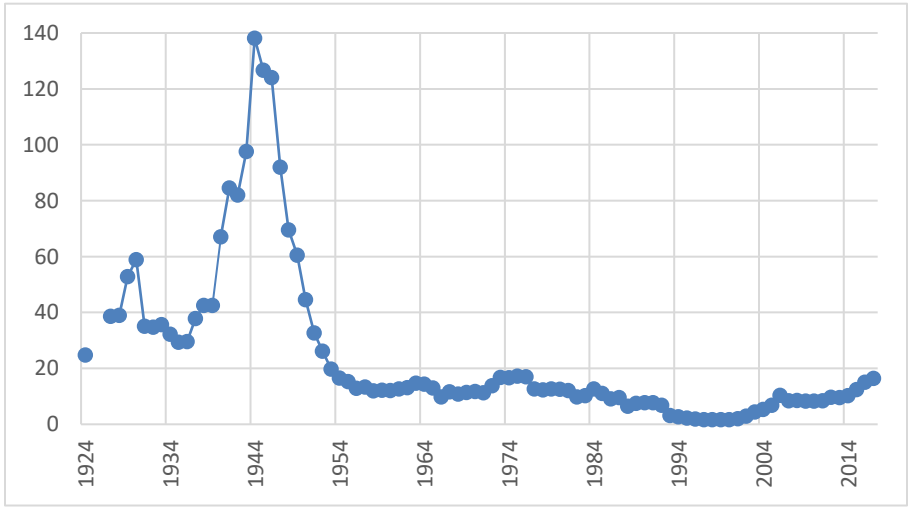
This primer and management guide intends to describe the natural history, transmission, diagnosis, and treatment of syphilis, and provide guidance for organizing syphilis care in Yukon.

Yukon's *Public Health and Safety Act* and *Regulations for the Control of Communicable Diseases in the Yukon Territory* include syphilis as a reportable disease. The *Act* and *Regulations* allow the Chief Medical Officer of Health to provide guidance to medical practitioners to manage the communicable disease of public health importance. The guidance in this document is from Yukon's Chief Medical Officer of Health and YCDC, in collaboration with Dr. Troy Grennan of British Columbia Centre for Disease Control (BCCDC).

As the syphilis response evolves in Yukon, health care providers and leadership may develop further policies and activities to maintain high quality syphilis care in Yukon.

Epidemiology of syphilis in Canada and Yukon

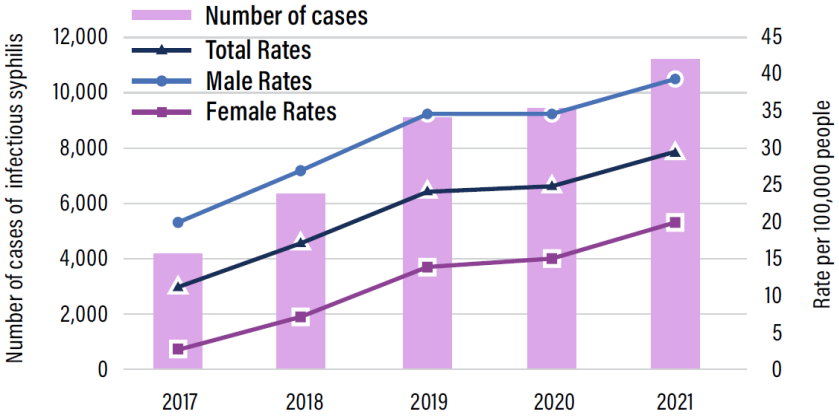
Figure 1: Rate of Syphilis per 100,000 of reported cases over time in Canada, 1924-2017[1]



Since notification of communicable diseases started in Canada, national syphilis incidence likely peaked in the early 1940s, around the time of penicillin introduction, with an estimated 140 infections per 100,000 people yearly. Incidence remained below 20 per 100,000 per year between 1954 and 2017, with lowest incidence in the late 1990s and early 2000s (less than 5 infections per 100,000 per year). In the last 20 years, localized syphilis outbreaks occurred, often in priority populations (e.g., men who have sex with men) and continue to disproportionately impact these groups in many parts of the country.

[1] Public Health Agency of Canada. (2022). Infectious syphilis and congenital syphilis in Canada, 2021. *CCDR*, 48, 11-12. Retrieved from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2022-48/issue-11-12-november-december-2022/infectious-congenital-syphilis-canada-2021.html

Figure 2: Number of cases and rates of infectious syphilis by sex in Canada, from 2017 to 2023[2]



Between 2017 and 2021, the incidence of syphilis infections in Canada has more than doubled and reached rates not seen since the early 1950s. Rates for males exceeds that for females, but both are increasing at similar rates. The relative rate for females, however, has increased over 7 times between 2017 and 2021. Alberta, Saskatchewan, Manitoba and some northern jurisdictions report the highest national increases in syphilis rates in females in recent years, and this represents an expansion in syphilis impacts to heterosexual populations, in addition to continued impact in priority populations such as men who have sex with men.

The re-emergence of syphilis in Canada has important regional differences. By 2020, at least nine provinces or territories declared regional or provincial outbreaks after seeing up to 10-fold increases in their rates since 2016.

There has been a steep increase in congenital syphilis in Canada between 2017 and 2021. Nationally, there were 96 notifications of congenital syphilis in 2021 (including stillbirths and children less than 2 diagnosed with syphilis) compared to 7 in 2017. The Public Health Agency of Canada expects the number of notifications of congenital syphilis to increase as provinces and territories report in 2022 and 2023.

[2] Public Health Agency of Canada. (2015) Syphilis among gay, bisexual, two-spirit and other men who have sex with men: A resource for population-specific prevention. Retrieved from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/syphilis-resource-population-specific-prevention.html

Epidemiology in Northern Territories and Yukon

Between July 2000 and early 2004, Yukon saw an abrupt increase in infectious syphilis, with a total of 45 infections diagnosed. In this period, 40% of individuals with syphilis were from the Whitehorse area, and 60% were rural residents. The majority (96%) were reported in a heterosexual population, with no congenital syphilis infections identified in this timeframe. Nunavut and NWT experienced syphilis re-emergence in about 2012 and 2018 respectively.

