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SYPHILIS RESURGENCE IN CANADA

GUEST EDITOR: JULIE THÉRIAULT

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CANADA COMMUNICABLE DISEASE REPORT

The *Canada Communicable Disease Report* (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious diseases to clinicians, public health professionals, and policy-makers to inform policy, program development and practice.

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Contact the Editorial Office

ccdr-rmtc@phac-aspc.gc.ca
613.301.9930

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The cover photo represents a pregnant woman silhouette plus abstract watercolor painted. Digital art painting. Syphilis is called the "great imitator" as it can present very similar to a large variety of other diseases. Image from Adobe Stock (https://stock.adobe.com/ca/images/double-exposure-illustration-of-pregnant-woman/120999725?prev_url=detail).

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SYPHILIS RESURGENCE IN CANADA

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Julie Thériault is a nurse consultant at the Public Health Agency of Canada (PHAC) and she is currently the manager of the Health Professionals Guidance Unit. Upon joining PHAC, she worked on the Canadian Guidelines for Sexually Transmitted Infections, and prior to this, she worked at Ottawa Public Health in the case management of sexually transmitted and bloodborne infections. She holds a Master's in public health from the London School of Hygiene and Tropical Medicine.

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Rising syphilis rates in Canada, 2011–2020

Josephine Aho[1]*, Cassandra Lybeck[1], Ashorkor Tetteh[1], Carmen Issa[1], Fiona Kouyoumdjian[2], Jason Wong[3,4], Alexandrea Anderson[1], Nashira Popovic[1]

Abstract

Background: Syphilis rates are of public health concern in Canada, with multiple jurisdictions reporting outbreaks over the past five years. The objective of this article is to describe trends in infectious and congenital syphilis in Canada 2011–2020.

Methods: Routine surveillance of syphilis is conducted through the Canadian Notifiable Disease Surveillance System (CNDSS). In response to rising rates of syphilis, all provinces and territories (P/Ts) have also submitted enhanced surveillance data on infectious syphilis to the Public Health Agency of Canada through the Syphilis Outbreak Investigation Coordinating Committee (SOICC) starting in 2018. Descriptive analyses of CNDSS and SOICC surveillance data 2011–2020 by age, sex, pregnancy status, male sexual orientation and P/Ts were performed.

Results: The national rate of infectious syphilis increased from 5.1 per 100,000 population in 2011 to 24.7 per 100,000 population in 2020.The rates increased in almost all P/Ts, with the Prairie provinces reporting the greatest relative increases from 2016 to 2020 (more than 400%). Rates in males were consistently higher than rates in females over the past 10 years; however, from 2016 to 2020, rates among females increased by 773%, compared with 73% among males. Although the proportion of cases who self-identify as gay, bisexual and other men who have sex with men decreased from 54% to 38% between 2018 and 2020, they still represent a high proportion of cases (according to data from eight P/Ts). From 2016 to 2020, rates of infectious syphilis increased in every age group, especially in females aged 15–39 years. Confirmed early congenital syphilis cases for 2020 increased considerably from prior years, with 50 cases reported in 2020, compared with 4 cases in 2016.

Conclusion: Infectious and congenital syphilis rates are a growing concern in Canada and the nature of the syphilis epidemics across Canada appears to be evolving, as evidenced by recent trends. More data and research are needed to better understand the drivers associated with the recent changes in the epidemiology of syphilis in Canada.

Affiliations

[1] Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada, Ottawa, ON

[2] Ontario Ministry of Health, Toronto, ON

[3] BC Centre for Disease Control, Vancouver, BC

[4] School of Population and Public Health, Faculty of Medicine, University of British Columbia, Vancouver, BC

***Correspondence:**

josephine.aho@phac-aspc.gc.ca

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Keywords: infectious syphilis, congenital syphilis, surveillance, gbMSM, heterosexual females, pregnant individuals, Canada

Introduction

Syphilis is the third most reported notifiable sexually transmitted infection in Canada, after chlamydia and gonorrhea. A bacterial infection caused by *Treponema pallidum* subspecies *pallidum*, syphilis is primarily transmitted through genital, anal/or oral sexual contact and can also be vertically transmitted to the fetus during pregnancy or to the neonate at delivery. Syphilis can easily and effectively be treated with penicillin, but left untreated it can progress through several different stages: primary; secondary; early latent; late latent; and tertiary syphilis. Syphilis is only infectious during the first three stages of infection (primary, secondary or early latent), which occur within the first year. Acute neurosyphilis can also develop during this time. At more advanced disease stages, syphilis can lead to serious health consequences such as neurological, cardiovascular or musculoskeletal complications. Congenital syphilis, which is syphilis transmitted *in utero*, can have severe debilitating effects and can lead to stillbirth or neonatal death (1).

Following a long period of declining syphilis rates since the 1940s, Canada announced in 1998 a national goal of maintaining syphilis rates below 0.5 per 100,000 population (2). In 2016, the World Health Organization released global targets for reducing the health impact of sexually transmitted infections by 2030, which included a 90% reduction in rates of syphilis globally and a threshold of 50 or fewer cases of congenital syphilis per 100,000 live births in 80% of countries (3). The Government of Canada has endorsed these global targets (4).

In Canada, rates of infectious syphilis started to increase steadily in the early 2000s, with substantial increases after 2017. Cases of congenital syphilis also increased during the same period. Ten Canadian jurisdictions have reported province and territory-wide or regional outbreaks in the past few years (1). In July 2019, in response to rising rates of syphilis across jurisdictions in Canada, the Public Health Agency of Canada (PHAC), in collaboration with all provinces and territories (P/Ts), established a federal, provincial and territorial Syphilis Outbreak Investigation Coordinating Committee (SOICC). The aim of SOICC is to share information on the epidemiology of syphilis and best practices and challenges on responses to rate increases. All P/Ts share enhanced surveillance data on confirmed infectious syphilis and confirmed early congenital syphilis case counts directly with PHAC as part of the activities of the SOICC.

In this article, we describe recent trends in infectious and congenital syphilis rates in Canada using surveillance data from 2011–2020.

Methods

Data sources

Since 1924, provincial and territorial health authorities have routinely provided data on laboratory-confirmed cases of syphilis to PHAC through the Canadian Notifiable Disease Surveillance System (CNDSS) (5). While all stages of syphilis are notifiable, only confirmed infectious cases and confirmed early congenital cases were included in our analysis. National case definitions of all syphilis stages as well as congenital syphilis can be found online (6).

Case variables submitted to CNDSS included sex, age at time of diagnosis, year of diagnosis and province or territory of diagnosis, while variables submitted to the SOICC also included male sexual orientation and pregnancy status. All P/Ts submitted data on sex, age and year of diagnosis to CNDSS and the SOICC. Newfoundland and Labrador's data were stratified by age and by sex but not by age and sex concurrently. Male sexual orientation and pregnancy data were reported consistently to the SOICC for 2018 to 2020 by British Columbia, Alberta, Saskatchewan, Ontario, New Brunswick, Nova Scotia, Yukon and the Northwest Territories. These eight P/Ts represented 72% of the Canadian population. Confirmed early congenital syphilis cases (less than two years after birth) did not include stillbirths.

Data for the years prior to the SOICC data collection (2011–2017) were extracted from CNDSS while data from 2018 to 2020 were collected via the SOICC. Twelve P/Ts submitted data for the full calendar year of 2020, and one province (Newfoundland and Labrador) provided partial counts for 2020; thus, annual counts for 2020 for this province were extrapolated.

Data analysis

Case counts, proportions and rates are presented overall and by sex, male sexual orientation, age group and P/T. Counts of cases of pregnant individuals are also presented. For reporting P/Ts, the proportion of missing data for sex and age did not exceed 1%, while it ranged from 0% to 18% for male sexual orientation and pregnancy data. The rates of confirmed infectious and confirmed early congenital syphilis were calculated using reported case counts as numerators and Statistics Canada population and live birth estimates, last updated in July 2020, as denominators. Reported rates were calculated per 100,000 population and included overall annual rates as well as sex, age group and P/T-specific rates. Descriptive analyses were performed using R version 4.0.2 (7–9) and Microsoft Excel. Observed trends based on small numbers must be interpreted with caution, as rates based on small numbers are more prone to fluctuation over time.

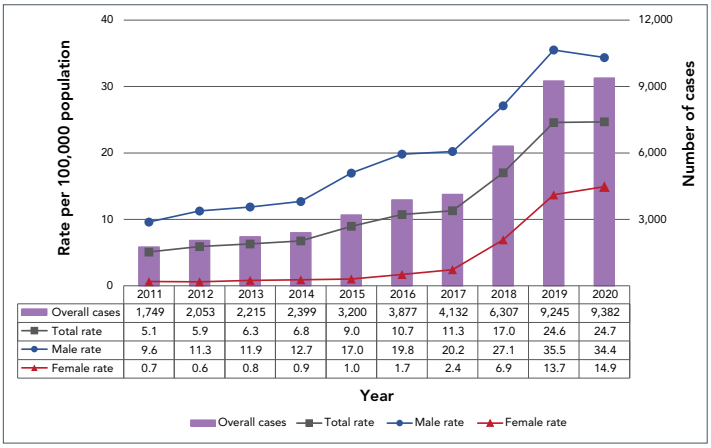
Results

Since 2011, there has been a consistent increase in the number of confirmed infectious syphilis cases reported, except for a slight decline in 2020 (**Figure 1**). The highest increases were observed in 2018 and 2019 (50% and 45% yearly increases, respectively), corresponding to the highest numbers of cases and rates recorded in the last 10 years. There were an estimated 9,382 cases in 2020, corresponding to a rate of 24.7 per 100,000 population (Figure 1). This reflects a 385% increase in rates compared to the 2011 rate of 5.1 per 100,000 population.

Rates of infectious syphilis increased among males and females, but faster in females

In the past decade, the annual rate of infectious syphilis has consistently been higher in males, compared with females (Figure 1). Rates of infectious syphilis increased in both males and females over 2011–2020; however, the magnitude of the rise has been more pronounced in females, especially in the past five years. From 2016 to 2020, while rates increased by 73% in males, they increased by 773% in females. Nonetheless, in 2020, the rate in males remained higher compared with females at 34.4 per 100,000 population and 14.9 per 100,000, respectively.

Figure 1: Total number of cases and sex-specific rates of infectious syphilis in Canada by year, 2011–2020



	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Overall cases	1,749	2,053	2,215	2,399	3,200	3,877	4,132	6,307	9,245	9,382
Total rate	5.1	5.9	6.3	6.8	9.0	10.7	11.3	17.0	24.6	24.7
Male rate	9.6	11.3	11.9	12.7	17.0	19.8	20.2	27.1	35.5	34.4
Female rate	0.7	0.6	0.8	0.9	1.0	1.7	2.4	6.9	13.7	14.9

The proportion of all infectious syphilis cases reported in females has also considerably increased. The national proportion of infectious syphilis cases among females was 6% in 2011 and remained under 10% until 2017. In 2019 and 2020, the proportion of all infectious syphilis cases reported among females was 28% and 30% respectively. In 2020, P/Ts with the highest proportions of female cases were Saskatchewan (51%), Manitoba (49%) and Alberta (43%). Although with low case counts (50 cases or fewer), Nunavut also reported a high proportion of female cases (60%). British Columbia, Ontario and Québec reported the lowest proportions of female cases in 2020 (less than or equal to 15%).

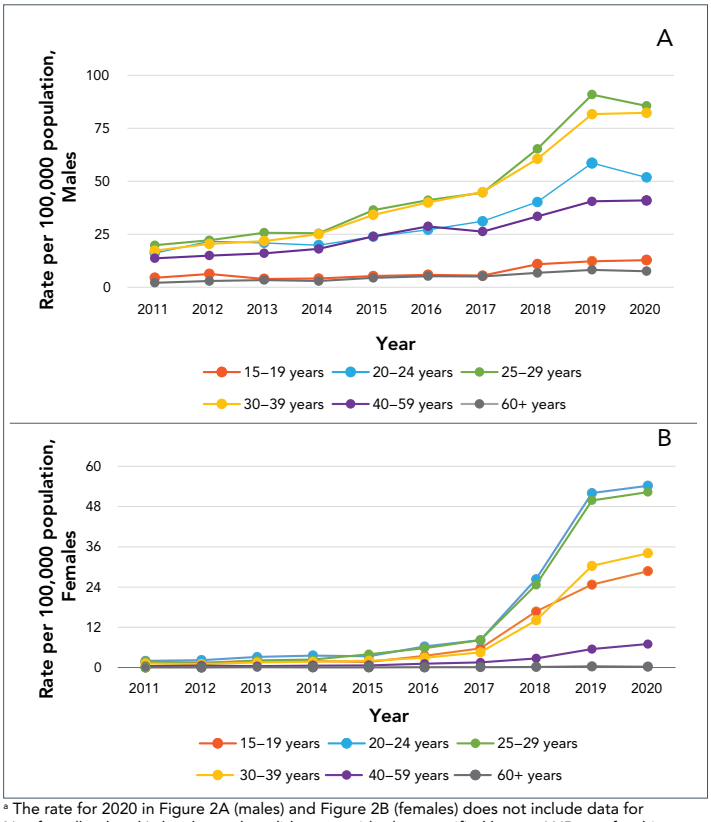
Proportion of infectious syphilis cases still highest among gay, bisexual and other men who have sex with men, but declining

The eight P/Ts that reported male sexual orientation accounted for 71% of all male cases reported in the country in 2020. Based on 2020 data provided by these P/Ts, 38% of all infectious syphilis cases were reported among gay, bisexual and other men who have sex with men (gbMSM), and 25% were reported among heterosexual males. In comparison, in 2018, the same eight P/Ts reported a proportion of 54% of cases identifying as gbMSM and 24% as heterosexual males.

