Canadian Public Health Laboratory Network national syphilis laboratory testing recommendations

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INTRODUCTION

The development of these recommendations arose in the spring of 2009 under the support and recommendation of the Canadian Public Health Laboratory Network (CPHLN). The initial group was formed of a federal co-chair (RT), a provincial co-chair (MM) and a CPHLN secretariat lead (SR). An initial environmental scan was performed in 2009, which was published in August 2011 (R. Tsang, SM Radons, M Morshed. Laboratory diagnosis of syphilis: A survey to examine the range of tests used in Canada. Can J Infect Dis Med Microbiol 2011;22[3]:83-87). National representation was added to the working group in 2010, including laboratory scientists from the provincial public health laboratories, STI clinicians, epidemiologists and researchers. The group divided into smaller groups for the drafting of each chapter, which was written and presented back to the larger group. Once the document was finalized by the Syphilis Working Group, it was reviewed and approved by the CPHLN Laboratory Directors Council (comprised of federal/provincial/territorial PHL directors or their representatives), before submission to the Journal.

TREPOBEMA PALLIDUM AND RELATED AGENTS

Syphilis is caused by the spirochaete, Treponema pallidum subsp. pallidum. The spiral-shaped bacteria is related to other species causing non-venereal diseases including Treponema pertenue, which causes yaws; Treponema endemicum, which causes endemic syphilis (bejel); and Treponema carateum, which causes pinta (1). There is a high degree of antigenic relatedness among the pathogenic treponemes (2,3). Available serological tests for syphilis are reactive in persons infected with any of the treponematoses, but none of these tests can distinguish between endemic treponemal infections from venereal syphilis (4,5).

MANIFESTATIONS OF SYPHILIS

T. pallidum is an obligate human parasite with no known reservoirs in animals or in the environment. Most cases of venereal syphilis occur due to direct sexual contact with lesions containing the bacteria. Studies of sexual partners of patients with syphilis report a risk of infection to approximately one-third (10% to 60%) of patients exposed to early syphilis (1). Transmission by sexual contact does not occur during the late latent and tertiary stages of infection. Untreated syphilis in pregnant women can lead to complications during pregnancy and delivery including neonatal death, still birth, blindness, deafness, abnormal bone growth and/or mental retardation.

T. pallidum is usually transmitted sexually through microabrasions in mucosal membranes or skin, and rapidly enters the bloodstream to disseminate to other tissues (5,6). To establish infection, T. pallidum adheres to epithelial cells and extracellular matrix components of the skin and mucosa (6). T. pallidum replicates at the site of initial inoculation, inducing a local inflammatory response that results in a painless chancre approximately three to six weeks after initial infection. Within three to eight weeks, the chancre heals, indicating clearance of T. pallidum locally. Once the organism breaches the epithelial layer, multiplication occurs locally, followed by dissemination through the blood vessels and lymphatics. Secondary syphilis results from the multiplication and dissemination of the spirochaetes and can occur up to six months after healing of the primary lesion. This stage can last from several weeks to months and may reoccur in approximately 25% of untreated patients. It is characterized by a range of clinical symptoms including malaise, headache, low-grade fever, rash (including on the palms and soles of the feet), and mucous patches in the oral cavity or genital tract. The symptoms of

IT IS NOTEWORTHY, HOWEVER, THAT A RECENT CASE REPORT FROM CANADA DESCRIBED THE USE OF GENOMIC TECHNIQUES TO DEMONSTRATE TRANSMISSION OF ENDEMIC SPHILIS IN CANADA (4).

TRANSMISSION, PATHOGENESIS AND CLINICAL MANIFESTATIONS OF SYPHILIS
secondary syphilis will resolve with or without treatment. Without treatment, however, the infection will progress to the latent and tertiary stages of syphilis. The latent stage is divided into early (within one year of infection) and late phases. Latency can last for many years and approximately 70% of untreated patients will remain in this stage for the rest of their lives. The last stage of syphilis, the tertiary stage, is rarely seen today given effective antibiotic therapy. It usually occurs in 15% to 40% of untreated individuals, and can occur between five and 40 years after infection. In this stage of syphilis, the bacteria invade the central nervous system, eyes, skin, cardiovascular system and other organs.

**EPIDEMIOLOGY OF SYphilIS**

Despite the existence of simple and validated screening tests, effective prevention measures, such as condoms and effective and relatively cheap treatment options, syphilis remains a global problem, with an estimated 12 million people infected annually (7). The World Health Organization (WHO) estimates that two million pregnant women each year are infected with syphilis globally and that approximately 25% end in stillbirth or spontaneous abortion (7).

In Canada, infectious syphilis (comprising of the primary, secondary and early latent stages) is notifiable. Based on nationally reported case reports, during the early and mid-1990s, Canada, like other high-income countries, was approaching or achieving its goal to eliminate endemic transmission of syphilis (8). Since 2000, however, there has been a re-emergence of syphilis in the country, driven, in part, by reported outbreaks among men who have sex with men, although recent reports suggest increased incidence among the heterosexual population. Between 2000 and 2012, the overall reported rate of infectious syphilis has increased by 481%, from 1.84 per 100,000 population to 8.85 per 100,000 population (Figure 1) (9).

**PUBLIC HEALTH IMPLICATIONS OF INCREASES IN INFECTIOUS SYphilIS**

The global increases in the reported prevalence of infectious syphilis is cause for public health concern (10). Syphilis is, in principle, entirely preventable and potentially eradicable because humans are the sole reservoir for this infection. Therefore, investment in syphilis prevention and treatment should result in reduced disease burden and associated costs in the future. In addition, HIV transmission is believed to be facilitated by ulcerative sexually transmitted infections. While the relationship between syphilis and HIV in the context of coinfection is complex, syphilis has been estimated to increase HIV transmission two- to ninefold and HIV acquisition two- to fourfold (11-13). Hence, treatment and prevention of syphilis will likely also reduce HIV transmission in that population. Finally, syphilis is an important public health marker for behavioural risk factors. In the United States, for example, the resurgence of syphilis among men who have sex with men has led researchers to suggest that increasing rates of syphilis among MSM may be an indicator of potential increases in other sexually transmitted infections.

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**DISCLOSURES**

The authors have no conflicts of interest to declare.

**REFERENCES**
