ALBERTA PRECISION LABORATORIES
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PROVLAB ALBERTA

Information on Syphilis Testing in Alberta

Diagnosis of syphilis

A diagnosis of syphilis should be considered in anyone with signs or symptoms compatible with syphilis and also in the individuals at risk for sexually transmitted infections (STI), such as:

- those having sexual contact with person(s) with a known STI
- those with early sexual debut
- those with a new sexual partner or ≥ 2 sexual partners in the past year
- persons who inject drugs or use other substances
- persons who exchange sex for goods or money and their clients
- persons who have been incarcerated and their sexual partners
- those who are street involved/homeless
- anonymous sexual partnering
- previous STI
- victims of sexual assault/abuse

Types of tests:

A: Direct Testing

Syphilis PCR

Molecular detection of *Treponema pallidum* subsp. *pallidum* can be performed on:

- swabs of primary syphilitic lesions, chancres, on skin and mucosal surfaces
- wet skin lesions and nasal discharge of babies with congenital syphilis
- CSF in patients with suspected neuro-syphilis
- fetal or placental tissue from stillborn babies whose suspected cause of death is congenital syphilis

PCR is an important diagnostic tool in early syphilis since serology can take up to 12 weeks to become positive.

B: Serology

1) Syphilis enzyme immunoassay (EIA)

This is the screening test for syphilis and measures IgM and IgG antibody specific for Treponema pallidum (antitreponemal antibodies). Estimated turnaround time for test result is within 48 hours of receipt at the lab.

2) Rapid Plasma Reagin (RPR)

This is used for staging infection, following response to treatment and determining re-infection. It is a non treponemal test, and measures antibody against cardiolipin (nontreponeme specific antibodies), providing a crude indicator of disease activity. Estimated turnaround time for test result is 48 hours.

3) Treponema pallidum Particle Agglutination (TPPA) Test

This is an internationally well-established confirmatory serological test for syphilis. It is highly sensitive and extremely specific. The test uses purified *T. pallidum* antigens (Nichols strain) to sensitise gelatin particles. Agglutination occurs when the trepomenal specific antibodies are present in the patient's serum. Although this is a manual test, the estimated turnaround time is 72 hours from time of specimen receipt.

The reverse syphilis testing algorithm is used in Alberta. This form of testing involves the use of a treponeme specific test as a screening test – the EIA. All specimens with positive EIAs subsequently have the RPR test and a confirmatory treponeme specific test performed. The current confirmatory test is the TPPA.

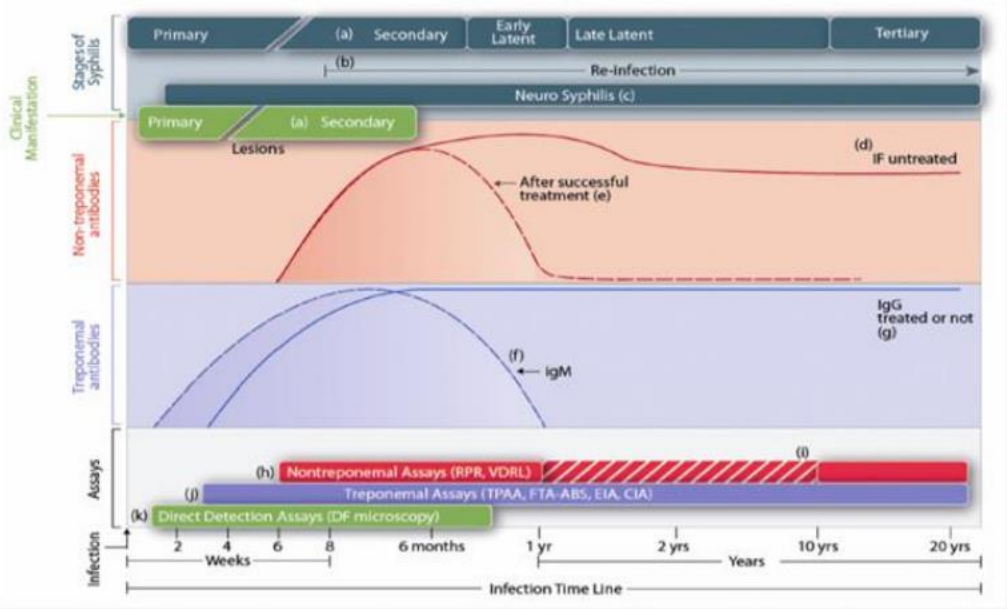

Figure 11.4.1–1 Diagram to provide insight into the immunology and clinical manifestations of syphilis. (a) Primary and secondary stages can overlap, with secondary lesions appearing before primary lesions are healed (1). (b) Reinfection can occur after treatment during any stage of infection (27). (c) Neurosyphilis can occur during any stage of infection (1, 9). (d) Nontreponemal antibodies rise and peak at about 6 months and remain elevated if untreated (28). (e) With adequate treatment, nontreponemal antibodies decline and may become undetectable in about a year (1). (f) Treponemal IgM antibody titers rise early infections, peak at about 6 months, and gradually decline regardless of treatment, and they are usually undetectable after about a year (29). (g) Treponemal IgG antibodies usually persist for life regardless of treatment (9). (h) Nontreponemal assays become reactive at about 6 weeks postinfection but may not be detectable in early primary syphilis (28). (i) Nontreponemal assays become reactive at about 6 weeks postinfection but may not be detectable in late latent syphilis (28). (j) Treponemal tests detect antibodies about 3 weeks postinfection (28). (k) Direct detection assays are useful when lesions are present in early syphilis (28).