Rates of infectious syphilis increased faster in young adults

Overall, rates of infectious syphilis have been increasing between 2011 and 2019 in almost all age group but remained relatively unchanged from 2019 to 2020 (**Figure 2**). The highest rate in 2020 was observed in those aged 25–29 years (69.8 per 100,000 population).

Figure 2: Rate of infectious syphilis in males and females per 100,000 by age group in Canada, 2011–2020[a,b]



[a] The rate for 2020 in Figure 2A (males) and Figure 2B (females) does not include data for Newfoundland and Labrador as they did not provide data stratified by sex AND age for this year
[b] Note that the scales of Figure 2A and 2B differ

Rates among males were consistently highest in all years (2011–2020) in those aged 25–29 years (85.5 per 100,000 population in 2020), followed closely by those aged 30–39 years (82.3 per 100,000 population in 2020) (Figure 2A).

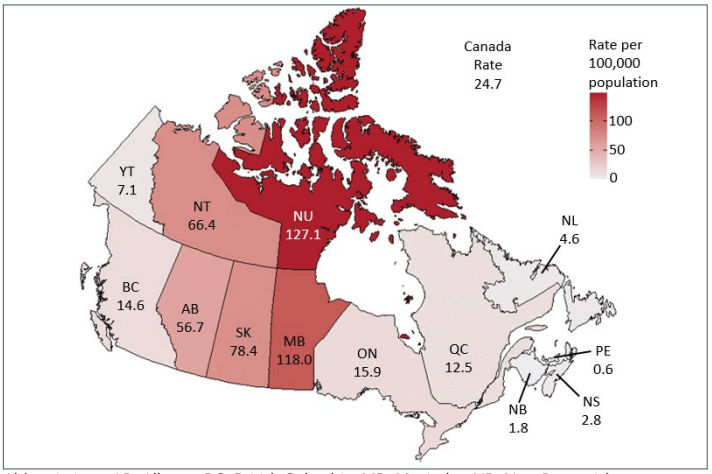
Rates of infectious syphilis in females were highest in younger age groups compared with their male counterparts (Figure 2B). Until 2017, there was a steady increase in rates of infectious syphilis in females, primarily in those aged 15–39 years. In 2018, rates in females in this age range tripled (increasing by over 200% from the previous year). In 2020, the highest rates of infectious syphilis in females were observed in those aged 20–24 years (54.2 per 100,000 population). Although only slightly higher than the rates observed in males (51.8 per 100,000 population), this is the first time in the period of interest (2011–2020) that female rates in this age group have surpassed males. The second highest rate of infectious syphilis among females was reported in females aged 25–29 years (52.3 per 100,000 population).

The proportion of all infectious syphilis cases that was reported in females aged 15–39 years has also increased rapidly. In 2011, 5.2% of all cases were reported in females aged 15–39 years, increasing five-fold to approximately a quarter (26%) of cases in 2020. From 2016 to 2020 (Figure 2B), an 858% increase in rates of infectious syphilis was observed in females aged 15–39 years. In 2020, females aged 15–39 represented 87% of all female cases.

Rates of infectious syphilis are increasing in almost all provinces and territories

In 2011, nine P/Ts reported cases of infectious syphilis, with rates ranging from 1.0 per 100,000 population in Newfoundland and Labrador to 7.8 per 100,000 population in Québec. Since then, there has been a steady rate increase in most P/Ts, with large increases observed in 2017 and 2018. From 2016 to 2020, the Prairie provinces reported the greatest relative increases (more than 400%). In most P/Ts, the highest rates of infectious syphilis reported in the last 10 years occurred in 2019. The P/Ts with the highest rates of infectious syphilis in 2019 were Nunavut (266.7 per 100,000 population), Manitoba (136.7 per 100,000 population), the Northwest Territories (97.7 per 100,000 population), Alberta (51.9 per 100,000 population) and Saskatchewan (33.7 per 100,000 population). Rates declined from 2019 to 2020 in Manitoba, the Northwest Territories and Nunavut but increased in Alberta and Saskatchewan (**Figure 3**).

Figure 3: Rates of reported infectious syphilis cases in Canada, by province and territory, 2020

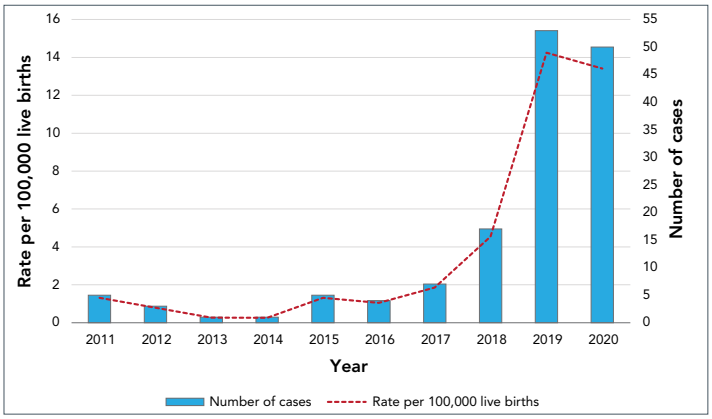


Abbreviations: AB, Alberta; BC, British Columbia; MB, Manitoba; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; NT, Northwest Territories; NU, Nunavut; ON, Ontario; PE, Prince Edward Island; QC, Québec; SK, Saskatchewan; YT, Yukon Territory

Early congenital syphilis cases also on the rise

The reported number of confirmed early congenital syphilis cases has increased over the last 10 years in Canada (**Figure 4**). From 2011 to 2017, 10 or fewer cases of confirmed early congenital syphilis were observed per year. Reported cases of confirmed early congenital syphilis more than doubled between 2017 and 2018, from 7 cases in 2017 to 17 cases in 2018. In 2019 and 2020, total case counts increased to 53 and 50, respectively, corresponding to a rate of 14.2 per 100,000 live births in 2019 and 13.4 per 100,000 live births in 2020.

Figure 4: Number and rate of reported confirmed early congenital syphilis cases per 100,000 live births in Canada, 2011–2020



In 2019, Alberta and Manitoba reported 79% of all confirmed early congenital syphilis cases in Canada, while other P/Ts reported three or fewer congenital cases. In 2020, the majority (86%) of all confirmed early congenital syphilis cases reported were observed in Alberta, Manitoba and Saskatchewan. These P/Ts also had the highest rates of infectious syphilis among females aged 15–39 years.

In the eight P/Ts that submitted data on pregnancy status, there were 230 cases of infectious syphilis reported among pregnant individuals in 2020. The same P/Ts reported 71 cases of infectious syphilis in pregnant individuals in 2018 and 133 cases in 2019.

Discussion

Rates of infectious syphilis in Canada have increased substantially in the past decade and especially since 2017. Similar to the United States (US), the United Kingdom and Australia, the majority of cases (based on partial data) in Canada have occurred among males, especially among gbMSM (10–12). However, while rates in Canada have remained higher among males than females, rates of infectious syphilis among females have risen quickly in recent years. Similar trends have also been observed in other countries. The US, the United Kingdom and Australia have all reported rising rates of infectious syphilis, with rates increasing more than 175% between 2015 and 2019, and rates in females increasing faster than in males (10–12).

The reasons for the ongoing high rates of syphilis among males, and particularly among gbMSM, and the more recent increases among heterosexual populations, remain unclear as data on sexual behaviours and key populations are incomplete in national surveillance. Social and structural determinants of health and health inequities undoubtedly play a crucial role in the inequitable occurrence of syphilis across different populations (1,13). These determinants include housing instability, experiences of violence, lack of access to culturally appropriate care, and experiences of stigma, discrimination and racism, particularly within the healthcare system (1,14–19).

Available evidence from Canada and the US suggests that substance use may potentially help explain the recent trends in syphilis rates. Substance use, including opioids and crystal methamphetamine ("crystal meth"), has become more frequent in recent years (20–23). While the prevalence of crystal meth use is low overall in Canada (less than 1% of the general population and 11 times lower than in the US), its availability, use and related harms have dramatically increased since 2013 (20). Crystal meth use can influence decision-making on safer sex practices (24,25). Among gbMSM, *chemsex*, which is the use of substances (such as crystal meth) to prolong and intensify sexual experiences, has been described as a major trend (24,26,27). Among other behaviours, injection drug use and problematic alcohol use in gbMSM have been shown to increase the risk of syphilis and human immunodeficiency virus coinfection (28–30). Crystal meth use was also reported in a heterosexual outbreak in Winnipeg in 2017–2018 and identified as a driver in 2019 during the syphilis outbreak in Saskatchewan (16,31). Recent data from the US similarly show associations between crystal meth and opioid use and syphilis outbreaks in heterosexual populations (32–34).

In the last 10 years, females aged 15–39 years accounted for an average of 96% of live births in Canada (35). From 2016 to 2020, an almost 10-fold increase in infectious syphilis cases (858%) was reported in females aged 15–39 years, with this group representing 87% of all female syphilis cases in 2020. The increase in infectious syphilis cases among this age cohort of females has led to subsequent increases in congenital syphilis in Canada. Record-high numbers of confirmed early congenital syphilis cases were reported in 2019 and 2020 (at least 50 cases in each year, compared with 10 or fewer cases up until 2017). This is the highest number of confirmed early congenital syphilis cases reported since congenital syphilis became reportable in 1993. The US also experienced a similar situation with 1,870 reported cases of congenital syphilis in 2019, a 291% increase from 2015 (10). Females face unique challenges in early diagnosis due to anatomical or biological differences that may make primary lesions take longer to identify (1). This may play a role in delaying early testing and access to care. It is worth noting that some jurisdictions have changed their clinical practice guidelines around prenatal screening over the past decade, to increase the frequency of testing for syphilis over the course of a pregnancy (36–42). This change in guidelines might have resulted in more consistent and more frequent screening for syphilis—and greater detection of cases—in pregnant individuals, and females of reproductive age in general, compared to males. In addition, US studies indicated that potential factors associated with increasing rates of syphilis during pregnancy and of congenital syphilis included lack of access to prenatal care and missed opportunities for timely and effective treatment of pregnant individuals (43,44).

Various structural barriers, including lower income, insecure housing and rural or remote residence, have been associated with syphilis infection, especially during pregnancy (1,36,45–47). In addition, systemic discrimination, racism and stigmatization in healthcare settings due to substance use may contribute to mistrust of healthcare systems and serve as barriers to care for individuals with syphilis (1,13,43,48,49). At least one province has anecdotally reported more frequent diagnoses of latent stages, indicating missed diagnoses at earlier stages of infection possibly linked to structural barriers to care. Rapid tests that can be performed at the site of patient care, such as point-of-care tests, may play an important role in the control of syphilis in remote or marginalized populations (50,51). However, no point-of-care tests for syphilis diagnosis have been licensed in Canada (1,52).

The rates of infectious syphilis reported in this article may underestimate true rates, as individuals living with the infection may not necessarily access health care or sexually transmitted and bloodborne infections (STBBI) services for testing. This underestimation may especially have occurred during the coronavirus disease 2019 (COVID-19) pandemic as a result of public health measures to control the pandemic limiting access to and provision of STBBI services. As the pandemic was declared in March 2020, the decreases observed in 2020 may not reflect the true incidence. An online survey conducted by PHAC in 2021 indicated that the COVID-19 pandemic has impacted STBBI detection and response (53). The survey reported that the pandemic led to a decrease in demand for and the ability to deliver STBBI prevention, testing and treatment services but an increase in demand for harm-reduction and drug-treatment services (53). The impact of the pandemic on STBBI surveillance has also been reported in other countries, highlighting decreased screening and testing and limited resources, which resulted in underdiagnosis and underreporting (54–56).

Given the disruption in services and reports of increased substance use, the impact of the pandemic on the true incidence of syphilis is yet to be seen. This may be reflected in 2021 and 2022 national surveillance data depending on how the COVID-19 pandemic evolves and its related impact on STBBI screening and testing (53,57). It is important to note that there are limitations in the enhanced national surveillance system, such as incomplete data on variables such as male sexual orientation and substance use (the latter not presented in this article due to high levels of missing data), which are not collected systematically and consistently across jurisdictions. In addition, data collection and research on other social determinants of health including

ethnicity and Indigeneity data would be instrumental in better understanding the epidemics, although data collection on ethno-cultural identity is still controversial. Nonetheless, there is a growing consensus, especially emerging from lessons learned during the COVID-19 pandemic, that disaggregated data are important to better describe epidemics and appropriately target interventions (58–60).

