

SYPHILIS

Case definition

CONFIRMED CASE – early congenital syphilis (within 2 years of birth)

Laboratory confirmation of infection:

- Identification of *Treponema pallidum* by dark-field microscopy, fluorescent antibody or equivalent examination of material from nasal discharges, skin lesions, placenta, umbilical cord or autopsy material of neonate (up to four weeks of age)

OR

- Reactive serology (non-treponemal and treponemal) from venous blood (not cord blood) in an infant/child with clinical, laboratory or radiographic evidence of congenital syphilis (including evidence on physical examination, on radiographs of long bones, a reactive cerebral spinal fluid (CSF) venereal disease research laboratory test (VDRL) an elevated CSF cell count or protein without other cause), whose mother is without documented evidence of adequate treatment

OR

- Detection of *T. pallidum* DNA in an appropriate clinical specimen.

CONFIRMED CASE – primary syphilis

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, nucleic acid testing, 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, nucleic acid testing 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 (i.e. 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 (<1 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 (>1 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 vs noninfectious)

Infectious neurosyphilis (<1 year after infection)

Laboratory confirmation of infection:

- Fits the criteria for Primary, Secondary **OR** Early Latent **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 neurosyphilis (>1 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

Causative agent

Treponema pallidum (*T. pallidum*), a bacterium of the order spirochaeta. Non-venereal treponemal infections cause pinta, yaws, and bejel.

Source

Bacterial (spirochetes) from a chancre that may be in the mouth, on the genitalia, or other parts of the body. It is also present in the blood of untreated individuals.

Incubation

See table below.

Transmission

The primary mode of transmission is vaginal, anal, and oral sexual contact (direct contact with infectious exudates from obvious or concealed moist, early lesions of skin, and with mucous membranes of infected people during sexual contact). Kissing, sharing of needles and injection equipment, blood transfusion, accidental inoculation (i.e. needle stick injury) and solid organ transplantation have rarely been reported as routes of transmission. The majority of infants with congenital syphilis are infected in utero, but they can also be infected by contact with an active genital lesion at the time of delivery. Breastfeeding does not result in syphilis transmission to the child unless an infectious lesion is present on the breast.

Communicability

An infected individual can transmit the infection to his/her sexual partner usually during the primary, secondary and early latent stages of the disease. Transmission of syphilis from mother to fetus is most probable during early maternal syphilis, but can occur throughout the latent period.