Figure 3: Rates of reported cases of infectious syphilis in Yukon, Northwest Territories and Nunavut, Canada[3]

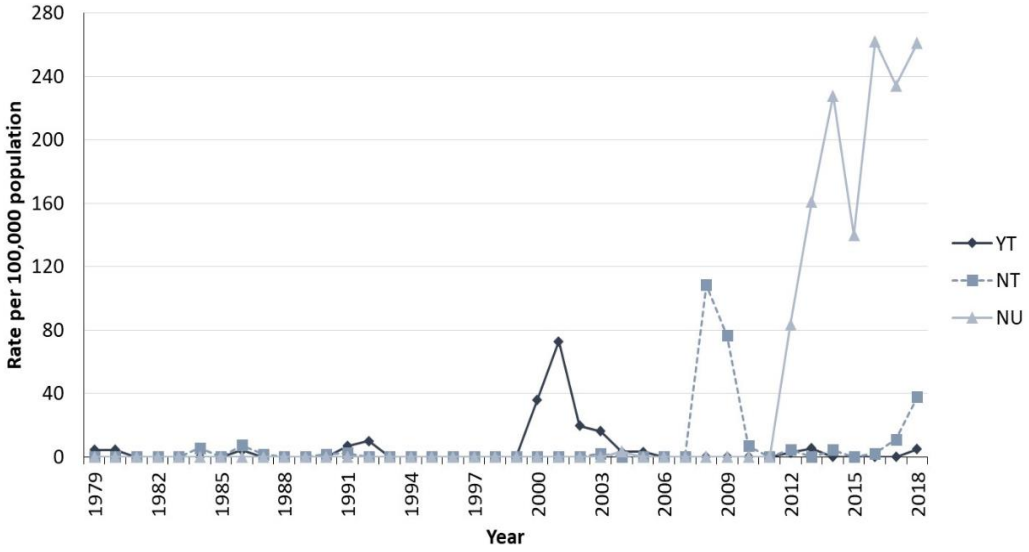
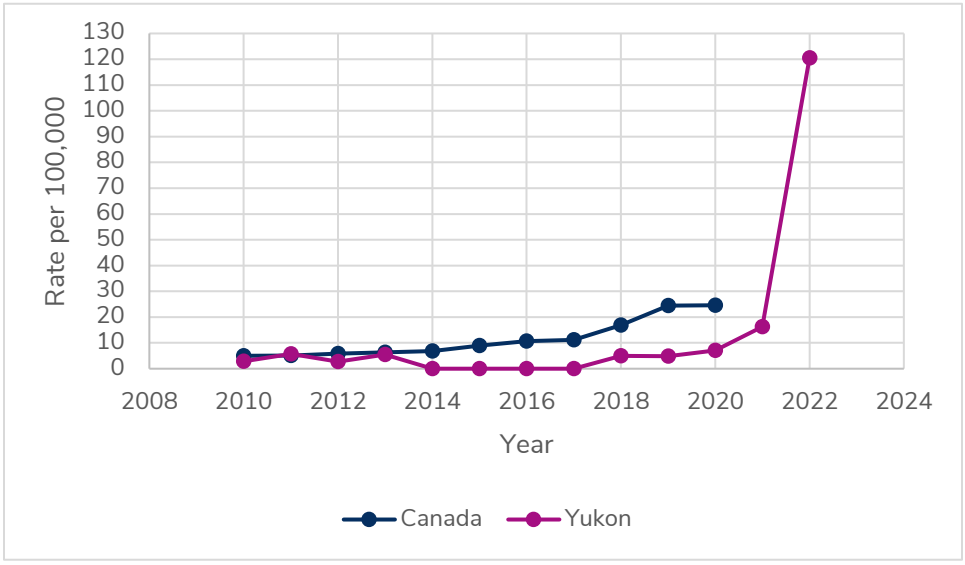


Figure 4: Yukon and Canada Rate of Infectious Syphilis per 100,000 of Reported Cases, 2010-2022



[3]Centre for Communicable diseases and infection Control, Public Health Agency of Canada. (2015). Infectious syphilis in Canada 2003-2012. *CCDR*, Volume 41(02). Retrieved from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2015-41/ccdr-volume-41-02-february-5-2015/ccdr-volume-41-02-february-5-2015-2.html

[4] Public Health Agency of Canada. (2020) Syphilis in Canada, Technical Report on Epidemiological Trends determinants and interventions: Appendix A: clinical algorithm for syphilis staging and treatment. Retrieved from: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/syphilis-epidemiological-report/syphilis-eng.pdf and Yukon Government, Internal report.

In 2022, 53 Yukoners were diagnosed with infectious syphilis, representing 121 infections per 100,000 people per year. The 2022 rate is 7 times higher than the 2021 rate, 17 times higher than 2020 rate, and is Yukon's highest rate of syphilis infections in many decades.

Categorizing syphilis into "infectious" and "non-infectious" depends on the duration and stage of syphilis infection. Because syphilis can produce a chronic, life-long infection if untreated, jurisdictions report recent infections, as opposed to those acquired many years ago, to provide the best estimate of current syphilis activity and the extent of transmission in a community. Established clinical algorithms, however, use a precautionary approach to categorize individuals into a later stage ('non-infectious') to ensure they receive sufficient treatment. This process likely misclassifies some individuals who are truly "infectious" as "non-infectious" and underestimates rates of recently acquired infections in populations. Yukon and Canada are likely underreporting the number of people with infectious syphilis per year.

As of August 2023:

- Syphilis infections are occurring in Whitehorse residents and in residents of small communities throughout Yukon.
- Syphilis is affecting primarily the heterosexual community in Yukon.
- The highest rates are in those aged 20-39, with a rate of 250 per 100,000 people in this age group in 2022.

Surveillance Case Definitions

Surveillance and communicable disease control teams use case definitions for valid and reliable reporting and monitoring of infectious diseases. These case definitions often overlap with clinical diagnostic criteria, but do not replace clinical guidelines or judgement. Yukon health care providers, if they suspect syphilis, should follow guidance for diagnosis, treatment, and referral as outlined in this primer.

Confirmed case – Primary syphilis

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, nucleic acid testing (NAT), or equivalent examination of material from a chancre or a regional lymph node;
  OR
- presence of one or more typical lesions (chancres) and reactive treponemal serology, regardless of non-treponemal test reactivity, in individuals with no previous history of syphilis;
  OR
- presence of one or more typical lesions (chancres) and a fourfold or greater increase in the titre over the last known non-treponemal test in individuals with a past history of syphilis treatment.