Conclusion

This article provides a national picture of the syphilis epidemic in Canada over the past 10 years and discusses potential factors associated with the considerable recent increases in syphilis rates. Syphilis incidence has surged over time and the nature of epidemics across Canada appear to vary and evolve, with a persisting impact on gbMSM and an increasing number of outbreaks in heterosexual men and women. The number of congenital syphilis cases has also risen significantly. Greater understanding of the social, structural and behavioural factors affecting syphilis could help identify opportunities for interventions using a syndemic approach. More research is needed to understand the full extent of syphilis and its associated determinants in Canada. Such evidence could inform efforts to reduce the health impact of STBBI and to reach the World Health Organization's global target for reducing syphilis incidence by 2030.

Authors' statement

JA — Conceptualization, writing–original draft, writing–review and editing, supervision
CL — Data curation, validation, visualization, data analysis, literature review, writing–original draft, writing–review and editing
AT — Writing–original draft, literature review, writing–review and editing, validation
CI — Data collection and curation, validation, data analysis, literature review, writing–original draft, writing–review and editing
FK — Writing–review and editing
JW — Writing–review and editing
AA — Data collection, writing–review and editing
NP — Conceptualization, writing–review and editing

Competing interests

None.

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Outcomes of infectious syphilis in pregnant patients and maternal factors associated with congenital syphilis diagnosis, Alberta, 2017–2020

Jennifer Gratrix[1], Jennifer Karwacki[1], Lynn Eagle[1], Lindsay Rathjen[1], Ameeta Singh[2], Angel Chu[1,3], Petra Smyczek[1,2]*

Abstract

Background: Congenital syphilis (CS) is a significant public health challenge, requiring early diagnosis and treatment to improve infant outcomes. The aim of this study is to describe public health outcomes of infectious syphilis cases among pregnant patients and factors associated with a CS diagnosis for their infant.

Methods: We conducted a retrospective review of demographic and clinical characteristics of infectious syphilis cases diagnosed during pregnancy and resulting infant outcomes in Alberta from 2017 to 2020 from the provincial communicable disease database. Adequate maternal treatment was defined as receiving at least one dose of Benzathine penicillin G-LA 2.4 million units IM at least 28 days before delivery. Univariate and multivariate analysis was performed to determine factors associated with CS diagnosis using SPSS version 25.

Results: A total of 374 cases of infectious syphilis were diagnosed in pregnancy, with two patients being diagnosed twice in a single pregnancy. The majority (79.1%; n=296) of women had a live birth, followed by therapeutic abortion (9.4%; n=35), stillbirth (7.5%; n=28) and spontaneous abortion (4.0%; n=15). Infant records (n=265) were available for review (n=117 CS cases and 148 non-cases). Correlates associated with CS were screening time in third trimester (adjusted odds ratio [AOR] 8.4, 95% confidence interval [CI], 2.9–24.6) and fewer than 28 days before delivery (AOR 8.1, 1.4–47.8 [vs. first and second trimester] and inadequate treatment (AOR 86.1, CI, 15.9–466.5). Among the CS cases, 23.1% (n=27) were stillborn compared with one (0.7%) stillbirth in the non-CS infants (p<0.001).

Conclusion: The early identification and treatment of syphilis in pregnancy is crucial to preventing poor infant outcomes.

Affiliations

[1] Sexually Transmitted Infections (STI) Services, Alberta Health Services, Edmonton, AB

[2] Department of Medicine, University of Alberta, Edmonton, AB

[3] Department of Medicine, Cumming School of Medicine, Calgary, AB

***Correspondence:**
petra.smyczek@albertahealthservices.ca

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Introduction

Congenital syphilis (CS) is a worldwide public health challenge and reflects the incidence of infectious syphilis in the heterosexual female population (1). Untreated syphilis during pregnancy can profoundly affect pregnancy outcomes, resulting in spontaneous abortion, stillbirth, perinatal death and serious sequelae in infected infants.

The World Health Organization has set global targets for 2030 to reduce the incidence of syphilis by 90% and to reduce CS to 50 or fewer cases per 100,000 live births in 80% of countries (2). The estimated global CS rate in 2016 was 473 (range=385–561) per 100,000 live births and 661,000 (range=538,000–784,000) total CS cases (3).

A provincial syphilis outbreak was declared in Alberta in 2016, after rates of infection doubled from 3.9/100,000 in 2014 to 8.8/100,000 in 2015 and have climbed to 56.7/100,000 in 2020. During this time, the rate among women has increased 90-fold

from 0.6/100,000 in 2014 to 49.6/100,000 in 2020 (4). The proportion of pregnant cases climbed from 0% in 2014 to 15% in 2020 (*unpublished data*). From 2012 to 2016, only a single CS case had been reported compared with 121 CS cases reported from 2017 to 2020, with 45 and 56 cases diagnosed in 2019 and 2020, respectively (4). Twenty-eight infants were stillborn during this time.

The aim of this study is to describe the epidemiology of infectious syphilis cases diagnosed during pregnancy and to report pregnancy and neonatal outcomes.

Methods

A retrospective review was conducted of demographic and clinical characteristics of infectious syphilis cases diagnosed during pregnancy and resulting pregnancy and neonatal outcomes in Alberta (current population 4.3 million) from 2017 to 2020. In Alberta, prenatal syphilis screening is universally recommended during the first trimester, at delivery, and throughout pregnancy for those with ongoing risk (5,6). All cases of syphilis are reportable by laboratories and clinicians to the provincial sexually transmitted infections (STI) program that is responsible for ensuring adequate treatment and partner notification of all confirmed cases. Partner notification nurses (PNN) act as case managers for patients by collaborating with the patient, the testing and treating healthcare providers, and the STI medical consultant to facilitate appropriate assessment, treatment and follow-up of patients and their sexual partners. All patients are assessed for pregnancy through patient or healthcare provider interviews by the PNN. For pregnant patients, the PNN also coordinates care with the delivery site to ensure serology at delivery and appropriate follow-up of infants.

Sexually transmitted infections medical consultants completed maternal staging of syphilis according to provincial case definitions (7) and reviewed infants for possible diagnoses with CS.

De-identified data were extracted from the provincial communicable disease database on June 25, 2021; mothers and infants were linked by unique record numbers. Variables extracted for each syphilis case included demographic, behavioural and clinical factors. Ethnicity, history of transactional sex, injection drug use (IDU), sex with a person who injects drugs (PWID) were self-reported during PNN interviews as part of routine public health follow-up and reporting requirements. A symptom inquiry for sores, rashes, lesions and neurological signs was completed through client self-report or by the healthcare provider. Correctional involvement included any case where the patient was initially diagnosed or treated in a correctional facility. Alberta is split into five geographic zones and these zones were assigned based on the patient's postal code. Healthcare proximity was defined based on population density and travel times to health services: metro/urban (municipalities with a population density of at least 20,000 per km2 and their adjacent communities with a tertiary or regional hospital); rural (population density between 100–10,000 per km2); and rural remote (population density fewer than 100 per km2 and more than 200 km to a regional centre). Public health contact was defined as patients contacted by PNN versus patients who PNN were unable to contact. Screening time was the difference between the delivery date and the collection date of the first positive specimen and then stratified into three categories: first and second trimester (at least 91 days); third trimester (28–90 days), and fewer than 28 days prior to delivery as this timing was insufficient for adequate treatment. Adequate maternal treatment was defined as receiving at least one dose of Benzathine penicillin G-LA 2.4 million units IM or aqueous crystalline penicillin G 18-24 million units per day for at least 10 days and more than 28 days before delivery. Time to treatment was calculated from the date of the first positive test result to the initial dose of medication. For birth outcomes, stillbirth was defined as a fetal death after 20 weeks gestation and spontaneous abortion was fetal demise at or before 20 weeks gestation.

Descriptive analyses were completed for IDU, sex with a PWID and transactional sex; however, due to large proportions of missing data (25%–31%), these variables were excluded from additional analysis. To identify factors associated with CS, analyses were performed by comparing CS and non-CS cases. Univariate analyses were performed using Chi-square or Fisher's exact test for categorical variables and Mann-Whitney tests for continuous variables, excluding missing data. To identify independent factors associated with CS, multivariable logistic regression was performed. All variables significant at $p \leq 0.10$ at the univariate level were assessed for multicollinearity. The number of days to treatment and adequate treatment were found to be highly correlated, so number of days to treatment was not included in model building. Models were built using all significant variables and forward step-wise approach was found to have the best Hosmer-Lemeshow Goodness-of-Fit score. Analyses were completed using IBM SPSS Statistics 19 (IBM, Armonk, New York, United States).

Results

A total of 374 cases of infectious syphilis were diagnosed in pregnancy between January 1, 2017 and December 31, 2020, with two patients being reinfected during the same pregnancy. The majority of cases self-reported First Nations ethnicity, resided in the Edmonton zone, were from a metropolitan/urban area, were diagnosed with early latent syphilis, were contacted by a PNN, and had a live birth. All cases were HIV-negative. A significant proportion of women reported IDU (21.0%; n=58/276), sex with a PWID (18.1%; n=47/259), and transactional sex (11.0%; n=31/281); however, these variables had high proportions of missing data (**Table 1**).

Table 1: Maternal characteristics of infectious syphilis cases among pregnant patients in Alberta, 2017–2020 (N=374)

Characteristics	N=374	%[a]
Median age at diagnosis (years, IQR)	26	22–30
Ethnicity		
White	58	15.5
First Nations	228	61.0
Métis	36	9.6
Other	6	1.6
Unknown/missing	46	12.3
Correctional facility		
No	342	91.4
Yes	32	8.6
Geographic zone		
South	2	0.5
Calgary	16	4.3
Central	30	8.0
Edmonton	217	58.0
North	109	29.1
Healthcare proximity		
Metro/urban	229	61.2
Rural	103	27.5
Rural remote	42	11.2
Diagnosis year		
2017	15	4.0
2018	66	17.6
2019	145	38.8
2020	148	39.6
Public health contact		
Client contacted	325	86.9
Unable to contact	49	13.1
Syphilis stage		
Primary	114	30.5
Secondary	21	5.6
Early latent	238	63.6
Early neurosyphilis	1	0.3
Median days to treatment[b] (IQR)	6	3–13
Birth outcome		
Live birth	296	79.1
Stillbirth	28	7.5
Spontaneous abortion	15	4.0
Therapeutic abortion	35	9.4

Abbreviation: IQR, interquartile range
[a] This table represents 374 cases of infectious syphilis among 372 pregnancies: two patients were reinfected during the same pregnancy
[b] Five cases had no treatment record at time of diagnosis

Of the 324 cases with a live birth or stillbirth, infant records were available for all but three cases. Seven sets of twins were born, resulting in a total of 328 infant records for review. Nearly one-third (35.7%; n=117) of the infants were diagnosed with CS, 45.1% (n=148) of infants did not meet CS case definitions (non-CS) and 19.2% (n=63) of infants remain unstaged and are continuing follow-up. Maternal characteristics associated with CS in univariate analysis were no contact with PNN, having two or more partners in the last year, screening time in third trimester or fewer than 28 days before delivery, and not receiving adequate treatment (**Table 2** and **Table 3**). Of the total 265 cases, one-third (35.8%; n=95) of cases were screened less than a month before delivery, with many of these (25.3%; n=67) being within two days of delivery. The majority (61.1%; n=162) of patients received adequate treatment for the prevention of CS; 161 patients received Benzathine penicillin G-LA 2.4 million units IM at least 28 days prior to delivery and one patient received aqueous crystalline penicillin G 24 million units per day for 14 days. The remaining 39.2% (n=104) of patients were not treated adequately. One-quarter (24.5%; n=65) of patients were treated with at least a single dose of Benzathine penicillin G-LA 2.4 million units IM at or post-delivery, 11.3% (n=30) were treated 1–27 days prior to delivery, two (0.8%) cases received doxycycline 100 mg b.i.d. for 14 days post-delivery, and one case received insufficient treatment with aqueous crystalline penicillin G 5 million units intravenously in a single dose post-delivery. An additional five cases (1.9%) had no treatment record at the time of analysis. Correlates that remained independently associated with CS upon multivariable analysis were screening time in third trimester (adjusted odds ratio [AOR] 8.4, 95% confidence interval [CI], 2.9–24.6) and fewer than 28 days before delivery (AOR 8.1, 1.4–47.8 [vs. first and second trimester], and inadequate treatment (AOR 86.1, CI, 15.9–466.5). Among the CS cases, 23.1% (n=27/117) were stillborn compared with one (0.7%) stillbirth in the non-CS infants ($p<0.001$). Despite diagnosis during the first and second trimester of nine CS cases, four cases were treated within fewer than 28 days before delivery. Of the 237 live births, all CS cases received treatment. Thirty (20.4%) of the non-CS cases also received treatment; these cases did not meet Alberta case definition for CS (8) but were treated at the time of delivery based on clinical judgement and maternal history known at the time of admission after assessment by paediatric Infectious Diseases specialists.