Symptoms

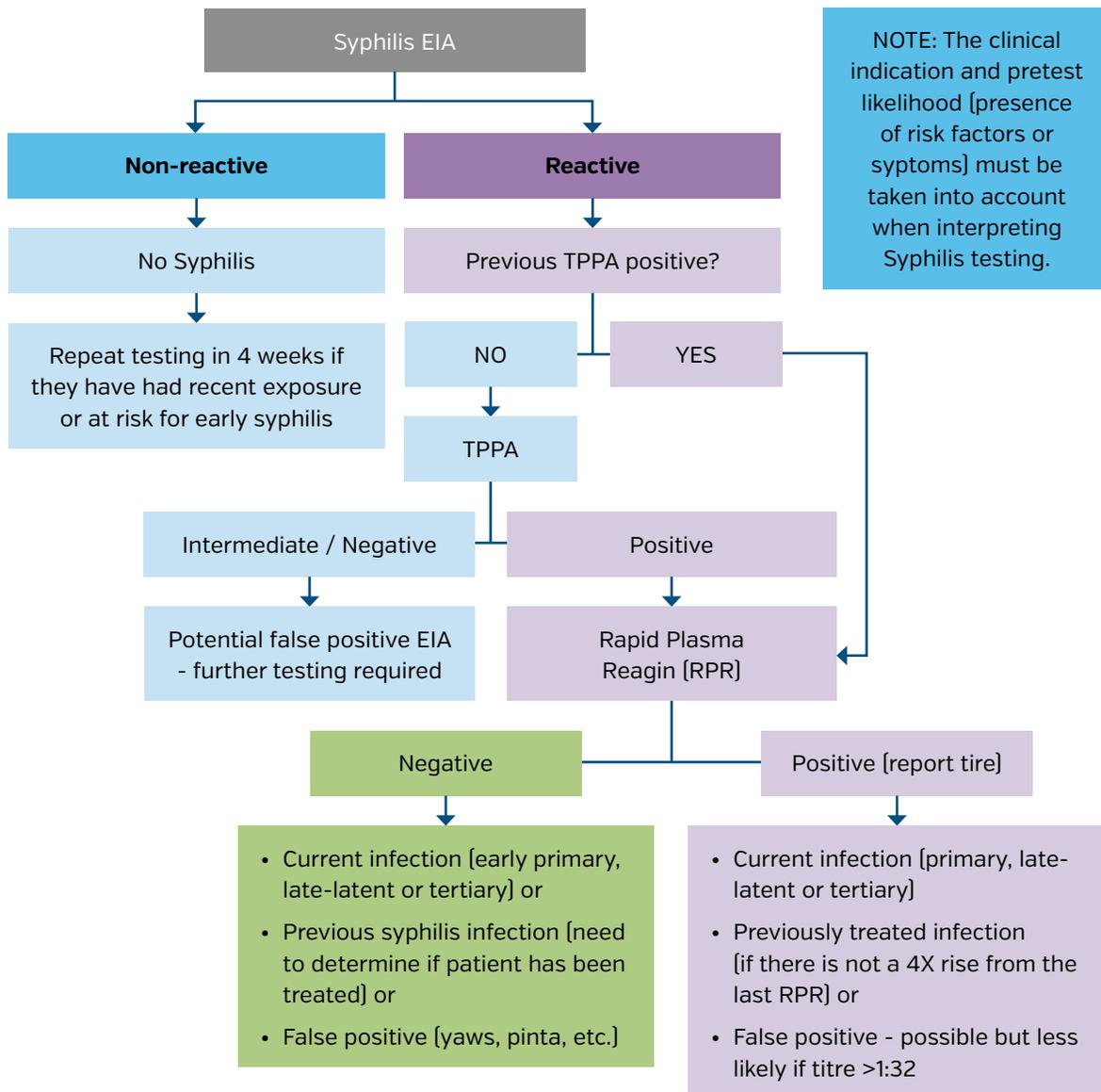
Syphilis is classified into stages that reflect the degree of infectivity and progression of the disease.

Stage	Incubation period	Clinical manifestations
Primary	3 weeks [3-90 days]	Chancre, regional lymphadenopathy
Secondary	2-12 weeks [2 weeks-6 months]	Rash, fever, malaise, lymphadenopathy, mucus lesions, condyloma lata, patchy or diffuse alopecia, meningitis, headaches, uveitis, retinitis
Latent	Early <1 year Late ≥1 year	Asymptomatic
Tertiary Cardiovascular syphilis	10-30 years	Aortic aneurysm, aortic regurgitation, coronary artery ostial stenosis
Neurosyphilis	<2years-20 years	Ranges from asymptomatic to symptomatic with headaches, vertigo, personality changes, dementia, ataxia, presence of Argyll Robertson pupil
Gumma	1-46 years [most cases 15 years]	Tissue destruction of any organ; manifestations depend on site involved
Congenital–Early	Onset < 2 years	2/3 may be asymptomatic, fulminant disseminated infection, mucocutaneous lesions, osteochondritis, anemia, hepatosplenomegaly, neurosyphilis
Congenital–Late	Persistence > 2 years after birth	Interstitial keratitis, lymphadenopathy, hepatosplenomegaly, bone involvement, anemia, Hutchinson's teeth, neurosyphilis

Diagnostic testing

Traditionally syphilis serology is a two-step algorithm where the patient's serum is initially screened with a non-treponemal test [e.g. RPR] followed by a confirmatory treponemal test [e.g. Treponemal pallidum Particle Agglutination [TPPA]]. However, recently laboratories in Nova Scotia have moved to using the “reverse algorithm” serum where a patient's serum is first tested with an EIA that detects IgM and IgG to *T. pallidum* and reactive specimens are subsequently tested with TPPA and an RPR [Figure 1]. The RPR result is quantitative and the titre is important to follow over time to ensure that the patient has responded to treatment. Although slightly more sensitive for early infection, false positives can occur, and confirmation can be more challenging [Table 1].