Confirmed case – Secondary syphilis

Laboratory evidence of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, NAT or equivalent examination of mucocutaneous lesions, condylomata lata and reactive serology (non-treponemal and treponemal);
  OR
- presence of typical signs or symptoms of secondary syphilis (e.g., mucocutaneous lesions, alopecia, loss of eyelashes and lateral third of eyebrows, iritis, generalized lymphadenopathy, fever, malaise, or splenomegaly) AND either a reactive serology (non-treponemal and treponemal OR a fourfold or greater increase in titre over the previous known non-treponemal test.

Confirmed case – Early latent syphilis (< one year after infection)

Laboratory confirmation of infection:

- An asymptomatic patient with reactive serology (treponemal and/or non-treponemal) who, within the previous 12 months, had one of the following:
  - non-reactive serology;
  - symptoms suggestive of primary or secondary syphilis;
  - exposure to a sexual partner with primary, secondary, or early latent syphilis.

Confirmed case – Late latent syphilis (> one year after infection or of unknown duration)

Laboratory confirmation of infection:

- An asymptomatic patient with persistently reactive treponemal serology (regardless of non-treponemal serology reactivity) who does not meet the criteria for early latent disease and who has not been previously treated for syphilis.

Confirmed case – Neurosyphilis

Infectious (< one year after infection)

Laboratory confirmation of infection:

- Fits the criteria of primary, secondary, OR early latent syphilis above AND one of the following:
    - reactive CSF-VDRL in non-bloody CSF;
    - clinical evidence of neurosyphilis AND either elevated CSF leukocytes OR elevated CSF protein in the absence of other known causes.

Non-infectious (> one year after infection)

Laboratory confirmation of infection:

- Reactive treponemal serology (regardless of non-treponemal serology reactivity) AND one of the following:
- reactive CSF-VDRL in non-bloody CSF;
- clinical evidence of neurosyphilis AND either elevated CSF leukocytes OR elevated CSF protein in the absence of other known causes.

Confirmed case – Tertiary syphilis other than Neurosyphilis

Laboratory confirmation of infection:

- Reactive treponemal serology (regardless of non-treponemal test reactivity) together with characteristic late abnormalities of the cardiovascular system, bone, skin, or other structures, in the absence of other known causes of these abnormalities (*T. pallidum* is rarely seen in these lesions although, when present, it is diagnostic);
  AND
- no clinical or laboratory evidence of neurosyphilis.

Confirmed case – Early congenital syphilis (within two years of birth)

This case definition is currently in revision. Please see Diagnosing congenital syphilis for further information.

If they suspect congenital syphilis, health care providers should consult YCDC and should organize consultation with BC Children's Hospital pediatrician and/or Dr. Troy Grennan (BCCDC) or a pediatric infectious disease specialist experienced in diagnosing and treating congenital syphilis.

Syphilis—natural history

After causing infection and if untreated, syphilis evades immune response and progresses through stages of infection including **primary syphilis, secondary syphilis, latent syphilis (early latent, late latent), and tertiary syphilis**. Neurosyphilis is a distinct collection of CNS impacts or syndromes, which may occur at various stages of infection, including the early infectious stages. Congenital syphilis results after infection in utero or contact with an active genital tract lesion during delivery, or possibly during maternal infant interactions in infancy.

Primary syphilis:

- A chancre (single, sometimes multiple) develops about three weeks after infection, but with an incubation range of 10 – 90 days.
- Often, there is regional lymphadenopathy.
- Health care workers or individuals often miss primary syphilis due to its location (e.g. rectum, cervix) and because it is typically asymptomatic.
- Chancre usually resolves without treatment in four to six weeks.

Secondary syphilis:

- Develops between 2 weeks and 6 months after untreated primary syphilis.
- Can involve many organ systems.
- Vast majority (> 95%) have skin or mucous membrane manifestations. The classic maculopapular rash usually begins on the trunk and proximal extremities as bilateral macules that often evolve into papules and may involve palms of hands and soles of feet.
- Other signs and symptoms include fever, malaise, pharyngitis, other skin and mucous membrane lesions (e.g., mucous patches, condyloma lata, alopecia) weight loss, arthralgia, lymphadenopathy).

Latent syphilis:

- Develops a few months after secondary syphilis.
- Asymptomatic and without signs.
- In about a quarter of untreated cases of early latent syphilis, recurrence of secondary syphilis can occur.
- Categorized as **early latent** or **late latent** based on time since infection and capacity for sexual transmission. Public Health Agency of Canada and US CDC categorize early latent as within one year of infection.
- Syphilis is transmissible through sexual contact during **early latent**, but **not late latent** syphilis.

Tertiary syphilis:

- Occurs years to decades after primary infection, possibly in up to 1/3 of those untreated.
- Includes cardiovascular syphilis or presence of gummas of bone, viscera, or skin.
- Not transmissible.

Neurosyphilis:

- Can occur shortly after infection, or years/decades after infection.

- Neurologic syndromes include chronic meningitis, neuro-ophthalmologic manifestations, otosyphilis (hearing loss, tinnitus, vertigo), meningo-vascular stroke syndromes, tabes dorsalis, and dementia.

Congenital syphilis:

- Severe outcomes can occur, including fetal death, stillbirth (born without signs of life at or after 20 weeks gestation), or death shortly after delivery. Estimates from a major systematic review and meta-analysis are that untreated syphilis in pregnancy produce an incremental 21% risk of fetal loss or stillbirth, 9% risk of neonatal death compared to outcomes in pregnant people without syphilis.
- Earlier stages of maternal infection increase the risk of transplacental transmission. Transmission occurs in up to 90% of cases of primary and secondary syphilis, versus roughly 40% of early latent cases. Untreated late latent syphilis, still has a risk (~10%) of transplacental transmission, particularly in the first several years following infection.
- Clinical pattern is variable in congenital syphilis, and most infected infants are asymptomatic at birth, but two-thirds develop symptoms by 8 weeks. Symptoms include rhinitis ("snuffles") followed by diffuse maculopapular desquamative rash, or severe rash which may slough, especially on palms and soles and around the mouth and anus.
- Other manifestations in newborns or infants include pneumonia, nephrotic syndrome, splenomegaly, hepatomegaly, lymphadenopathy, anemia, thrombocytopenia, and jaundice.
- Longer term outcomes in children older than one year include a spectrum of musculoskeletal, neurological, dental, ocular, cutaneous or other organ manifestations.