Table 2: Univariate analysis of maternal characteristics associated with infant outcomes from infectious syphilis cases among pregnant patients in Alberta, 2017–2020 (N=265)

Maternal characteristics	Congenital		Non-cases		Total		*p*-value	Unadjusted OR	
	(n=117)	%	(n=148)	%	(N=265)	%		Rate	95% CI
Median age at diagnosis (years, IQR)	27	23–31	26	21–30	26	22–31	0.18	1.0	1.0–1.1
Ethnicity									
White	17	14.5	24	16.2	41	15.5	0.37	Ref	Ref
First Nations	71	60.7	96	64.9	167	63.0	-	1.0	0.5–2.1
Métis	13	11.1	7	4.7	20	7.5	-	2.6	0.9–8.0
Other	1	0.9	3	2.0	4	1.5	-	0.5	0.1–4.9
Unknown/missing	15	12.8	18	12.2	33	12.5	-	1.2	0.5–3.0
Correctional facility									
No	107	91.5	133	89.9	240	90.6	0.66	Ref	Ref
Yes	10	8.5	15	10.1	25	9.4	-	0.8	0.4–1.9
Geographic zone									
Calgary	4	3.4	5	3.4	9	3.4	0.05	Ref	Ref
Central	16	13.7	6	4.1	22	8.3	-	3.3	0.7–16.7
Edmonton	63	53.8	90	60.8	153	57.7	-	0.9	0.2–3.4
North	34	29.1	47	31.8	81	30.6	-	0.9	0.2–3.6
Healthcare proximity									
Metro/urban	65	55.6	93	62.8	158	59.6	0.09	Ref	Ref
Rural	39	33.3	32	21.6	71	26.8	-	1.7	1.0–3.1
Rural remote	13	11.1	23	15.5	36	13.6	-	0.8	0.4–1.7
Diagnosis year									
2017	5	4.3	9	6.1	14	5.3	0.01	1.6	1.2–2.1
2018	16	13.7	43	29.1	59	22.3	-	-	-
2019	44	37.6	52	35.1	96	36.2	-	-	-
2020	52	44.4	44	29.7	96	36.2	-	-	-
Public health contact									
Client contacted	89	76.1	136	91.9	225	84.9	<0.001	Ref	Ref
Unable to contact	28	23.9	12	8.1	40	15.1	-	3.6	1.7–7.4
Symptoms[a]									
No	49	48.0	64	44.8	113	46.1	0.61	Ref	Ref
Yes	53	52.0	79	55.2	132	53.9	-	0.9	0.5–1.5
Number of partners in last 12 months									
Fewer than 2	21	17.9	10	6.8	31	11.7	0.005	Ref	Ref
At least 2	96	82.1	138	93.2	234	88.3	-	0.3	0.2–0.7
Maternal syphilis stage									
Primary	34	29.1	43	29.1	77	29.1	1.00	1.0	0.6–1.7
Secondary	8	6.8	9	6.1	17	6.4	-	1.1	0.4–3.2
Early latent	75	64.1	95	64.2	170	64.2	-	Ref	Ref
Early neurosyphilis	0	0	1	0.7	1	0.4	-	-	0 cell precluded regression analysis
Median days to treatment[b]	5	2.0–8.5	6	3.0–10.0	6	3.0–10.0	0.03	1.0	0.999–1.01

Table 2: Univariate analysis of maternal characteristics associated with infant outcomes from infectious syphilis cases among pregnant patients in Alberta, 2017–2020 (N=265) (*continued*)

Maternal characteristics	Congenital		Non-cases		Total		*p*-value	Unadjusted OR	
	(n=117)	%	(n=148)	%	(N=265)	%		Rate	95% CI
Screening time									
First to second trimester	9	7.7	111	75.0	120	45.3	<0.001	Ref	Ref
Third trimester	18	15.4	32	21.6	50	18.9	-	6.9	2.8–16.9
At least 28 days from delivery	90	76.9	5	3.4	95	35.8	-	222	71.9–685.9
Adequate treatment									
No	99	84.6	4	2.7	103	38.9	<0.001	198.0	65.0–602.7
Yes	18	15.4	144	97.3	162	61.1	-	Ref	Ref

Abbreviations: CI, confidence interval; IQR, interquartile range; OR, odds ratio; Ref, reference; -, no applicable
[a] Excludes 20 cases with missing data
[b] Excludes six cases with missing treatment date

Table 3: Multivariate analysis of maternal characteristics associated with infant outcomes from infectious syphilis cases among pregnant patients in Alberta, 2017–2020 (N=265)

Maternal characteristics	Adjusted OR	95% CI	*p*-value
Screening time			
First to second trimester	Ref	-	-
Third trimester	8.4	2.9–24.6	<0.001
At least 28 days from delivery	8.1	1.4–47.8	0.02
Adequate treatment			
Yes	Ref	-	-
No	86.1	15.9–466.5	<0.001

Abbreviations: CI, confidence interval; OR, odds ratio; Ref, reference; -, no applicable

Discussion

In Canada, the rates of infectious syphilis have been increasing sharply in the past five years; particularly alarming is an increase of infectious cases by 740% among females between 2016 and 2020 (8). Similar epidemiological trends have been seen in the United States with nearly 2,100 cases of CS in 2020 (9). Since the current syphilis outbreak started in 2015, Alberta has seen an unprecedented number of infectious syphilis cases among pregnant women resulting in CS cases and stillbirths. Inadequate maternal treatment was the most important predictor for a diagnosis of CS in our study. Several factors contributed to inadequate treatment during pregnancy. Firstly, the odds of giving birth to an infant with CS were eight times higher among patients screened in the third trimester and for patients screened in the last month of pregnancy as the late diagnosis leaves inadequate time for treatment. Furthermore, four of the nine CS cases with maternal screening during the first and second trimesters did not receive treatment four weeks prior to delivery due to barriers to care. Our findings are similar to those in a recent study on maternal syphilis treatment that showed that no pregnant patient with treatment in the first trimester delivered a neonatal CS case. Patients who initiated treatment in the third trimester had an increased risk of stillbirth, preterm birth and low birth weight (10). Another study examining the determinants associated with CS and adverse pregnancy outcomes found that every week of delay in treatment was related to 2.82-fold increased risk for adverse pregnancy outcomes (11).

While screening in the first trimester and at mid-gestation aims at preventing CS, the goal of screening at delivery is early diagnosis and treatment of infants born to mothers with infectious syphilis. A cost effectiveness analysis in the United States in 2018 found that repeat screening in the third trimester is superior to single screening during the first trimester and is both cost-effective and results in improvement in maternal and neonatal outcomes (12). During the last infectious syphilis outbreak in Alberta in the mid-2000s, universal mid-gestation screening was introduced but, after a review of the Alberta prenatal screening program, it was discontinued in 2012 due to low uptake and limited utility for the diagnosis of additional new syphilis infections (13), although syphilis rates were lower at that time. Canadian and United States Centers for Disease Control and Prevention (CDC) syphilis screening guidelines recommend screening in the first trimester or at the first prenatal visit and repeat screening at 28–32 weeks' gestation and again at delivery for patients in areas with high rates of syphilis and for women at ongoing risk for syphilis acquisition (14,15). Our study results support current Alberta syphilis screening guidelines for pregnant patients recommending universal maternal screening in the first trimester, at delivery (5,6) and rescreening for those at ongoing risk. The majority of the mothers interviewed reported multiple partners in the last year and more than one-half reported symptoms, thereby meeting current recommendations for rescreening during pregnancy. Despite meeting current provincial screening recommendations for being at risk and requiring frequent re-screening throughout pregnancy, we found a high number of patients with an initial screen late in pregnancy (one-quarter within two days of delivery) and two cases of reinfection during the same pregnancy. We believe that frequent

testing and re-testing of pregnant women up to monthly after an initial negative test result but who are at ongoing risk is an important tool to prevent further newborn syphilis cases. Increasing overall knowledge on syphilis and awareness of existing screening guidelines among medical providers are important steps to improve health outcomes of pregnant women and their infants. Opportunistic screening when women at risk present to healthcare for non-pregnancy related causes can lead to earlier diagnosis and treatment thereby reducing morbidity and mortality related to CS. Use of point of care testing and symptomatic syphilis treatment should be considered for women at risk for being lost to follow up. Offering screening to women in non-traditional care settings, such as addiction treatment centers, correctional facilities or emergency room departments, can further increase screening among women otherwise not engaging in prenatal care. The high proportion of cases in our study diagnosed in the third trimester underlines the need for non-traditional approaches for testing and treatment, as many patients who access services late in pregnancy are affected by adverse social determinants of health including poverty and mental health and addictions issues. In addition, a significant proportion of patients were Indigenous, demonstrating the need for culturally appropriate services. In response to the mid-2000s resurgence of infectious syphilis in Alberta, an outreach team in Edmonton geographical zone expanded to include registered nurses with the team of Indigenous community health representatives; offering culturally appropriate care. Outreach services can be a valuable strategy in reaching persons at risk for STIs since services are delivered to populations that would not normally be aware of or able to access services due to their life circumstances (16). Previous evaluations of outreach services in Edmonton, including the use of incentives, have highlighted the utility of these services in identifying new cases (17).

Nurse case management has been found to increase linkage to care and improve patient outcomes (18,19). In our study population, patients without public health contact had worse outcomes with a 3.6-fold increased risk of giving birth to an infant with CS. Overall, the median time from first specimen collection to initiating treatment was six days and only five cases remained untreated. We hypothesize that our treatment success is related to the case management role that PNNs play in client engagement and prioritization of pregnant patients and their sexual contacts.

Limitations

This is the first Canadian study describing outcomes of infants born to patients with infectious syphilis during pregnancy. One possible limitation of our study is that our reported cases may underestimate the number of pregnant patients with syphilis, especially with the reduction of health services and patients choosing not to access care during the coronavirus disease 2019 pandemic, as well as cases that PNNs were unable to contact. Additionally, since we used retrospective data collected for surveillance purposes, data on behavioural characteristics, like IDU and transactional sex, was missing in a significant proportion of our study population, which may be related to underlying stigma and social desirability bias, and therefore underestimate their impact.

Conclusion

Our study shows that early identification of syphilis in pregnancy through adherence to prenatal screening guidelines and a strong public health program to link patients to timely care are key in the prevention of CS cases. As syphilis rates increase and infections spread to rural and remote areas with limited access to health and social programs, it is imperative that sufficient resources for public health follow-up are available to facilitate the engagement of patients in care. In addition, a review of current screening practices in combination with increased awareness not only among members of the healthcare team but also in the general public may be required to respond to the changing epidemiology of syphilis, particularly to the increased prevalence of syphilis in young heterosexual populations. Lastly, we need to continue to engage with and work with affected communities to deliver services in a culturally and societally appropriate way.

Authors' statement

JG — Contributed to the concept of this report, performed statistical analysis, contributed to acquisition of data, contributed to interpretation of data, revising the manuscript critically for important intellectual content, and approved the final version
PS — Contributed to the concept of this report, drafted the initial manuscript, contributed to interpretation of data, revising the manuscript critically for important intellectual content, and approved the final version
JK — Contributed to acquisition of data
LE, LB, AES, AC — Contributed to interpretation of data, revising the manuscript critically for important intellectual content, and approved the final version

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Competing interests

None.

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Characterizing female infectious syphilis cases in British Columbia to identify opportunities for optimization of care

Kaylie Willemsma[1]*, Lindsay Barton[2], Rochelle Stimpson[2], Irene Pickell[2], Venessa Ryan[2], Amanda Yu[2], Ann Pederson[1,3], Gina Ogilvie[1,2,3], Troy Grennan[1,2], Jason Wong[1,2]

Abstract

Introduction: The rate of infectious syphilis continues to increase among females in British Columbia (BC) and Canada, raising concerns of increased incidence of congenital syphilis. We characterized syphilis cases among females in BC to identify opportunities to prevent syphilis and optimize its care.

Methods: All cases of infectious syphilis diagnosed in BC between March 13, 2018 and December 31, 2020 and reported as female gender were reviewed. Demographics, risk factors and concurrent conditions were collected from a provincial surveillance system. Subgroup analyses comparing cases with and without housing instability, substance use, mental illness and a recent sexually transmitted infection (STI) were conducted to understand differences between these subgroups. Statistical associations were calculated using chi–square or t-tests.