FIGURE 1:



The interpretation of syphilis serology should be made in conjunction with someone experienced in this area [i.e. microbiologist, infectious disease physician]. Every attempt should be made to obtain and document prior history of treatment for syphilis and prior serologic results in order to avoid unnecessary retreatment.

TABLE 1: INTERPRETATION OF SYPHILIS SEROLOGY

EIA result	TPPA	RPR	Interpretation
Negative	Not done	Not done	No evidence of syphilis. Repeat serology if at risk for early syphilis (window period is approximately 3-4 weeks)
Reactive	Negative	Negative	May represent a false positive EIA result or early seroconversion. Repeat testing in 4 weeks if unchanged represents false positive EIA
Reactive	Reactive	Non-reactive	Current or previously treated syphilis OR Yaws, pinta, bejel in patients from an endemic country
Reactive	Reactive	Reactive (dilutions may vary)	Current or previously treated syphilis OR Yaws, pinta, bejel in patients from an endemic country

IMPORTANT CAVEATS FOR SEROLOGIC DIAGNOSIS:

Serology may be falsely negative in early syphilis. As outlined in Figure 1, serology can be falsely negative in the first 4 weeks of infection. If there is a high index of suspicion, then the tests should be repeated in 2-4 weeks.

Diagnosis of Re-Infection: The EIA and TPPA will remain positive for life in previously infected patients. If the RPR increases 4-fold (ie two dilutions 1:8 – 1:32) this would indicate serologic evidence of reinfection

Patients from areas where other treponemal diseases (Pinta, Yaws, Bejel) may have false positive EIA/TPPA. It would be reasonable to seek expert advice if a patient from these regions presents with a positive test.

Patients may remain serofast. Although the reactivity to the RPR will disappear in the majority of patients who are successfully treated with benzathine penicillin, a small majority will have a persistent low titre [e.g.1:8]

Treatment

Although regimens containing daily IM procaine penicillin for 10-14 days are equally efficacious to regimens containing benzathine penicillin G, the latter are preferred because of better adherence with less frequent dosing [weekly].

Monitoring of serologic tests and other follow-up and adequate serologic response after treatment of each stage are outlined in the table below.

NOTE: Public Health Agency of Canada has indicated that there have been reports of inappropriate use of short-acting benzylpenicillin (penicillin G) intramuscularly (IM) for the treatment of infectious syphilis rather than the standard long-acting benzathine penicillin G (Bicillin-LA). Practitioners, pharmacists and purchasing agents should be aware of the similar names of these two products to prevent and avoid inappropriate and inadequate treatment. Long-acting benzathine penicillin achieves detectable serum levels of penicillin for 2-4 weeks in non-pregnant adults and is required to adequately treat infectious syphilis; short-acting penicillin agents are not adequate for achieving cure.

Stage	Preferred treatment
ALL NON-PREGNANT ADULTS Primary Secondary Early latent (<1 year duration)	Benzathine penicillin G 2.4 million units IM as a single dose*
ALL NON-PREGNANT ADULTS Late latent syphilis Latent syphilis of unknown duration Cardiovascular syphilis and other tertiary syphilis not involving the central nervous system	Benazthine penicillin G 2.4 million units IM weekly for 3 doses
ALL ADULTS Neurosyphilis	Penicillin G 3-4 million units IV q4h (16-24 million units per day) for 10-14 days
PREGNANT WOMEN Primary Secondary Early latent (<1 year duration)	Benazthine penicillin G 2.4 million units IM weekly for 1-2 doses*‡
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Stage	Preferred treatment
<p>PREGNANT WOMEN Late latent syphilis Latent syphilis of unknown duration Cardiovascular syphilis and other tertiary syphilis not involving the central nervous system</p>	<p>Benzathine penicillin G 2.4 million units IM weekly for 3 doses</p>
<p>Congenital syphilis</p>	<p><1 month of age–Crystalline penicillin G 50,000 units/kg IV every 12 hours for the first week of life and every 8 hours thereafter for 10 days total therapy. Addendum: Benzathine penicillin G 50,000 units/kg IM in a single dose has been recommended by some experts for infants not diagnosed with congenital syphilis but born to mothers with infectious syphilis:</p> <ul style="list-style-type: none"> • in whom adequate maternal treatment is confirmed AND • where there is no concern regarding re-infection in the mother AND • in infants with no clinical or laboratory evidence of congenital syphilis Alternatively, meticulous follow-up (e.g. monthly clinical/laboratory follow-up) until clearance of passively transferred antibodies may be indicated if there is good indication that adequate maternal treatment occurred. <p>≥ 1 month of age–Crystalline penicillin G 50,000 units/kg IV every 6 hours for 10-14 days.</p>

*some experts recommend 3 weekly doses (total of 7.2 million units) of benzathine penicillin G in HIV-infected individuals.