Transmission of syphilis

- Person to person transmission occurs almost exclusively through direct sexual contact including vaginal, oral, or anal sex when source has infectious syphilis (primary, secondary, early latent).
- Vertical transmission (maternal-fetal or maternal-newborn) occurs, producing congenital syphilis. Risk of vertical transmission in pregnancy is highest in primary and secondary stages but may occur during the first four years after maternal infection if untreated or inadequately treated. Vertical transmission also occurs during vaginal delivery if there are syphilis lesions to the genital tract or may occur through maternal infant interactions after birth (e.g., breastfeeding if syphilis lesions are present to breast).
- *Treponema pallidum* is not known to transmit through breast milk.
- There are reports of transmission through direct, non-sexual contact with skin or mucous membrane lesions (for example from family members to children). Avoiding contact with lesions should be part of client teaching.
- There are historical reports of transmission to health care workers not wearing gloves when in contact with skin or mucous membrane lesions.
- There are also rare reports of syphilis transmission after solid organ transplantation, needlestick injury, blood transfusion, or sharing of needles and injection equipment.
- Studies continue to investigate the role of non-sexual transmission in households (e.g., through close contact amongst parents and children).

Diagnosing Syphilis

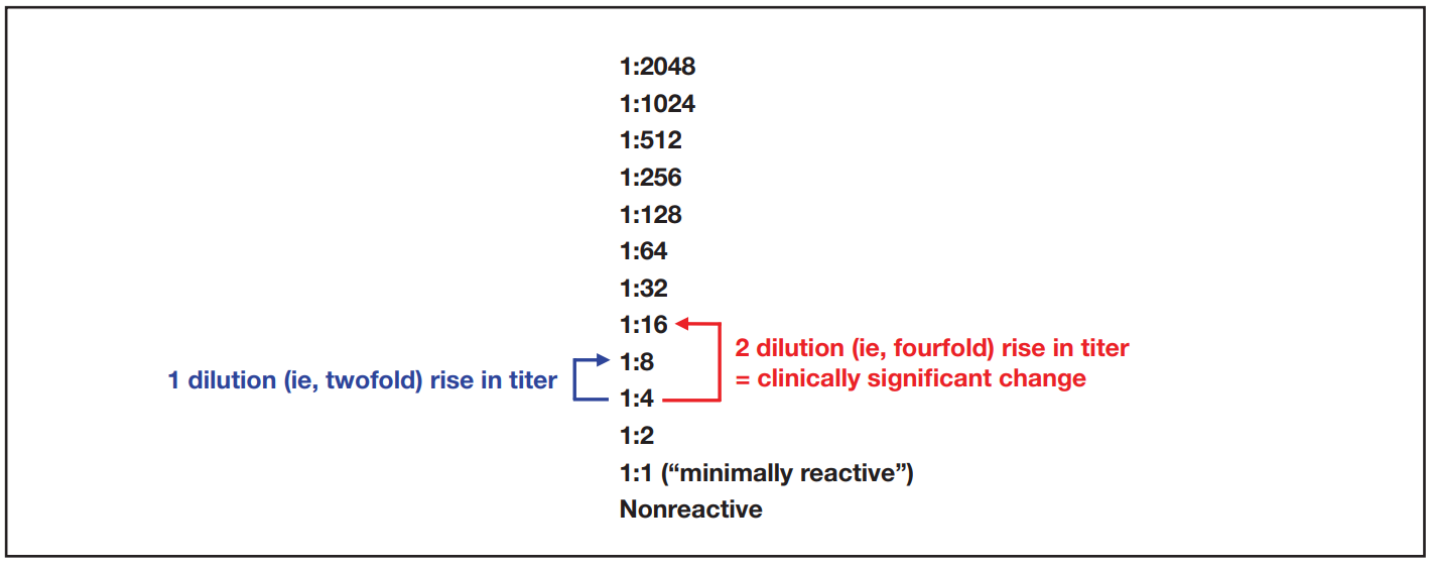
T. pallidum does not grow easily in vitro. Diagnosis relies on serologic tests to detect immunologic response and polymerase chain reaction (PCR) from swabs of lesions to identify bacterial DNA.

Serologic testing

Serologic testing is the standard method for syphilis diagnosis and should be ordered when a health care provider suspects syphilis to establish diagnosis and to monitor response to treatment. BCCDC serology includes syphilis EIA (enzyme immunoassay), RPR (rapid plasma reagin), and TPPA (*Treponema pallidum* Particle Agglutination).

BCCDC utilizes EIA as an initial screening test. If this is positive, a more specific test (TPPA) confirms the diagnosis. RPR quantifies the serologic response and is reported in dilutions (or dils) and is essential for monitoring treatment response and to determine reinfection.

Figure 5: Example of Quantitative Nontreponemal Titers That Indicate a Clinically-significant Change[5]



[5] New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections and the New York City STD Prevention Training Center. (2019) The Diagnosis, Management and Prevention of Syphilis New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections. Retrieved from: https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

RPR is a test that visually detects agglutination produced by antibodies in a serum sample that bind to a "non-treponemal" antigen suspension in the test kit. Antibodies produced in syphilis infection, as well as in immune responses to other pathology, bind to the test antigen and induce visible agglutination. With serial dilution of the serum sample, lab technicians quantify the amount of antibodies present by reporting agglutination in the most diluted sample. For example, compared to RPR positive at 1:4 dils, an RPR positive at 1:16 dils is fourfold higher. Similarly, a drop from positive at 1:16 to positive at 1:4 is a fourfold drop in titres. Importantly, because presence or absence of agglutination is a qualitative variable (i.e., agglutination either appears present or absent), interobserver variability may produce minor variation in reported positive RPR dilution. A fourfold change in titers is less likely due to interobserver variability.

Practice Point

Health care providers should refer to BCCDC eLab Handbook for details about collection of syphilis tests, available at:

http://www.elabhandbook.info/PHSA/Test/PrintPageWithMaster.aspx

PCR

PCR is highly specific and sensitive for diagnosing syphilis if a chancre or other infectious lesion (e.g., mucous patch) is present. PCR detection supports staging (and subsequently treatment).