Results: There were 226 reported cases of female infectious syphilis in BC during this period: 38 (16.8%) in 2018; 74 (32.7%) in 2019; and 114 (50.4%) in 2020. Mean age was 32 years (range 15–75 years). Of those who reported concurrent conditions, most cases had experiences with housing instability (71.1%), substance use (68.2%) and mental illness (83.9%), while 42.9% had a recent STI. Cases who reported housing instability or substance use were significantly more likely to have experiences with a recent STI, street involvement, transactional sex, mental illness and income assistance (all $p<0.01$).

Conclusion: Our findings highlight the importance of fostering an enabling environment for syphilis care. Concurrent services to support individuals with syphilis as well as housing instability, substance use and mental illness, may help prevent syphilis and improve wellbeing.

Affiliations

[1] Faculty of Medicine, University of British Columbia, Vancouver, BC

[2] BC Centre for Disease Control, Vancouver, BC

[3] BC Women's Hospital, Vancouver, BC

***Correspondence:**
kaywill@student.ubc.ca

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Keywords: female infectious syphilis, sexually transmitted infections, syndemics, social determinants of health, substance use, housing instability, Canada

Introduction

Rates of infectious syphilis have been increasing in British Columbia (BC) and across Canada. While infectious syphilis disproportionately affects gay, bisexual and other men who have sex with men (gbMSM), an increasing number of cases are being reported among the female and heterosexual populations, raising concern of increased incidence of congenital syphilis. From 2016 to 2020, the rates of female infectious syphilis increased by 740% in Canada (1). Currently, one in three cases of infectious syphilis in Canada was among females (1).

Concurrently, there has been an increase in congenital syphilis cases nationally, from four cases in 2016 to 50 cases in 2020 (1).

In BC, the rate of infectious syphilis increased 138% among females from 2018 to 2020 (2). The male-to-female ratio of cases of infectious syphilis in BC decreased from 15.9 in 2018 to 6.7 in 2020 (2). Of note, the number of infectious syphilis cases reported in 2020 may be an underestimate due to reduced access to healthcare services and concerns related to coronavirus

disease 2019 (COVID-19) (3). British Columbia reported three cases of early congenital syphilis in 2019; the first cases reported in six years (4). In response, the BC Centre for Disease Control (BCCDC) sought to update its provincial Syphilis Action Plan (5), with an added focus on the prevention of syphilis and related complications among females.

To inform the refresh of the Syphilis Action Plan, the BCCDC led consultations with stakeholders based on the pillars described in the *Pan-Canadian Sexually Transmitted and Blood-Borne Infections (STBBI) Framework for Action* (6,7). The consultations emphasized the need for a syndemics approach to address syphilis (7,8). Syndemics theory postulates that health problems tend to co-occur, are synergistic, and combine to exacerbate the health burden among marginalized populations (8). In particular, the consultations highlighted the need to address concurrent conditions, including housing instability, substance use and mental illness, as well as system factors such as relationship with a healthcare provider as part of the provincial syphilis response (6,7). To better understand the prevalence of these concurrent conditions and risk factors and to identify opportunities to optimize care for females affected by syphilis, we reviewed all cases of infectious syphilis among females reported in BC.

Methods

Context

Clinicians at the BCCDC conducted and/or coordinated case and partner management with testing providers for all infectious syphilis cases diagnosed in BC to ensure appropriate testing, treatment and follow-up. Since March 13, 2018, all case and partner information have been entered into the provincial Intrahealth Profile electronic medical record (EMR) systems.

Inclusion criteria

This descriptive study involved a retrospective chart review of all female cases of infectious syphilis (i.e. primary, secondary or early latent stage) diagnosed in BC from March 13, 2018 to December 31, 2020. Case definitions for the infectious stages of syphilis are available on the BCCDC website (9).

Data sources

Cases of female infectious syphilis were identified through the Intrahealth Profile EMR system. Details of the cases, including demographics, risk factors and concurrent conditions, were collected through both the EMR system and the CareConnect system. CareConnect is an integrated viewer of clinical information from across BC, including clinical encounters and laboratory information (10).

Variables of interest

Geography was based on health authority boundaries in BC (11). Urbanity was defined as living in a metropolitan area with a population of more than 500,000.

The setting for syphilis testing was determined using the address of the ordering physician and classified as 1) community settings (including family practice, specialist and walk-in clinics), 2) hospital settings (including in-patient, out-patient and emergency departments) or 3) outreach settings (including clinics focused on caring for people living with human immunodeficiency virus [HIV], substance use, and/or mental illness).

The narrative notes were reviewed to understand the reason for testing that resulted in the syphilis diagnosis. Reason for testing was classified as 1) contact to a sexually transmitted infection (STI), 2) immigration medical examination, 3) incidental, 4) prenatal or at delivery, 5) routine screen or 6) symptomatic.

A recent STI was defined as a diagnosis of chlamydia, gonorrhea or syphilis in the five years prior to the syphilis diagnosis date.

Concurrent conditions (e.g. housing instability, street involvement, substance use and mental illness) were based on documentation of the condition in the clinical notes or as a diagnosis in the EMR with an International Classification of Diseases code. For simplicity, mental illness was categorized as yes/no. The types of substances used and housing status at the time of diagnosis were also collected when documented.

The number of partners included all those reported during the infectious period of syphilis. Partner notification was considered complete if syphilis clinicians were able to inform all partners or made all reasonable attempts to do so, or if the case indicated they would inform their partners themselves. Connection to a primary care provider was based on evidence of repeated visits and testing from the same provider.

Postal codes were used to estimate socioeconomic status using Statistics Canada's Canadian Index of Multiple Deprivation quintiles in four domains: 1) ethno-cultural composition; 2) situational vulnerability; 3) economic dependency; and 4) residential instability (12). If the client had no fixed address or an unknown postal code, the postal code of the ordering physician was used instead.

Statistical analyses

Descriptive analyses were conducted on the full cohort of female infectious syphilis cases, with further sub-analysis done on the maternal cases. Chi-square or t-tests were conducted on four subgroups: 1) housing instability; 2) substance use; 3) mental illness; and 4) a recent STI to explore associations between concurrent conditions. These subgroups were chosen because of their known association with syphilis and potentiality for prevention of syphilis, as described in the Pan-Canadian STBBI Framework and BC's Syphilis Action Plan (5–7). Statistical significance was defined as $p<0.01$.

Ethics

This study was undertaken to support syphilis surveillance and prevention efforts which are under BCCDC's public health mandate; thus, ethics approval was not required.

Results

In BC, there were 226 reported female cases of infectious syphilis between March 13, 2018 and December 31, 2020. The number of cases increased from 38 (16.8%) in 2018 to 74 (32.7%) in 2019 and 114 (50.4%) 2020. The mean number of cases per month was 4.0, 6.2 and 9.5 for 2018, 2019 and 2020, respectively. Mean age at diagnosis was 32 years (range 15–75 years). Cases were distributed across BC, with over half residing in BC's two most populated health authorities (i.e. Vancouver Coastal Health and Fraser Health Authority). Over two-thirds were diagnosed in the early latent stage of infection (**Table 1**).

Table 1: Descriptive statistics of female infectious syphilis cases

Variables	n	%
Age (years) (n=226)		
Mean	32.5	N/A
Median	30.9	N/A
Min	15.5	N/A
Max	75.4	N/A
Age categories (n=226)		
Younger than 20 years	18	8.0%
20–30 years	81	35.8%
30–40 years	92	40.7%
40–50 years	16	7.1%
Older than 50 years	19	8.4%
Year—total (n=226)		
2018[a]	38	16.8%
2019	74	32.7%
2020	114	50.4%
Year—mean cases per month (n=226)		
2018[a]	4.0	N/A
2019	6.2	N/A
2020	9.5	N/A
Health Authority (n=223)		
Northern	9	4.0%
Interior	24	10.8%
Vancouver Island	59	26.5%
Fraser	61	27.4%
Vancouver Coastal	70	31.4%
Urbanity (n=213)		
Metropolitan	106	49.8%
Non-metropolitan	107	50.2%
Ethnicity (n=92)		
White	31	33.7%
Non-white	61	66.3%
Stage (n=226)		
Primary	22	9.7%
Secondary	49	21.7%
Early latent	155	68.6%
Pregnancy (n=116)		
Yes	24	20.7%
No	92	79.3%
Diagnosis setting (n=148)		
Community	71	48.0%
Hospital	28	18.9%
Outreach	49	33.1%
Reason for testing (n=217)		
Contact to STI	34	15.7%
Immigration medical examination	5	2.3%
Incidental	22	10.1%
Prenatal or at delivery	23	10.6%
Routine screen	60	27.7%
Symptomatic	73	33.6%
Recent STI (n=198)		
Yes	85	42.9%
No	113	57.1%
HIV positive (n=198)		
Yes	8	4.0%
No	190	96.0%
Housing (n=97)		
Stable	28	28.9%
Not stable	69	71.1%
No fixed address	43	44.3%
Single room occupancy/hotel	15	15.5%
Modular/subsidized	7	7.2%
Shelter	4	4.1%
Street involved (n=89)		
Yes	64	71.9%
No	25	28.1%
Transactional sex (n=42)		
Yes	26	61.9%
No	16	38.1%
Substance use (n=157)		
No	50	31.9%
Yes	107	68.2%
Alcohol	10	6.4%

Table 1: Descriptive statistics of female infectious syphilis cases (*continued*)

Variables	n	%
Substance use (n=157) (*continued*)		
Stimulants	17	10.8%
Opioids	3	1.9%
Benzodiazepines	1	0.6%
Polysubstance	76	48.4%
Mental illness (n=87)		
Yes	73	83.9%
No	14	16.1%
Income assistance (n=59)		
Yes	39	66.1%
No	20	33.9%
History of incarceration (n=20)		
Yes	17	85.0%
No	3	15.0%
Gender of partners (n=199)		
Female only	2	1.0%
Male only	191	96.0%
Male and female	6	3.0%
Number of partners (n=188)		
Mean	2.6	N/A
0	8	4.3%
1	94	50.0%
2–5	75	39.9%
6 or more	11	5.8%
Partner notification completion (n=217)		
Yes	146	67.3%
No	71	32.7%
Connected to primary care provider (n=220)		
Yes	176	80.0%
No	44	20.0%

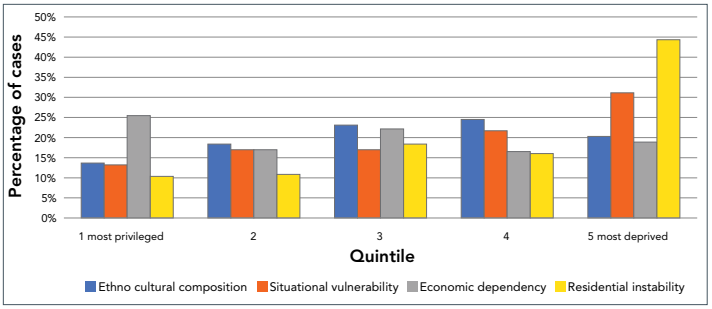
Abbreviations: HIV, human immunodeficiency virus; N/A, not applicable; STI, sexually transmitted infection
[a] Data from March 13 to December 31, 2018

The most common setting of diagnosis was community (n=71/148, 48.0%) followed by outreach (n=49/148, 33.1%) and hospital (28/148, 18.9%). The most common reason for testing was the presentation of symptoms consistent with syphilis (n=73/217, 33.6%), followed by routine screening (n=60/217, 27.7%) and due to notification of exposure to an STI (n=34/217, 15.7%). Prenatal/at delivery screening for syphilis was the reason for diagnosis in about 10% of cases (n=23/217). Eight cases were co-infected with HIV, representing 4.0% of the 198 cases with known HIV status. On average, each case had 2.6 previous partners. Most cases completed the partner notification process (n=146/217, 67.3%) and were connected to a primary care provider (n=176/220, 80.0%) (Table 1).

Among cases where concurrent conditions were reported, 42.9% (n=85/198) had a recent STI and the majority had experiences with housing instability (n=69/97, 71.1%), street involvement (n=64/89, 71.9%), transactional sex (n=26/42, 61.9%), substance use (n=107/157, 68.2%), mental illness (n=73/87, 83.9%) and income assistance (n=39/59, 66.1%). Additionally, 17 cases reported a history of incarceration, which represented 85.0% (n=17/20) of those with known incarceration history, or 7.5% (n=17/226) of all cases (Table 1).

Over half the cases were in the two lowest quintiles for situational vulnerability and residential instability (52.8% and 60.3%, respectively), of Statistics Canada's Canadian Index of Multiple Deprivation Quintiles. The ethno-cultural and economic dependency composition quintiles were more evenly distributed (**Figure 1**).