‡Given the complexity of accurately staging early syphilis, some experts recommend that primary, secondary and early latent cases in pregnancy be treated with two doses of benzathine penicillin G 2.4 million units 1 week apart; the efficacy of this regimen in preventing fetal syphilis is not known.

PUBLIC HEALTH MANAGEMENT & RESPONSE

Case management

Upon receiving a report of syphilis it is very important to confirm the diagnosis [see case definition] and initiate follow-up. The interpretation of syphilis serology should be made in conjunction with a physician experienced in this area. *Close collaboration between Public Health and the physician is crucial to ensure there is sufficient information to identify syphilis stage. This will allow PH nurse to identify appropriate trace-back period and locate sexual contacts in a timely manner.*

Some initial information that should be collected from the physician prior to contacting the case are:

- prior history of treatment for syphilis and prior serologic results *[every attempt should be made to obtain this prior history in order to avoid unnecessary retreatment]*
- reason for testing
- symptoms
- risk factors
- referral to specialist
- appropriate treatment initiated
- is case pregnant [in an attempt to prevent congenital syphilis pregnant cases and their infant should be clinically assessed/managed by a specialist]
- any pregnant contacts
- staging of syphilis
- tested for other sexually transmitted infections [STI] [i.e. HIV]
- co-infection [Persons co-infected with HIV may require a longer course of treatment, as well as closer and longer follow-up]

Also, during the initial conversation with the physician, it is important to determine the clinical plan of action for the case. It is a good time to educate the physician regarding the role of Public Health and contact tracing/education. Refer the treating physician to the appropriate syphilis sections of the revised January 2010 syphilis chapter in the 2006 edition of the [Canadian STI Guidelines](#) [i.e. Management, Follow-up, Special considerations] so they are aware of their role in ongoing monitoring of serologic tests and other follow-up which can last up to 2 years.

The following tables can be used as a guide:

Monitoring of serologic tests and other follow-up

Primary, secondary, early latent	[*], 3, 6, 12 months after treatment
Late latent, tertiary [EXCEPT NEUROSYPHILIS]	12 and 24 months after treatment
Neurosyphilis	6, 12 and 24 months after treatment. Patients with CSF abnormalities require follow up CSF at 6 month intervals until normalization of CSF parameters [see revised January 2010 syphilis chapter in the 2006 edition of the <i>Canadian STI Guidelines</i> for more info] Other clinical follow-up may be indicated on a case-by-case basis
HIV infected (any stage)	[*], 3, 6, 12 and 24 months after treatment and yearly thereafter
Pregnant women with reactive syphilis serology	See revised January 2010 syphilis chapter in the 2006 edition of the <i>Canadian STI Guidelines</i>
Babies born to mothers with reactive syphilis serology	See revised January 2010 syphilis chapter in the 2006 edition of the <i>Canadian STI Guidelines</i>

[*] Some experts recommend follow up testing at 1 month after treatment to ensure that non-treponemal test titre is not rising; a rising titre may be indicative of either treatment failure or re-infection.

Note: Consultation with a specialist is strongly recommended in syphilis cases who are pregnant or HIV-infected.

Note: Consult District Medical Officer's of Health (MOH) for advice/guidance if any questions/discrepancies arise regarding the confirmation of diagnosis and staging.

Adequate serologic response

Primary	4-fold* drop at 6 months, 8-fold drop at 12 months, 16-fold drop at 24 months
Secondary	8-fold drop at 6 months and 16-fold drop at 12 months
Early latent	4-fold drop at 12 months

*A four-fold drop = 2- tube drop [i.e., change from 1:32 dilutions to 1:8 dilutions].