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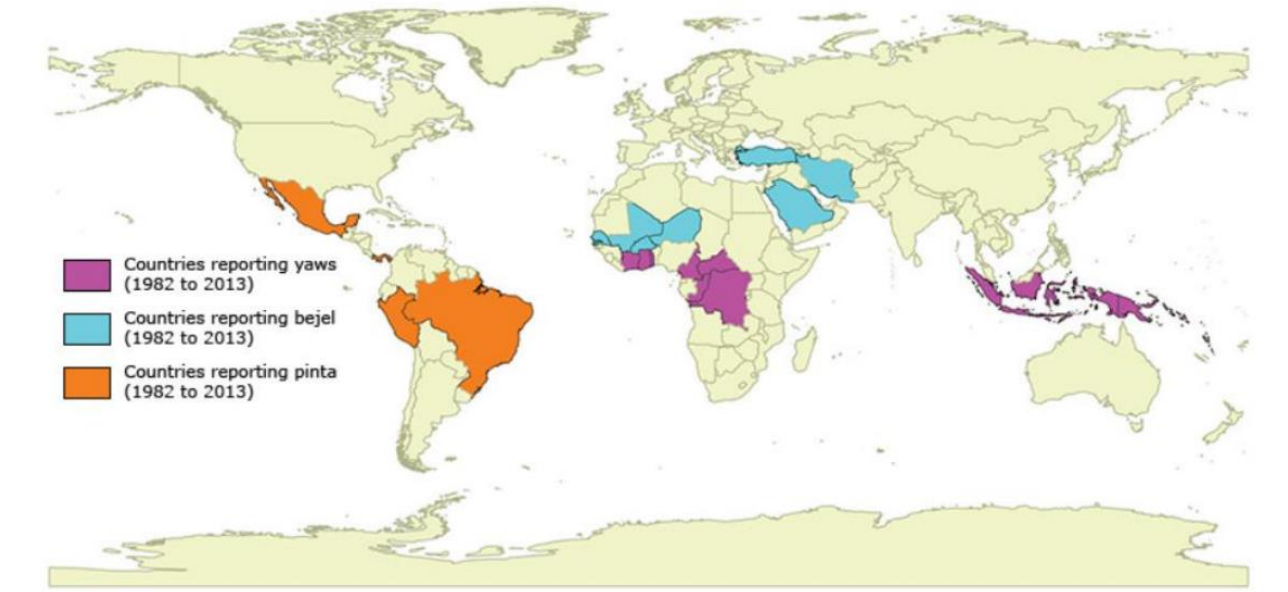
Other subspecies

Note that all serological tests for syphilis will also pick up antibody against other subspecies of *T. pallidum,* i.e. *T. pallidum* subsp. pertenue, “yaws”, and *T. pallidum* subsp. *endemecium* “bejel”, as well as the closely related *Treponema carateum*, “Pinta”.These non-venereal treponemal infections are reported to be on the increase related to deteriorating social conditions in some parts of the world. Consider patient origin and travel, patient age (these are usually acquired in childhood), distribution of lesions (if any). Generally speaking because of the difficulty in distinguishing between reactive serologic tests for syphilis and non-venereal trepanematoses, most clinicians in Canada would manage the patient as a case of syphilis (often late latent syphilis). For a good review see Farnsworth and Rosen, Clinics in Dermatology, 24: 181-90, 2006. (2).

Geographic distribution of yaws, bejel, and pinta



Countries where endemic treponemal diseases have recently been reported.

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The interpretation of syphilis serology should be made in conjunction with a colleague experienced in this area.

For additional information:

1) Syphilis chapter in *Canadian Guidelines on Sexually Transmitted Infections, 2010 Edition*. Ottawa, ON: Public Health Agency of Canada, available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

2) Contact:
- Your local Sexual and Reproductive or STI clinic, OR
- STI Clinics in:
  - Calgary 1-855-945-6700, option 1
  - Edmonton: 1-855-945-6700, option 2
  - Ft. McMurray: 1-855-945-6700, option 3 OR
- STD partner notification nurse OR
- STI Centralized Services at 1-855-945-6700, option 4 during business hours
  For afterhours consultation, please refer to Infectious Diseases.

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Further information on syphilis testing and management can be obtained from:
1. Levett, et al. Canadian Public Health 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 2015; 26(suppl. A): 6A -12A.
2. Morshed, et al. Recent Trends in the Serological Diagnosis of syphilis. Clinical and Vaccine Immunology 2015; 22(2): 137-147.
3. UK Standards for Microbiology Investigations. Virology 2015; 44(9): https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/421801/V44i2.pdf
4. Workowski, et al. Sexually Transmitted Diseases Treatment Guidelines, 2015. MMWR 2015; 64(3): 34-41.
5. Syphilis Antibody by TP-PA, Serum. Mayo Clinic. http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/61480