Health care providers should collect chancre fluid or swab of any syphilis skin or mucous membrane lesion using:

- **Aptima swab (preferred);** i.e., the same 'orange' swab as for vaginal CT/GC **OR**
- **Universal Transport Medium (UTM) / viral transfer media; OR**
- **BD ProTech swab**

Diagnosing neurosyphilis

Symptomatic neurosyphilis includes early syndromes (acute meningitis and meningovascular disease) and late complications (tabes dorsalis or general paresis). Ocular and otologic involvement may occur at any stage of infection.

Individuals with serologic evidence of syphilis and signs or symptoms consistent with ocular, otic, or neurosyphilis require further investigation including prompt lumbar puncture and CSF testing (typically CSF VDRL or FTA-Abs, cell count and differential, and protein). Evaluation by ophthalmology or otolaryngology/audiology may also be warranted.

If they suspect neurosyphilis, health care providers should consult YCDC and should organize consultation with Dr. Troy Grennan (BCCDC), or another infectious disease specialist who is experienced in diagnosing and treating neurosyphilis.

Diagnosing congenital syphilis

Diagnosing congenital syphilis requires consideration of maternal serology and treatment and testing in infants. Testing in infants may include syphilis serology, PCR, CBC, long bone radiographs, and CSF.

The Canadian Pediatric Society published guidance on diagnosing congenital syphilis (reaffirmed in 2018) and is available here: https://cps.ca/documents/position/congenital-syphilis

If they suspect congenital syphilis, health care providers should consult YCDC and should organize consultation with BC Children's Hospital pediatrician and/or Dr. Troy Grennan (BCCDC) or a pediatric infectious disease specialist experienced in diagnosing and treating congenital syphilis.

Treating Syphilis

Refer to Yukon Treatment Guidelines for Sexually Transmitted Infections (STI) in Adolescents and Adults:
https://yukon.ca/sites/yukon.ca/files/hss/hss-imgs/sti_guidelines_2020_web_final.pdf

NAME ALERT:
BICILLIN LA® IS LONG-ACTING AND SHOULD NOT BE CONFUSED WITH BENZYLPENICILLIN G WHICH IS SHORT-ACTING AND NOT APPROPRIATE FOR SINGLE DOSE OR WEEKLY THERAPY TREATMENT OF SYPHILIS

A single dose of 2.4 million units IM of ***long acting benzathine penicillin G (Bicillin LA)*** (provided in two prefilled syringes of 1.2 million units each) achieves detectable blood levels for 2 to 4 weeks and is preferred treatment for **primary, secondary, and early latent syphilis.** See table for treatment recommendations.

The Public Health Agency of Canada provides treatment recommendations for syphilis[24], available at: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/treatment-follow-up.html

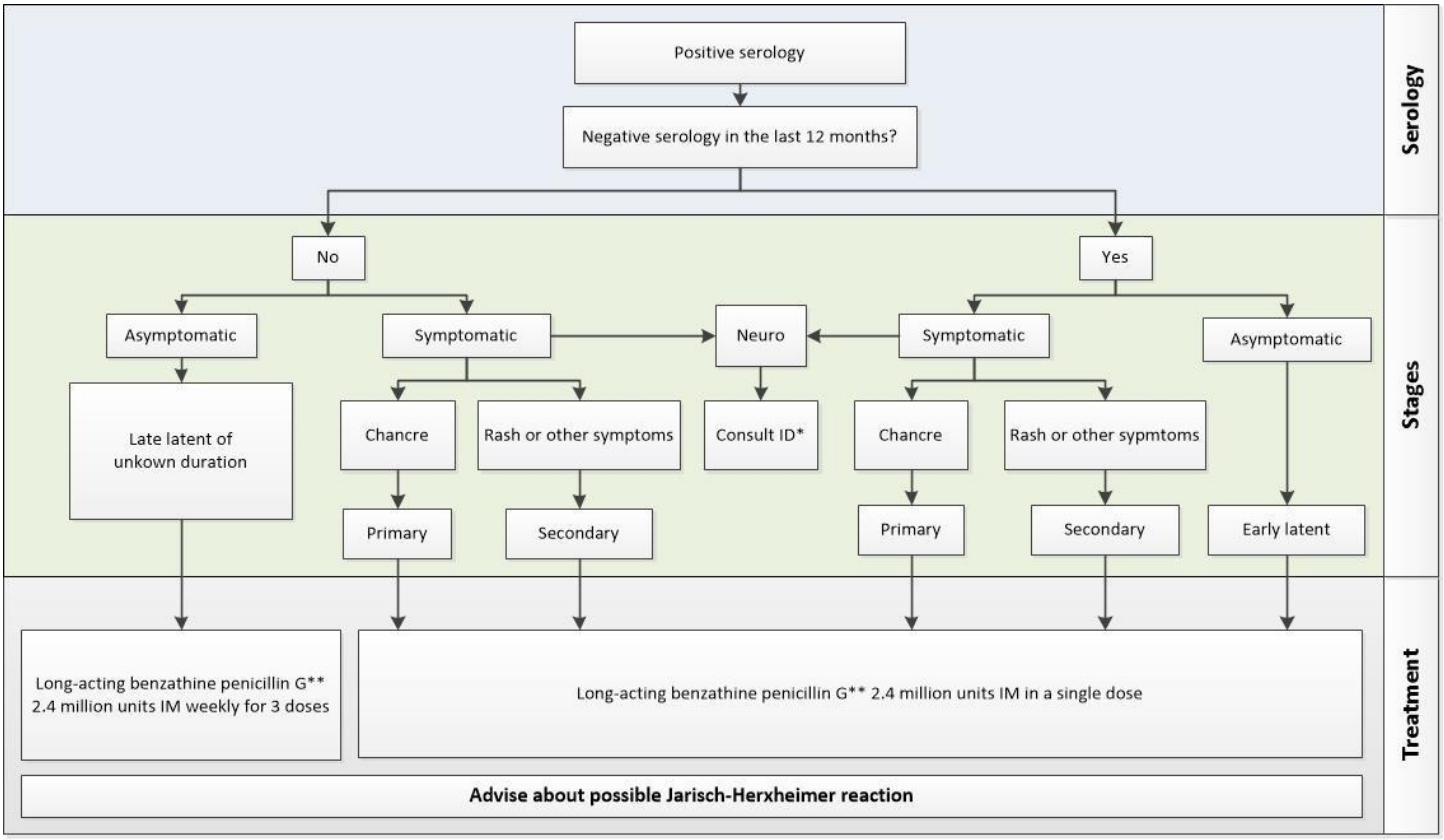
Figure 6: Recommended treatment of syphilis in non-pregnant adults[6]