- Once preliminary information is obtained contact and interview the case.
- Discuss Public Health's role regarding contact tracing [see below].
- Review with the case the importance of adequate treatment and follow-up with their physician [see above].
- Obtain details about current and past symptoms and risk factors. Collect prior history of syphilis and treatment information, if applicable.
- During the interview it is important to build trust and rapport so that the case feels safe in disclosing sensitive details regarding his/her sexual history and partners.
- It is very important to reassure the case that their personal information will not be disclosed in any way during the contact tracing process.
- Take the opportunity to provide education regarding other sexually transmitted infections and prevention measures.
- Public Health should follow case until treatment is completed and there is an adequate serologic response [refer to tables above].
- Once Public Health follow-up is complete ensure that case understands the importance of ongoing follow-up with their physician as mentioned above.
- Advise the case of community clinics/groups as appropriate [i.e. local STI clinics, AIDS Coalition, Pride Health, Addiction Services, etc].

Exclusion

In most situations, no exclusion is necessary. If syphilis case's work involves activity that could potentially put the public at risk [i.e. sex trade work], consult MOH.

Education

- Explain to the case the importance of contact tracing and Public Health's role in preventing or controlling a current or potential outbreak.
- Educate the case regarding abstaining from unprotected sex until he/she is considered non-infectious.

- Educate the case regarding the risks associated with various sex acts, including the risk of transmission via oral sex, and ensure the use of a barrier method for oral sex [i.e., although the risk of STI transmission is lower via oral sex than vaginal or anal sex, many STIs, including syphilis, can be transmitted through unprotected oral sex].
- Discuss the importance of complying to the treatment regimen and subsequent follow-up.
- Cases should be made aware of the possible Jarisch-Herxheimer reaction to treatment, especially with penicillin.

NOTE: The reason the Jarisch-Herxheimer reaction occurs is not clear. It may be caused by the toxins released from the syphilis bacteria as they are destroyed by antibiotics. Other important points about this reaction:

- more common in secondary syphilis (70-90%), but can occur at any stage of infection
 - an acute febrile illness with headache, myalgia, chills, rigors which can occur as early as 2 hours after treatment and resolves within 24 hours
 - not clinically significant unless there is neurologic or ophthalmic involvement or in pregnancy where it may cause fetal distress and premature labour
 - not a drug allergy
 - can be treated with antipyretics
 - steroids may be indicated for the management of severe reactions –consult an expert in this area
- Depending on risk factors identified during interview, educate the case regarding prevention and harm reduction measures to prevent exposure to communicable diseases in the future.
 - Educate the case that reinfection can occur. Having syphilis once does not protect a person from getting it again. Following successful treatment, people are still susceptible to re-infection.
 - It is also important for Public Health to educate health care professionals that a diagnosis of syphilis should be considered in anyone with signs or symptoms compatible with syphilis and also in the following individuals:
 - those who have had sexual contact with a known case of syphilis
 - males who have sex with males (MSM)
 - sex workers
 - those with street involvement/homelessness
 - those with a history of syphilis, HIV and other STIs

- those originating from or having sex with an individual from a country with a high prevalence of syphilis; it should be noted that screening for syphilis (using a non-treponemal test) is routinely performed in all immigration applicants to Canada who are older than 15 years
- sexual partners of any of the above
- Sexual activity of any mucosal type (oral, anal, genital) can be a mode of transmission for syphilis. Since lesions may not be readily apparent (i.e., painless lesions on the internal genital tract in females, intra-anal lesions, etc.) all patients with infectious syphilis should be considered potentially infectious regardless of the presence or absence of obvious lesions.
- In patients with confirmed infectious (primary, secondary and early latent) syphilis, patients and their partners should abstain from all forms of sexual activity until treatment of both partners is complete and an adequate serologic response is determined. If the case can not abstain then it is important to educate the person that condoms are most commonly used in safe sex practice to reduce the risk of transmission of infectious diseases. There are male and female condoms. Dental dams are effective barriers that can also be used for oral sex.
- Syphilis can also be passed from mother to child during pregnancy and therefore routine prenatal screening for syphilis is an important means of prevention. If there is ongoing high-risk activity, test again later in pregnancy. See revised January 2010 syphilis chapter in the 2006 edition of the *Canadian STI Guidelines* for more information regarding special considerations in pregnant women and newborn infants.
- In cases where a child is born to a mother who was diagnosed with syphilis in pregnancy, and where the child is placed under the care of child protection services, medical information about the mother's diagnosis may be critical to the ongoing protection and monitoring of the infant's health.