Figure 1: Statistics Canada's Canadian Index of Multiple Deprivation Quintiles (n=212)[a]



[a] This population-level data is based on the 2016 Canadian census, the definitions of each index and factors considered to classify postal code into the quintiles of privilege-deprivation is available from: https://www150.statcan.gc.ca/n1/pub/45-20-0001/452000012019002-eng.htm

There were 24 cases of maternal infectious syphilis, representing 20.7% of the 116 cases of those with known pregnancy status. Mean age was 30 years (range 23–41 years). Nearly half (n=11/23, 47.8%) resided in a metropolitan area. Over 90% were diagnosed in the early latent stage of infection. With regard to concurrent conditions, many maternal cases of syphilis had a recent STI (n=8/21, 38.1%) and had experiences with housing instability (n=7/17, 41.2%), street involvement (n=7/12, 58.3%), substance use (n=10/17, 58.8%) and mental illness (n=6/9, 66.7%) (**Annex Table A1**).

Our analysis on the four subgroups found that cases with unstable housing were significantly more likely to have experiences with diagnosis of a recent STI, street involvement, transactional sex, substance use, mental illness, income assistance and to not complete partner notification ($p<0.01$ for all). Cases who used substances were significantly more likely to have experiences with diagnosis of a recent STI, unstable housing, street involvement, transactional sex, mental illness and income assistance ($p<0.01$ for all). Cases who were diagnosed with mental illness were significantly more likely to have experiences with housing instability, street involvement and substance use ($p<0.01$ for all). Lastly, cases who had a recent STI

were significantly more likely to reside in a metropolitan area and to have experiences with unstable housing, street involvement and substance use (p<0.01 for all) (**Table 2**).

Table 2: Subgroup analyses

Variables	Subgroups			
	Housing instability (n=97)	Substance use (n=157)	Mental illness (n=87)	Recent STI (n=198)
Urbanity	N/S	N/S	N/S	0.0123
Recent STI	0.0003	0.0025	N/S	N/A
Housing instability	N/A	<0.0001	0.0006	0.0003
Street involvement	<0.0001	<0.0001	0.0005	0.0062
Transactional sex	<0.0001	<0.0001	N/S	N/S
Substance use	<0.0001	N/A	0.0003	0.0025
Mental illness	0.0006	0.0003	N/A	N/S
Income assistance	0.0028	0.0003	N/S	N/S
Partner notification not completed	0.0082	N/S	N/S	N/S

Abbreviations: N/A, not applicable; N/S, not significant; STI, sexually transmitted infection

Discussion

We described all female infectious syphilis cases diagnosed in BC between March 2018 to December 2021 to better understand the drivers of syphilis infection and opportunities to optimize care for females affected by syphilis. We found that a high proportion of the female cases of syphilis in BC reported housing instability, street involvement, substance use, mental illness and income assistance. Our analysis on each of the four subgroups found strong associations between these conditions.

There are few studies focused on female infectious syphilis globally. Recent studies from Manitoba, Canada have found a similarly high prevalence of concurrent conditions (13,14). A descriptive study of female syphilis from 2003–2015 found that compared with male syphilis cases, female cases were more likely to report co-infection with chlamydia and alcohol use (13). Furthermore, the proportion of heterosexual cases of syphilis reporting co-infection with chlamydia, housing instability and substance use, were higher in 2015–2018 compared with 2011–2014, which coincided with a decrease in the ratio of male to female cases in Manitoba (14). The authors concluded there were two simultaneous epidemics of syphilis: one amongst gbMSM and a second amongst the heterosexual population, with the latter being more challenging to control (14).

We also found a high proportion of maternal infectious syphilis cases had a recent STI; a finding similar to that reported in an American national case study from 2012–2016 (15). Our analysis of maternal cases found a high proportion of street involvement, substance use, mental illness and income assistance, consistent with a recent review by the Public Health Agency of Canada (16). These factors may also contribute to experiences of discrimination and impact access to prenatal care affecting the overall health and wellbeing of both the mother and baby (16).

The strong association between the socioeconomic determinants, concurrent conditions and syphilis infection support the need for a syndemics-based approach to respond to the current syphilis epidemic (6,7,17–20). This includes recognizing and deconstructing structural barriers such as those for affordable and stable housing (16). Our study found an overrepresentation of females with syphilis were in the most deprived residential instability quintiles, emphasizing the marginalization of female cases of syphilis in BC.

Incarceration is also a key factor that intersects and can exacerbate STBBI infection. Two recent Canadian reviews found that the incarcerated population was more mobile and had high rates of experiences with substance use, mental illness, transactional sex, and financial and housing instability (21,22). These concurrent conditions are mutually reinforcing, and complicate STBBI diagnosis and follow-up care, related to stigma and a lack of connection to a consistent care provider, ultimately contributing to worse health outcomes (21,22). Thus, partnerships with federal and provincial correctional institutions can help support people infected with syphilis. While most correctional institutions have STBBI screening programs, these programs vary greatly with regard to diseases screened, approach to testing (i.e. opt-in or opt-out) and whether individuals need to be symptomatic to be tested for STBBIs (23–25). Our study adds to existing literature supporting the implementation of universal client-centred STBBI screening in all correctional settings (23,25).

Our study can offer insights into opportunities to improve syphilis care. We found almost half of diagnoses were in the community setting, which may be an area for investment to better address both syphilis and the other intersecting epidemics, such as housing instability, substance use and mental illness, through co-location of additional supports like social worker and counselling services (19). Moreover, engagement with emergency departments, urgent care centres and correctional institutions to develop standards and tailored resources for those settings may help identify cases of syphilis and improve linkage to care and public health outreach teams. While not the setting where the majority of cases in our study were diagnosed, emergency departments are frequently used by populations who do not have a primary care provider or who experience marginalization through financial instability, lack of housing and other support systems (16).

Limitations

This study has several limitations. First, the chart review did not capture the full medical and social history of every case. As a result, presence or absence of risk factors and concurrent

conditions was not known for all cases and certain variables had smaller sample sizes. For instance, there was limited and non-specific data documented in client's charts regarding the ethnicity of cases. Improved understanding of differential experiences by ethnic groups has previously been identified as a priority for further work in BC (26,27). Second, only cases of infectious syphilis that were diagnosed could be analyzed; thus, certain populations who lack access, awareness or agency to seek syphilis testing would have been under-represented in this study. Lastly, this study was descriptive in nature and does not demonstrate causality between the drivers of infection and the diagnosis of syphilis. However, our findings are consistent with the literature and strengthen the evidence for increased services to address socioeconomic and concurrent conditions in the response to the syphilis epidemic.

Conclusion

Overall, this study characterized all female cases of infectious syphilis diagnosed in BC over a nearly three-year period. We found that of the 226 female cases of infectious syphilis, a substantial proportion had concurrent conditions, including housing instability, substance use and mental illness. To our knowledge, this is the largest descriptive analysis of infectious syphilis among females in Canada. Additionally, the use of comprehensive, provincial clinical information systems allowed for a more in-depth understanding of the socioeconomic context of infectious syphilis cases. The findings from our study can help inform interventions to foster enabling environments to prevent and optimize the care for females affected by syphilis, such as integrating mental illness and substance use supports with STI care.

Authors' statement

KW — Conceptualization, methodology, investigation, data curation, writing–original draft, review and editing
LB — Conceptualization, methodology, investigation, review and editing
RS — Review and editing
IP — Investigation, review and editing
VR — Conceptualization, methodology, data curation, review and editing
AY — Data curation, review and editing
AP — Review and editing
GO — Review and editing
TG — Conceptualization, review and editing
JW — Conceptualization, methodology, writing–original draft, review and editing, project administration

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

The authors have no conflicts of interest to declare.

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Annex Table A1: Maternal syphilis descriptive statistics (n=24)

Variables	n	%
Age (years) (n=24)		
Mean	30.6	N/A
Median	30.0	N/A
Min	23.3	N/A
Max	41.7	N/A
Year—total (n=24)		
2018[a]	2	8.3%
2019	7	29.2%
2020	15	62.5%
Year—mean cases per month (n=24)		
2018[a]	0.2	N/A
2019	0.6	N/A
2020	1.3	N/A
Health Authority (n=23)		
Northern	1	4.3%
Interior	4	17.4%
Vancouver Island	4	17.4%
Fraser	7	30.4%
Vancouver Coastal	7	30.4%
Urbanity (n=23)		
Metropolitan	11	47.8%
Non-metropolitan	12	52.2%
Ethnicity (n=11)		
White	5	45.5%
Non-White	6	54.5%
Stage (n=24)		
Primary	0	0%
Secondary	1	4.2%
Early latent	23	95.8%
Diagnosis setting (n=17)		
Community	13	76.5%
Hospital	2	11.8%
Outreach	2	11.8%
Reason for testing (n=24)		
Contact to STI	1	4.2%
Prenatal or at delivery	21	87.5%
Routine screen	2	8.3%
Symptomatic	0	0%
Recent STI (n=21)		
Yes	8	38.1%
No	13	61.9%
HIV positive (n=21)		
Yes	0	0%
No	21	100%
Housing (n=17)		
Stable	10	58.8%
Not stable	7	41.2%
Housing (n=17) (*continued*)		
No fixed address	5	29.4%
Single room occupancy/hotel	2	11.8%
Modular/subsidized	0	0%
Shelter	0	0%
Street involved (n=12)		
Yes	7	58.3%
No	5	41.7%
Transactional sex (n=4)		
Yes	1	25.0%
No	3	75.0%
Substance use (n=17)		
No	7	41.2%
Yes	10	58.8%
Alcohol	1	5.9%
Stimulants	3	17.6%
Opioids	0	0%
Benzodiazepines	0	0%
Polysubstance	6	35.3%
Mental illness (n=9)		
Yes	6	66.7%
No	3	33.3%
Income assistance (n=4)		
Yes	3	75.0%
No	1	25.0%
Incarceration (n=2)		
Yes	2	100%
No	0	0%
Gender of partners (n=19)		
Female	0	0%
Male	19	100%
Male and female	0	0%
Number of partners (n=21)		
Mean	1.8	N/A
1	15	71.4%
2–5	5	23.8%
6 or more	1	4.8%
Partner notification completion (n=23)		
Yes	17	73.9%
No	6	26.1%
Connected to primary care provider (n=24)		
Yes	20	83.3%
No	4	16.7%

Abbreviations: HIV, human immunodeficiency virus; N/A, not applicable; STI, sexually transmitted infection

[a] Data from March 13 to December 31, 2018

Syphilis in Ottawa: An evolving epidemic

Lauren Orser[1,2]*, Paul MacPherson[3,4,5], Patrick O'Byrne[1,2]

Abstract

Background: The incidence of infectious syphilis in Canada has declined throughout the latter decades of the last century; however, in Ottawa, an upsurge in new cases began in 2001. The local epidemic continues to involve predominantly gay, bisexual and other men who have sex with men (gbMSM), but in recent years, has expanded further into heterosexual populations. This has coincided with an increase in the number of pregnant women testing positive for syphilis on antenatal screening. The aim of this study is to understand the changing epidemiology in infectious syphilis cases diagnosed in Ottawa to strengthen primary care management and public health response.

Methods: Surveillance data from the Ontario Ministry of Health were used to describe the evolving epidemiology of infectious syphilis in the Ottawa region from 2010 to 2019, including a comprehensive chart review of cases from 2015–2019.

Results: The number of cases of infectious syphilis in Ottawa rose from 50 cases in 2010 to 171 cases in 2019. These rates were consistently high among males, and increased from 10.9/100,000 in 2010 to 30.9/100,000 in 2019. The rates among females, in comparison, increased from 0.4/100,000 in 2010 to 3.2/100,000 in 2019, with corresponding increases during antenatal screening (with no congenital syphilis cases to date).

Conclusion: As the syphilis epidemic continues to evolve in Ottawa, ongoing surveillance plays a crucial role. Public health resources must address the needs of populations already impacted but at the same time be flexible enough to respond to changes in trends and support clinicians providing care to populations where the epidemic is emerging.

Affiliations

[1] School of Nursing, Faculty of Health Sciences, University of Ottawa, Ottawa, ON

[2] Ottawa Public Health, Sexual Health Services Unit, Ottawa, ON

[3] Division of Infectious Diseases, The Ottawa Hospital, Ottawa, ON

[4] Clinical Epidemiology Program, The Ottawa Hospital Research Institute, Ottawa, ON

[5] Department of Medicine, Faculty of Medicine, University of Ottawa, Ottawa, ON

***Correspondence:**
lorse060@uottawa.ca

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Keywords: syphilis, syphilis priority groups, antenatal syphilis, surveillance data

Introduction

Across Canada, there has been an upsurgence in infectious syphilis. While cases reached an all time low through the 1990s, the incidence of infectious syphilis began to increase in 2001 with most diagnoses occurring among gay, bisexual and other men who have sex with men (gbMSM) (1). Since 2010, however, there has been a secondary surge in the incidence of infectious syphilis with an increasing number of cases now being reported among persons previously thought to be at low risk including heterosexual men and, in particular, women of childbearing age (2,3). Indeed, over just a three-year period from 2015 to 2018, the rate of infectious syphilis among Canadian women aged 20 to 24 years increased nearly eight-fold from 3.4 to 26.0 per 100,000 (4). Such reports have coincided with an increase in the number of pregnant women testing positive for syphilis on antenatal screening and a 1,725% increase in cases of congenital syphilis in Canada (5).