Stage	Preferred treatment	Alternative treatment for people with penicillin allergies
Primary, secondary and early latent syphilis	Benzathine penicillin G-LA 2.4 million units IM as a single dose [A-II]	• Doxycycline 100 mg PO BID for 14 days [B-II] • In exceptional circumstances and when close follow-up is assured: o Ceftriaxone 1g IV or IM daily for 10 days [B-II]
Latent, late latent, cardiovascular syphilis and gumma	Benzathine penicillin G-LA 2.4 million units IM weekly for three (3) doses [AII]	• Consider penicillin desensitization o Doxycycline 100 mg PO Bid for 28 days [B-II] • In exceptional circumstances and when close follow-up is assured: o Ceftriaxone 1g IV or IM daily for 10 days[C-III]
All adults: neurosyphilis	• Refer to a neurologist or infectious disease specialist	

[6] Public Health Agency of Canada. (2021) Syphilis guide: Treatment and follow-up. Retrieved from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/treatment-follow-up.html

Because of uncertainty with staging syphilis, Dr. Troy Grennan (BCCDC), YCDC, Yukon's Office of the Chief Medical Officer of Health, and the Public Health Agency of Canada recommend that health care providers follow the following algorithm (Figure 5) for simplified staging and treatment of syphilis for non-pregnant adults. This algorithm does not address treating neurosyphilis, syphilis in pregnancy, or congenital syphilis.

Figure 7: Clinical Algorithm for syphilis staging and treatment[7]



** Infectious Disease Specialist*
*** Alternative treatment to be considered in case of penicillin allergy.*

[7] Public Health Agency of Canada. (2020) Syphilis in Canada, Technical Report on Epidemiological Trends determinants and interventions: Appendix A: clinical algorithm for syphilis staging and treatment. Retrieved from: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/syphilis-epidemiological-report/syphilis-eng.pdf

Treating syphilis in pregnancy and congenital syphilis in the newborn

Prompt diagnosis and treatment of syphilis in pregnancy and newborns, including asymptomatic newborns, reduces the risk of health impacts in infancy or after one year of age. Maternal testing and treatment during pregnancy/delivery and/or the newborn at birth is therefore critical.

Treating syphilis in pregnancy

Refer to Yukon Treatment Guidelines for Sexually Transmitted Infections (STI) in Adolescents and Adults: https://yukon.ca/sites/yukon.ca/files/hss/hss-imgs/sti_guidelines_2020_web_final.pdf

Non-HIV Infected Pregnant Adults
Primary, Secondary, Early Latent Syphilis: Long acting benzathine penicillin G (Bicillin) 2.4 mu IM weekly for 2 consecutive weeks (Must be ordered through YCDC)
Late Latent: Long acting benzathine penicillin G (Bicillin) 2.4 mu IM weekly for 3 consecutive weeks (Must be ordered through YCDC)

When treating syphilis in pregnancy, health care providers should contact YCDC and should consult Dr. Troy Grennan (BCCDC) or an infectious disease specialist experienced in treating syphilis in pregnancy. The treating health care provider should notify the maternal care team including primary care, midwife, or specialist obstetrician to arrange clinical follow up and monitoring including fetal imaging.

During pregnancy there is uncertainty whether the Jarisch-Herxheimer (JH) reaction might induce preterm labour. When treating pregnant women who are ≥ 20 weeks gestation, the treatment team, including obstetrics, should determine whether the pregnant person should be near a facility which can perform fetal monitoring after syphilis treatment.

Treating congenital syphilis

When treating congenital syphilis, health care providers should contact YCDC and consult assessment with BC Children's Hospital pediatrician and/or Dr. Troy Grennan (BCCDC) or another infectious disease specialist experienced in diagnosing and treating congenital syphilis.

- Prompt diagnosis and treatment of maternal syphilis in pregnancy reduces the risk of poor fetal and neonatal outcomes.
- Because an infant with congenital syphilis may be asymptomatic, or have minimal symptoms, maternal syphilis screening at birth is critical.
- Prompt diagnosis and treatment of newborns reduces the incidence or severity of outcomes in infancy or after one year of age.

If maternal syphilis has been diagnosed and treated during the pregnancy, follow up assessment of the pregnant person and newborn is critical to ensure adequacy of treatment.

The Canadian Pediatric Society published guidance on diagnosing and treating congenital syphilis and reaffirmed their recommendations in 2018: https://cps.ca/documents/position/congenital-syphilis

Treating neurosyphilis

Treating neurosyphilis requires a penicillin antibiotic regimen that achieves CNS penetration (e.g., aqueous crystalline penicillin G intravenously).

When considering treating neurosyphilis, health care providers should contact YCDC and should consult Dr. Troy Grennan (BCCDC), or another infectious disease specialist who is experienced in diagnosing and treating neurosyphilis.

Penicillin allergy

Penicillin regimens are the first choice for treating syphilis because of the effectiveness demonstrated in randomized controlled trials and observational studies.

There is a high prevalence of reported penicillin allergy in Canada. With limited data on the effectiveness of non-penicillin treatment regimens for syphilis, health care providers must clarify reported penicillin allergies as best as possible and individualize decisions for syphilis treatment in those who are allergic to penicillin. Documentation of allergic reactions or previous allergy assessments and testing will support decisions.

Health care providers should review syphilis treatment in those reporting penicillin allergy with YCDC or an infectious disease consultant.

Non-penicillin regimens are acceptable for a person with reported penicillin allergy with primary or secondary syphilis IF the health care provider does not identify risks suggesting the person will have difficulty completing treatment and following up for serologic testing following treatment.

Health care providers providing syphilis treatment for people who report penicillin allergy should contact YCDC and organize assessment with an allergist to review penicillin allergy skin testing and desensitization if a person has syphilis, reports a penicillin allergy, and:

- **is pregnant; OR**
- **has neurosyphilis; OR**
- **has early latent, late latent, or tertiary syphilis; OR**
- **has primary or secondary syphilis and are likely to have difficulty completing non-penicillin regimens and maintain follow up for serology after treatment.**

Treatment failure and repeat infections

There is no gold standard to define treatment success. Syphilis EIA and TPPA do not necessarily revert after treatment, and often remain positive for life after syphilis infection.