Contact tracing

The goal of partner elicitation is to obtain sufficient information to confidentially locate, notify, and refer the partners for necessary examination and treatment (if appropriate). Public Health takes the lead in coordinating this process.

Rapid identification and investigation of sexual partners/contacts is essential to locate persons with early (primary, secondary, early latent) or incubating syphilis and provide them with treatment to prevent further transmission.

Definition of close contact/exposure criteria

Primary, secondary, and early latent stages are considered infectious, with an estimated risk of transmission per partner of around 60%. Direct (often intimate) contact with lesions of primary and secondary syphilis poses the greatest risk of transmission. Early latent syphilis is considered infectious because of the 25% chance of relapse to secondary stage. Congenital transmission is most likely during the primary and secondary stage of maternal syphilis, but can occur in the latent period.

The risk of transmission from mother to baby in untreated women is 70-100% with primary or secondary syphilis, 40% with early latent syphilis and 10% in late latent stages in pregnancy. About 40% of pregnancies in women with infectious syphilis results in fetal demise.

Also, please see above for information regarding transmission and communicability.

Susceptibility

Susceptibility is universal. Infection leads to gradual development of immunity against *T. pallidum*; immunity often fails to develop because of early treatment in the primary and secondary stages.

Initiate contact tracing

- During interview with the case, identify contact[s].
- Discuss Public Health's role in potentially preventing infection to persons who are exposed. Explain that it is important that the contacts be referred to the appropriate health care provider and Public Health can assist with this. Reassure case that Public Health Nurses are trained in contact tracing procedures and that it is an anonymous process.
- Follow up with contact[s].
- Determine how contacts will be notified. This may be dependent on contact's culture and/or their social environment (i.e. place/venue where case and contact met).

All sexual or perinatal contacts within the following time periods need to be located, tested, and treated if serology is reactive- *if exposure to a primary, secondary or early latent syphilis case occurred within the past 90 days, presumptive treatment is recommended, even if the contact[s] are seronegative*. If exposure was more than 90 days ago, treatment should be based on serologic test results.

NOTE: Public Health will contact all of the contacts and will follow up contacts until above criteria are met.

Partner notification

Stage of syphilis	Trace-back period
Primary syphilis	3 months*
Secondary syphilis	6 months*
Early latent	1 year*
Late latent/tertiary	Assess marital or other long-term partners and children as appropriate; the decision to test these contacts depends on estimated duration of infection in source case.
Congenital	Assess mother and her sexual partner(s)
Stage undetermined	Assess/consult with a specialist experienced in syphilis management

*Trace-back period refers to the time period prior to symptom onset or date of specimen collection (if asymptomatic).

The length of time for the trace-back period should be extended:

1. To include additional time up to the date of treatment.
2. If the index case states that there were no partners during the recommended trace-back period, then the last partner should be notified.
3. If all partners traced (according to recommended trace-back period) test negative, then the partner prior to the trace-back period should be notified.

Public Health should be reviewing the contact's test results and other information (i.e. past cases and possible connections) in an attempt to determine the source case and to assess whether an outbreak may be occurring.

Prophylaxis

The preferred treatment of sexual contacts in the preceding 90 days to primary, secondary, and early latent syphilis is Benzathine penicillin G 2.4 million units IM as a single dose.

Public Health should ensure that all contacts are appropriately referred, tested and treated when appropriate.

Education

- Educate the contacts regarding the risks associated with various sex acts, including the risk of transmission via oral sex, and ensure the use of a barrier method for oral sex [i.e., although the risk of STI transmission is lower via oral sex than vaginal or anal sex, many STIs, including syphilis, can be transmitted through unprotected oral sex. Transmission through oral sex is well documented].
- Explain to the contact the importance of following up with public health recommendations and the rationale for the recommendation[s].

Ongoing Public Health follow-up

Ensure that all contacts are appropriately referred, tested and treated when appropriate.

Surveillance Guidelines

<https://novascotia.ca/dhw/populationhealth/surveillanceguidelines.asp>

General Information Sheet

REFERENCES

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