In light of the changing landscape of syphilis in Canada, we sought to re-evaluate what is known about syphilis epidemiology in Ottawa. We undertook a retrospective review of syphilis diagnoses from 2010 to 2019 with a more comprehensive analysis of persons diagnosed with infectious syphilis from 2015–2019. The objective of this review was to identify trends in syphilis epidemiology and case characteristics to better inform prevention and management efforts.

Background

While reports of syphilis infection were historically noted in Ottawa, these diagnoses were rare (fewer than 0.5/100,000) and most were of late latent infection (6). In 2001, however, Ottawa Public Health (OPH) reported four cases of early infectious syphilis (rate: 0.5/100,000) (6), the first sign of new transmission

within the region. By 2006, the number of new cases had increased 10-fold to 41 (rate: 4.8/100,000) (6). A review of cases from January 2001 to June 2006 (7), revealed a predominantly male epidemic with a male-to-female ratio of 19:1, with gbMSM accounting for the majority of cases (83.5%). Nearly half (43%) of those diagnosed with infectious syphilis were human immunodeficiency virus (HIV)-positive (7). Oral-genital contact was the most predominant form of transmission and nearly half of epidemiologically linked sexual partners resided outside Ottawa (7). Sexual networks involving Montréal and Toronto were the most common. Since 2006, the rate of new syphilis infections across Ontario has continued to rise with a 242% increase from 2010 to 2019 (8), and, like elsewhere in Canada (4), heterosexual men and women now make up an increasing proportion of new cases. In view of this, we sought to understand the changing epidemiology in Ottawa. Ongoing surveillance will play a crucial role in guiding clinicians and public health officials and informing screening and prevention efforts.

Methods

This review occurred in Ottawa, Canada, a city with a population of over one million based on 2019 data. The main objectives of this review were to 1) obtain a comprehensive picture of syphilis epidemiology in Ottawa and 2) improve our understanding of the characteristics and risk factors for infection among persons diagnosed with syphilis. To achieve these aims, we completed a review of all syphilis cases diagnosed in Ottawa from 2010 to 2019, focusing on local syphilis epidemiology. We also completed an in-depth chart review of infectious syphilis cases from 2015 (following a major increase in syphilis rates) to 2019 (the most recent available case data) and a review of cases diagnosed during pregnancy from 2015 to 2021 (using preliminary data from 2020–2021).

For the overall epidemiologic review (2010–2019), cases were classified as either infectious (primary, secondary and early latent) or late latent. Data were obtained using the following: 1) the Public Health Ontario (PHO) reportable diseases report, which provides counts of infectious syphilis diagnoses from OPH; 2) the City of Ottawa infectious diseases reports, which tabulate infectious and non-infectious syphilis diagnoses locally; and 3) the Integrated Public Health Information System database, which contains information about cases diagnosed within the province, including names, demographic, diagnosis and treatment information. Duplicate cases were removed. Case counts were logged in an Excel spreadsheet by year based on diagnosis (infectious or late latent syphilis).

A more in-depth analysis was conducted by chart review of public health charts (obtained from OPH) for cases of infectious syphilis diagnosed from 2015 to 2019. We considered only diagnoses of primary, secondary and early latent syphilis among persons who resided in Ottawa during this period. Cases were excluded if they were diagnosed as syphilis of unknown duration, late latent syphilis, or neurosyphilis. In addition, syphilis contacts (i.e. those with a known exposure but not diagnosed with syphilis) were also excluded. Of a total 672 cases of infectious syphilis in Ottawa identified using the above datasets, 637 charts (95% of the total cases) were available for review. The 35 charts not available for review related to a discrepancy in the number of infectious syphilis cases reported by PHO (672 cases) compared to the number retrieved during the chart review (637 cases). For data collection, we extracted age, gender (as reported), sexual orientation, history of other sexually transmitted infections, HIV status at time of diagnosis and pregnancy status (where applicable). All data were recorded in an Excel spreadsheet without identifiers. Z-tests were preformed to determine statistical significance between variables with the exception of age where Student t-test was used. A p-value ≤ 0.05 was considered significant. Initial data analysis was completed by one of the authors and reviewed by all authors to ensure agreement of observed trends and conclusions.

Ethics

Ethics approval for this study was obtained from the University of Ottawa Research Ethics Board (H-11-21-7333). In addition, we completed the ethics assessment tool from PHO which generated a score of zero, indicating no risk. Data pertaining to case numbers and distributions by gender were compiled based on publicly reported information from the Ontario Ministry of Health. Additional information on demographics and risk factors for syphilis infection did not include identifiable information. Data collection did not involve direct contact with cases.

Results

Epidemiology review of syphilis cases: 2010–2019

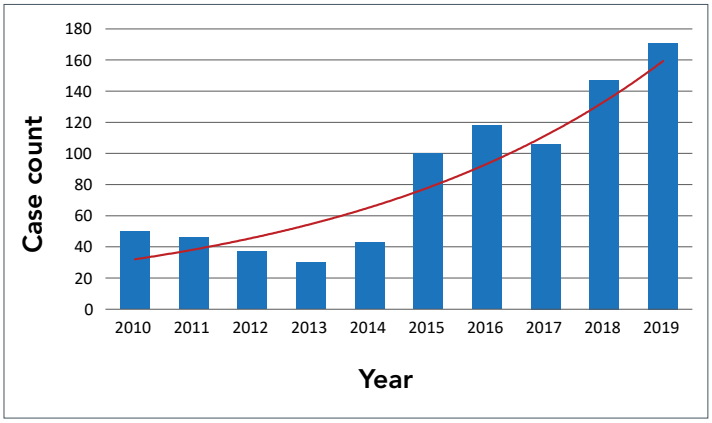
In Ottawa, from 2010-2019, 1,693 syphilis diagnoses were reported; 878 were infectious (primary, secondary, or early latent) and 815 were late latent (**Table 1**). For infectious syphilis, the annual number of reported cases remained relatively stable in the first half of our review period (2010–2014). During this time, 206 cases were reported, averaging approximately 41 cases per year (range 30–50); 96% of these cases were male and 4% were female. Interestingly, beginning in 2015, infectious syphilis cases began to surge increasing to 100 with incremental increases observed each year onward (**Figure 1**). In the latter half of the decade, infectious syphilis rates more than tripled, yielding 672 cases over these five years with 171 cases in 2019 alone (change from 10,7/100,000 persons in 2016 to 15,6/100,000 persons in 2019).

Though most diagnoses of infectious syphilis in Ottawa continue to involve gbMSM, the proportion of cases reported among this group decreased from 91% to 73% over the 10-year period. The proportion of cases diagnosed among HIV-positive persons also declined over the same period with 53% of syphilis cases

Table 1: Yearly count of syphilis diagnoses by stage

Year	Infectious syphilis (#)	Late latent syphilis (#)
2010	50	126
2011	46	104
2012	37	93
2013	30	77
2014	43	80
2015	100	65
2016	135	79
2017	106	63
2018	160	71
2019	171	57
Total	878	815

Figure 1: Infectious syphilis diagnoses



Note: The red line is the exponential trendline for infectious syphilis rates

in 2010 reported among persons living with HIV compared to 19% in 2019. The nearly 20% decrease in syphilis cases among gbMSM has corresponded with an increase in the number of syphilis cases reported among heterosexual men and women.

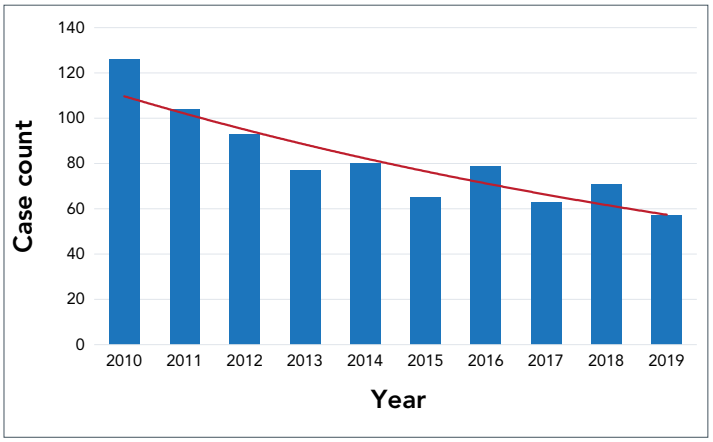
In terms of late latent diagnoses in 2010–2019, rates varied by year. Inversely to the rates of infectious syphilis which increased over the 10-year period, the rates of late latent syphilis decreased from 126 diagnoses in 2010 to 57 in 2019 (**Figure 2**).

Diagnoses of late latent syphilis were relatively similar between males and females and most commonly reported among individuals with opposite sex sexual partners, who immigrated from a syphilis endemic region (identified during immigration medical examination), and in those with new onset memory loss (identified during dementia workup).

In-depth review of infectious syphilis cases: 2015–2019

While the incidence of infectious syphilis remained relatively stable from 2010–2014 at an average 41 cases per year, new diagnoses doubled to 100 in 2015 and nearly doubled again to

Figure 2: Late latent syphilis diagnoses



Note: The red line is the exponential trendline for late latent syphilis rates

171 in 2019. Since 2015 marked a point of substantial increase in syphilis diagnoses, a more detailed chart review was completed for cases from 2015 to 2019. Of the total 672 cases of infectious syphilis in Ottawa reported during this period by the Ontario Ministry of Health, 637 charts (95%) were available for review (**Table 2**).

Table 2: Demographics of cases of infectious syphilis in Ottawa

Characteristic	2015	2016	2017	2018	2019
Number of cases	100	118	106	147	166
Male	98%	95%	93%	97%	90%
Female	2%	5%	7%	3%	10%
Average age (years)	46.8	41.1	38.9	38.0	39.6
MSM	86%	84%	87%	91%	73%
MSW	4%	7%	4%	4%	13%
WSM	1%	5%	5%	3%	10%
Bisexual	8%	4%	4%	2%	4%
Previous STI	64%	64%	72%	65%	60%
HIV+	38%	36%	36%	30%	20%

Abbreviations: HIV+, human immunodeficiency virus-positive; MSM, men who have sex with men; MSW, men who have sex with women; STI, sexually transmitted infection; WSM, women who have sex with men

Interestingly, the gender distribution and proportion of gbMSM accounting for new diagnoses remained stable during the initial surge from 2015 to 2018 but shifted in 2019. Similar to the period from 2010–2014, despite the increase in number, men still accounted for an average of 96% of cases of infectious syphilis from 2015–2018, while women made up about 4% of cases. In 2019, however, 10% of new diagnoses were among women (p=0.006). Further, while the proportion of new diagnoses

among women increased overall 2.5-fold, the absolute number increased 850%. Similarly, whereas heterosexual men made up, on average, 6% of cases of infectious syphilis from 2015–2018, they accounted for 13% in 2019 (p=0.0005), representing a 550% increase in absolute number. Taken together, the proportion of new diagnoses of infectious syphilis among heterosexual men and women in Ottawa increased from 5% in 2015 to 23% in 2019 (p=0.0003). Overall, the male-to-female ratio within this group remained relatively stable across the five years. With the increase in diagnoses among heterosexuals, gbMSM accounted for a lower proportion of new diagnoses in 2019; dropping from 86% in 2015 to 73% in 2019, although this difference did not reach statistical significance (p=0.24). The absolute number of cases of infectious syphilis among gbMSM still increased 41% from 86 cases in 2015 to 133 cases in 2018 and 121 in 2019. Interestingly, diagnoses among individuals who self-identified as bisexual remained low and stable in both proportion and number across the five years.

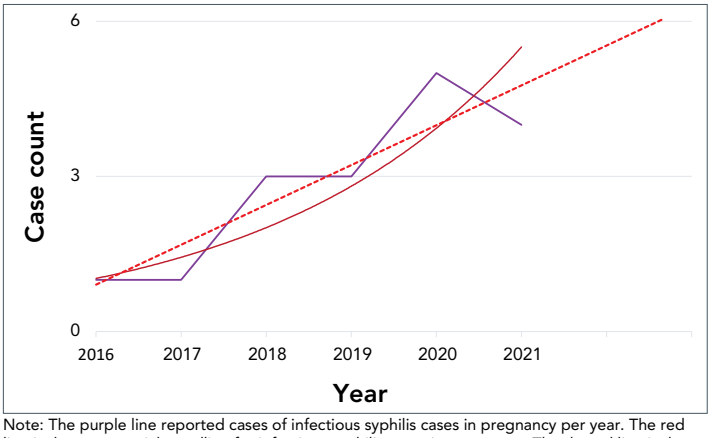
For risk factors, a previous diagnosis of a sexually transmitted infection (STI) was present in 60%–70% of cases of infectious syphilis in Ottawa in 2015–2019. Notably, the proportion of those with a prior STI was relatively stable over the five years. In contrast, the proportion of new syphilis cases with a prior or concurrent diagnosis of HIV infection, all among gbMSM, declined from 36%–38% in 2015–2017 to 20% in 2019 (p=0.002). This decrease is not solely accounted for by the shift of syphilis into the predominantly HIV-negative heterosexual population. Among gbMSM in Ottawa with a diagnosis of infectious syphilis, the proportion who were HIV-negative increased from 58% in 2015–2017 to 73% in 2019 (p=0.082) although this shift did not quite reach statistical significance.