One indicator of successful treatment is the reduction of quantifiable RPR after treatment, contingent on syphilis stage at the time of treatment. The Public Health Agency of Canada defines adequate serologic response as the following:

Figure 8: Adequate serologic response in infectious syphilis[8]

Stage	Adequate serologic response
Primary syphilis	• 4-fold drop at 6 months • 8-fold drop at 12 months
Secondary syphilis	• 8-fold drop at 6 months • 16-fold drop at 12 months
Early latent syphilis	• 4-fold drop at 12 months

[8] Public Health Agency of Canada. (2021) Syphilis guide: Treatment and follow-up. Retrieved from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/treatment-follow-up.html

If health care providers monitor and interpret syphilis serologic response, they should collaborate closely with YCDC and/or an infectious disease specialist for diagnosing and treating repeat infections.

Health care providers should consider the occurrence of re-infection if there is a 4 fold or higher increase in RPR titer. In addition to serology: history, clinical examination, and PCR of lesions are important to evaluate for repeat infections.

Health care providers should collaborate closely with YCDC and/or specialist consultants (e.g., Dr. Troy Grennan or another infectious disease specialist) for diagnosing and treating repeat infections.

Client teaching

Advise clients to avoid all sexual contact, even with a condom, with anyone while being treated and to wait at least 7 days after treatment before resuming sexual activity.

For those with mucocutaneous lesions, they should avoid sexual and other direct contact of lesions with others (e.g., avoid co-sleeping with infants) for until at least 7 days after treatment AND until all skin/mucous membrane lesions are healed.

There is a high risk of infection in sexual partners. People treated for syphilis should avoid sexual contact with ongoing sexual partners until those partners seek medical evaluation and until 7 days after their partner's treatment (see "Contacts" below).

Health care providers should provide information about the Jarisch-Herxheimer (JH) reaction which may occur within the first 24 hours (most often within 8 hours) after initiation of treatment, and usually resolves within 24 hours. Symptoms include exacerbation of skin lesions, fever, malaise, nausea, vomiting and headache and can be treated with antipyretics. In a pregnant person, this reaction can be associated with uterine contractions but usually resolves without incident. During treatment for syphilis in early pregnancy, the client should be advised to stay well hydrated and rest; acetaminophen may help uterine cramping, pelvic pain, and fever.

Contacts

Health care providers and Yukon Communicable Disease Control should make every effort to identify and communicate the syphilis exposure to all sexual contacts of those with infectious syphilis (primary, secondary, early latent, and unspecified duration presumed infectious). Index cases can support with partner notification as able, but health care workers and YCDC should make every effort to communicate with contacts. This may involve community outreach by health care practitioners (e.g., health centre nurses) or allied health care workers (e.g., social workers or community health representatives) as necessary, while minimizing the amount of personal health information disclosed as appropriate.

CMOH and YCDC recommend assessment and treatment of all contacts. If history and physical examination allow for staging, contacts should receive stage specific treatment of syphilis. Otherwise, contacts should receive benzathine penicillin G-LA (Bicillin LA) 2.4 million units IM as a single dose, unless there are contraindications. Health care practitioners should offer syphilis testing (serology and PCR) at the same time as treatment.

The trace back period is to identify contacts who should be located, tested and treated. The minimum trace back periods to identify sexual contacts relate to the stage of the index case, as follows.

- **Primary syphilis: 3 months**
- **Secondary syphilis: 6 months**
- **Early latent: 1 year**

Hospital infection prevention and control

- The Public Health Agency of Canada recommends routine precautions, which include gloves to examine rash or lesions, to prevent transmission to health care workers in health care settings.
- Multiple jurisdictions recommend extra precautions (i.e., contact precautions) for an infant with congenital syphilis until the infant has received 24 hours of antibiotics.

Further guidance for health care providers

In addition to the guidance in this document, YCDC and Yukon's CMOH issued an alert on February 3, 2023, notifying health care providers that they:

1. **Must notify YCDC/MOH if they suspect, diagnose, or treat syphilis infection in an individual (see https://yukon.ca/sites/yukon.ca/files/hss/hss-yukon-reportable-communicable-diseases.pdf for reporting process);**

2. **Should recommend that all pregnant people have at least three syphilis serologic tests during pregnancy, including:**

    a. **At the time of diagnosis of pregnancy;**
    b. **At 28 to 32 weeks gestation;**
    c. **At the time of delivery.**

3. **Should recommend pregnancy testing in any person capable of becoming pregnant who is diagnosed with syphilis;**

4. **Must notify YCDC/MOH by fastest means possible of any pregnant person who is diagnosed with syphilis for development of urgent treatment and follow up plan. (see https://yukon.ca/sites/yukon.ca/files/hss/hss-yukon-reportable-communicable-diseases.pdf for reporting process);**

5. **Should refer any pregnant person diagnosed with syphilis in the five years prior to their current pregnancy to YCDC for review of previous treatment adequacy;**

6. **Should consider more frequent testing of pregnant people at higher risk of sexually transmitted infections (STIs);**

7. **Should treat for syphilis at the time of ordering syphilis tests (and report as above) in the following situations:**

    a. **people with known untreated syphilis infection when they are seeking health care for other reasons,**
    b. ***if their clinical assessment establishes the client has a high risk of primary or secondary syphilis (e.g., risk factors and characteristic chancre or rash of secondary syphilis),***
    c. ***if public health or the individual identifies as a sexual contact of a person with infectious syphilis.***

8. **Should recommend syphilis serology for any pregnant person if they deliver a stillbirth after 20 weeks gestation;**

9. **Must, if they provide or manage services to pregnant people, ensure that any investigation protocols for stillbirths in Yukon include appropriate tests for syphilis stillbirth (e.g. swab of nasopharynx, placenta, oral mucosa, umbilical cord, or skin lesions for *T. pallidum* PCR).**

Health care providers should also continue with routine high quality sexual and reproductive health services, including:

a. Offering STI/HIV testing to all sexually active people and including syphilis testing as part of routine STI tests,
b. Confirming the best, and alternate ways to reach people with results as they undertake STI testing,
c. Referral to local health centre or YCDC for immunizations (e.g., HAV, HBV, HPV) as appropriate.

Contact Numbers

This guidance has been approved by the CMOH and is subject to change.

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References

1. Queen's Printer for the Yukon. (2002). Public Health and Safety Act. Retrieved from: https://laws.yukon.ca/cms/images/LEGISLATION/acts/puhesa.pdf

2. Commissioner of the Yukon. (1961). Regulations for the Control of Communicable diseases in the Yukon Territory. Retrieved from: https://laws.yukon.ca/cms/images/LEGISLATION/SUBORDINATE/1961/1961-0048/1961-0048_1.pdf?zoom_highlight=communicable+diseases#search=%22communicable%20diseases%22

3. Peeling RW, Mabey D, Kamb M, Chen X-S, Radolf JD, and Benzaken AS. (2017). Syphilis. *Nature Reviews: Disease Primers*, 3, 17073. Retrieved from: https://doi.org/10.1038/nrdp.2017.73

4. Kenyon CR, Osbak K, Tsoumanis A. (2016). The Global Epidemiology of Syphilis in the Past Century – A Systematic Review Based on Antenatal Syphilis Prevalence. Small PLC, editor. *PLOS Neglected Tropical Diseases*, 11;10(5):e0004711.

5. Government of Canada. (2023) Reported cases from 1924 to 2020 in Canada-Notifiable diseases on-line. Retrieved from: https://diseases.canada.ca/notifiable/charts?c=pl

6. Public Health Agency of Canada. (2022). Infectious syphilis and congenital syphilis in Canada, 2021. *CCDR*, 48, 11-12. Retrieved from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2022-48/issue-11-12-november-december-2022/infectious-congenital-syphilis-canada-2021.html

7. Public Health Agency of Canada. (2015) Syphilis among gay, bisexual, two-spirit and other men who have sex with men: A resource for population-specific prevention. Retrieved from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/syphilis-resource-population-specific-prevention.html

8. Public Health Agency of Canada. (2020) Syphilis in Canada, Technical Report on Epidemiological Trends determinants and interventions: Appendix A: clinical algorithm for syphilis staging and treatment. Retrieved from: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/syphilis-epidemiological-report/syphilis-eng.pdf

9. World Health Organization. (2008) Commission on Social Determinants of Health: Closing the gap in a generation: health equity through action on the social determinants of health. Retrieved from: https://apps.who.int/iris/rest/bitstreams/65985/retrieve

10. Centre for Communicable diseases and infection Control, Public Health Agency of Canada. (2015). Infectious syphilis in Canada 2003-2012. *CCDR*, Volume 41(02). Retrieved from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2015-41/ccdr-volume-41-02-february-5-2015/ccdr-volume-41-02-february-5-2015-2.html

11. Public Health Agency of Canada. (2018) Canadian Guidelines on Sexually Transmitted Infections: Management and treatment of specific infections – Syphilis. Retrieved from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections/canadian-guidelines-sexually-transmitted-infections-27.html

12. Singh AE, Romanowski B. (1999) Syphilis: review with emphasis on clinical, epidemiologic, and some biologic features. *Clin Microbiol Rev*, 12(2):187–209.

13. Bennett JE, Dolin R, Blaser MJ, Mandell GL, Douglas RG. (2015) Mandell, Douglas, and Bennett's principles and practice of infectious diseases: Chapter 239 Syphilis (Treponema pallidum). Retrieved from: https://doi.org/10.1016/C2012-1-00075-6

14. Alberta Health. (2012) Public Health Notifiable Disease Management Guidelines: Syphilis. Retrieved from: https://open.alberta.ca/dataset/e234483d-fc2d-4bbf-a248-e0442808187e/resource/244eaccc-c0ac-4933-9347-a908cbbc45f0/download/guidelines-syphilis-2012.pdf

15. WHO. (2003) Guidelines for the Management of Sexually Transmitted Infections: 3.4 Syphilis. Retrieved from: http://www.who.int/reproductivehealth/topics/rtis/treatment_syphilis.pdf

16. World Health Organization. (2018) Stillbirths. Retrieved from: http://www.who.int/maternal_child_adolescent/epidemiology/stillbirth/en/

17. Gomez GB, Kamb ML, Newman LM, Mark J, Broutet N, Hawkes SJ. (2013) Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. *Bulletin of the World Health Organization*, 91(3):217–26.

18. Levett PN, Fonseca K, Tsang RS, Kadkhoda K, Serhir B, Radons SM, et al. (2015) Canadian Public Health Laboratory Network laboratory guidelines for the use of serological tests (excluding point-of-care tests) for the diagnosis of syphilis in Canada. *Can J Infect Dis Med Microbiol*., 26 Suppl A:6A–12A.

19. Robinson JL; Canadian Paediatric Society Infectious Diseases and Immunization Committee. (2009) Congenital syphilis: No longer just of historical interest. (Updated Feb 8, 2018). Retrieved from: https://cps.ca/documents/position/congenital-syphilis

20. Province of British Columbia Provincial Health Services Authority eLab Handbook. Retrieved from: http://www.elabhandbook.info/PHSA/Default.aspx. Accessed: January 13, 2023.

21. New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections and the New York City STD Prevention Training Center. (2019) The Diagnosis, Management and Prevention of Syphilis: An Update and Review. Retrieved from: https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

22. Moscatelli G, Moroni S, García Bournissen F, Falk N, Destito A, González N, Ballering G, D'Amico I, García L, Altcheh J. (2021) Acquired Syphilis by Nonsexual Contact in Childhood. *Pediatr Infect Dis J*, 40(10):892-898. doi: 10.1097/INF.0000000000003215.

23. Public Health Agency of Canada. (2016) Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Healthcare Settings. Retrieved from: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/routine-practices-precautions-healthcare-associated-infections.html. Accessed: May 24, 2023.

24. Alberta Health Services. (2023) Infection Prevention and Control. IPC Diseases and Conditions Table Recommendations for Management of Patients Acute Care. Retrieved from: https://www.albertahealthservices.ca/assets/healthinfo/ipc/hi-ipc-resource-manual-main-document.pdf. Accessed: May 24, 2023

25. Government of Yukon. (2020) Yukon Treatment Guidelines for Sexually Transmitted Infections (STI) in Adolescents and Adults 2020. Retrieved from: https://yukon.ca/sites/yukon.ca/files/hss/hss-imgs/sti_guidelines_2020_web_final.pdf

26. Public Health Agency of Canada. (2021) Syphilis guide: Treatment and follow-up. Retrieved from: https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/treatment-follow-up.html