Finally, while the distribution in gender and sexual orientation among new syphilis diagnoses in Ottawa appears to have shifted late in the five years under study, the average age at diagnosis decreased somewhat from 46.8 years in 2015 to 41.1 years in 2016 and 38.0–39.6 years in 2017–2019 (p=0.094).

Review of antenatal syphilis diagnoses

Considering the increasing number of syphilis cases among women of childbearing age and risk of perinatal transmission from untreated syphilis in pregnancy, we reviewed all positive syphilis tests found on antenatal screening in Ottawa from January 2015 to July 2021. Of a total of 37 positive tests among pregnant females, 17 reported cases of syphilis were identified in 15 patients. As seen in **Figure 3**, the number of antenatal syphilis cases in Ottawa has been steadily increasing since 2015 (from no reported cases in 2015 to four cases in mid-2021). While the 2021 data for pregnant women was incomplete at the time of this review, the exponential trendline for antenatal syphilis indicates further upward trends in diagnoses over time. Of the 17 reported cases of syphilis during the review period, three were cases of early infectious syphilis and eight were latent syphilis—as either latent syphilis of unknown duration or late latent. The average age of women who tested positive

Figure 3: Infectious syphilis diagnoses in pregnancy



Note: The purple line reported cases of infectious syphilis cases in pregnancy per year. The red line is the exponential trendline for infectious syphilis cases in pregnancy. The dotted line is the linear forecast for future incidence of infectious syphilis in pregnancy

for syphilis during antenatal screening was 27.7 years (range: 17–39 years) and ethnicity varied. The remaining six positive tests were in pregnant women who had a reported case of syphilis in Ottawa, but reported having been previously treated for syphilis outside of Ontario (i.e. had no prior follow-up in Integrated Public Health Information System database) or had a reactive chemiluminescent microparticle immunoassay test with negative rapid plasma reagin and a negative *Treponema pallidum* particle agglutination test, which are laboratory results consistent with a false positive screening. Of the pregnancies that were maintained and/or completed at the time of this review, none was diagnosed with congenital syphilis based on serologic testing and physical examination of the infant. All infants were referred to the care of paediatric infectious diseases specialists for monitoring. To date, there have been no reported diagnoses of congenital syphilis in Ottawa.

Discussion

Our review of syphilis diagnoses in Ottawa from 2010–2019 showed a decrease in non-infectious (late latent syphilis) and a marked increase in the incidence of infectious syphilis over the study period and a shift in demographic distribution. Overall, the mean age at diagnosis decreased slightly with an increase in cases among heterosexual men and women and among HIV-negative gbMSM. The shift in syphilis toward heterosexual populations, particularly women, has been similarly observed across Canada with Public Health Agency of Canada (PHAC) reporting a 740% increase in infectious syphilis in this population from 2016–2020 (5), with the highest rates reported among women of childbearing age. While gbMSM still account for the vast majority of syphilis diagnoses, the proportion of cases in this population has decreased in tandem with increases among heterosexuals (4,5). Similar upwards trends are now observed among women during pregnancy, with forecasted increases anticipated; however, no congenital syphilis diagnoses have been observed in Ottawa to date.

Considerations for clinical and public health practices

First, the increasing rates of infectious syphilis among women, particularly those of childbearing age, pose a concern for possible future increases in congenital syphilis. Canada-wide, PHAC has already reported a significant increase in the number of confirmed congenital syphilis cases from four in 2016 to 73 in 2020 (5). PHAC noted that this increase is proportional to the increase in infectious syphilis diagnoses among women aged 15–24 years (5). While we have yet to document any confirmed or suspected cases of congenital syphilis in Ottawa, the changing landscape in our region augurs poorly that this will remain the case. As seen in Figure 3, the linear forecast for infectious syphilis among pregnant women in Ottawa projects continued future increases in this group. In view of this, clinicians and public health practitioners should consider more consistent screening of women of childbearing age for syphilis to avoid poor health outcomes in this group and prevent possible cases of congenital syphilis (9–11). Both increased awareness and robust clinical guidance are recommended to assist practitioners in screening for, treating and monitoring syphilis in pregnant women, including screening early in pregnancy and repeat testing in the third trimester if ongoing risk is identified (12). Locally, our public health unit provides comprehensive follow-up for all positive syphilis tests found on antenatal screening. This includes referrals to appropriate specialty care and follow-up syphilis serology during pregnancy and for the infant in the first year of life.

A second point of interest is the increasing proportion of new syphilis diagnoses in Ottawa among HIV-negative gbMSM. Commonly, the increasing incidence of syphilis in this group is attributed to the uptake of HIV preexposure prophylaxis (PrEP) and a concurrent decrease in condom use (13,14). A cause and effect here, however, is very unlikely (15). First, the surge in infectious syphilis in Ottawa first began in 2015. Accessed by some individuals through a single clinic in Ottawa began on November 2015. PrEP was not approved by Health Canada until 2016 (16) and has only become more generally available in recent years. Second, when we examined the rates of STIs, including syphilis, among gbMSM using PrEP in Ottawa in 2018, we did not find a higher incidence among men using PrEP compared to gbMSM in the general population (17). Thus, uptake of PrEP is unlikely to be the cause of the increase in infectious syphilis among HIV-negative gbMSM. In view of this, the vulnerability for HIV infection documented among individuals who acquire syphilis is of enhanced concern. The United States' Centers for Disease Control and Prevention estimates that one in 18 gbMSM are infected with HIV within one year of acquiring syphilis (18). This risk is amplified in racialized populations with the Centers for Disease Control and Prevention estimating the lifetime risk of HIV infection to be one in two for African, Caribbean or Black gbMSM, and one in four for Latino or Hispanic gbMSM (18). Given the enhanced risk of HIV infection among gbMSM diagnosed with syphilis, we suggest HIV PrEP be offered to persons in this group. Specifically, for any gbMSM diagnosed with primary, secondary or early latent syphilis, we recommend an active offer of HIV PrEP be made (15,19). In Ottawa, this is done routinely by public health staff during follow-up and contact tracing (15,19). Since doing so, we have seen a decline in HIV infections in Ottawa (20) though this observation is confounded by increasing uptake of PrEP through several clinics and family physicians across the city and by decreased HIV testing due to the coronavirus disease 2019 pandemic in 2020.

Considering the changes in syphilis epidemiology observed in Ottawa and elsewhere in Canada and the increasing proportion of new HIV diagnoses now occurring in heterosexual men and women locally, offers of PrEP should likely be expanded to other groups beyond gbMSM (21). To mitigate ongoing HIV transmission in heterosexual groups, we suggest applying some of the same criteria used for PrEP in gbMSM (19); 1) for all heterosexual groups with a repeat diagnosis of STI (including syphilis) and 2) women with a diagnosis of infectious syphilis, gonorrhea or hepatis C (21,22). While no heterosexual men or women in our review had a previous or concurrent diagnosis of HIV at the time of syphilis diagnosis, persons with opposite sex partners accounted for 9% (n=80/878) of all infectious syphilis diagnoses and 5% (n=21/413) of all patients with repeat STIs, which can potentially elevate HIV acquisition risk (21,22). Offering PrEP to these individuals, in addition to gbMSM, could be a useful strategy to improve HIV prevention efforts.

Our third point relates to the decrease in non-infectious—or late latent—syphilis diagnoses observed over the 10-year review period. Though the exact reasons for this decline in late latent syphilis cases is not certain, it could relate to 1) increased awareness, testing for and treatment of infectious syphilis over the past 20 years resulting in fewer cases becoming late latent, and/or 2) changes in case classification (12), particularly those classified as latent syphilis of unknown duration. While this latter classification supports longer treatment in individuals where syphilis may or may not have been recently acquired, it muddies surveillance data.

Lastly, based on our data, we suggest broader public awareness campaigns and increased screening among heterosexuals, and reinstatement of syphilis of undetermined duration as a reportable stage of infection (22). Given the known health complications of syphilis, it is concerning that despite the documented shift of new cases into the heterosexual population, screening efforts continue to target almost exclusively gbMSM. Social media campaigns and other strategies should be employed to ensure heterosexual men and women are aware of syphilis and the benefits of testing. From a public health perspective, we also advocate for the inclusion of syphilis of undetermined duration in surveillance data. Presently, these cases are typically captured as late latent though it is unknown if syphilis was recently acquired (23). Classifying syphilis of undetermined duration as late latent means these cases will not be included in the changing epidemiology and will bias surveillance away from non-gbMSM populations where routine

testing is less common. Also, public health follow-up and contact tracing will not occur in these cases, allowing the potential for onward transmission (12,23,24).

Limitations

Our study has several limitations. The data reported in this review are based on information collected and input by public health nurses during routine syphilis follow-up. It is possible that the consistency of the data was subject to some variation. Further, the breadth of information related to infectious syphilis is limited to information specified in the public health reporting system, which does not capture data on transgender, ethnicity and some infection-specific risk factors (e.g. sex with bisexual partners, group sex, etc.). There were some differences between the number of cases reported by PHO and the number reported by OPH. This likely relates to changes in diagnosis, staging, or responsible public health unit not adjusted for by PHO. Finally, in this review, we do not report on cases diagnosed as syphilis of unknown duration as this is no longer a reportable stage. It is possible that the distribution of cases of infectious syphilis, particularly among heterosexual groups, is higher than what is reported.

Conclusion

Findings from our review of syphilis epidemiology in Ottawa support our clinical suspicions and align with recent reports from other Canadian cities and provinces. While the incidence of infectious syphilis remained relatively stable in the first half of our review period (2010–2014), cases surged in the period of 2015 to 2019. Superimposed on this was the notable increase in diagnoses among individuals previously considered at low risk, specifically heterosexual men and women. While 10 years ago, heterosexuals accounted for approximately 5% of infectious syphilis cases in Ottawa, by 2019 they accounted for nearly one-quarter. Cases also increased among HIV-negative gbMSM with the proportion of cases with concurrent HIV infection decreasing from 38% to 20%. Based on our findings, we recommend clinicians and public health practitioners increase syphilis screening beyond the gbMSM population and strengthen contact tracing efforts for persons who may have been exposed to syphilis. Increased efforts should also be made to strengthen HIV prevention efforts, such as PrEP, to heterosexual men and women diagnosed with infectious syphilis. In response to rising rates of infectious syphilis among heterosexual women, future research must be done to help explore syphilis risk factors within this group. We also strongly advocate that prenatal syphilis screening be done as early as possible and, where indicated, screening be repeated during pregnancy and/or near term. As the syphilis epidemic continues to evolve in Ottawa, ongoing surveillance will continue to play a crucial role. While public health resources must ensure ongoing support for populations already impacted by syphilis, they must also be flexible and address emerging trends in the epidemic.

Authors' statement

LO completed the initial data extraction of syphilis diagnoses in Ottawa from 2010–2019. All authors were involved in the data analysis, article writing, editing, submission, and approval of this article.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

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Laboratory evaluation of two point-of-care test kits for the identification of infectious syphilis

Raymond SW Tsang[1]*, Michelle Shuel[1], Kristy Hayden[1], Paul Van Caeseele[2], Derek Stein[2,3]

Abstract

Background: Syphilis is a sexually transmitted disease that can have atypical clinical presentations. Conventional laboratory tests to confirm the diagnosis are not rapid enough to affect clinical decision on treatment and contact tracing. Rapid point-of-care tests (POCT) can be useful for control of infectious diseases; however, no POCT for syphilis detection is currently available in Canada. The aim of this study is to evaluate two POCTs (Reveal™ Rapid TP (*Treponema pallidum*) Antibody test and DPP® Syphilis Screen and Confirm test) for detection of infectious syphilis.

Methods: One hundred serum samples with known syphilis serological status, based on treponemal and non-treponemal test results, were analysed in the laboratory with two POCTs by two independent operators in a blind fashion. Results were analysed to evaluate their ability to detect infectious syphilis.

Results: The Reveal Rapid TP Antibody POCT showed an overall sensitivity of 95.0% and a specificity of 83.3%, while the DPP Syphilis Screen and Confirm POCT showed a sensitivity of 87.5% and a specificity of 98.3%. Both POCTs gave a sensitivity of 100% on active syphilis samples with Venereal Disease Research Laboratory (VDRL) titres of greater than 1:4, but their sensitivities decreased for samples with low VDRL titres. Both POCTs gave weakly or very weakly reactive results on 11.3%–25.0% of the treponemal antibody positive samples.

Conclusion: This laboratory evaluation has shown promising results for both POCTs to detect infectious syphilis. Further evaluations in the field would be required to confirm this preliminary finding.

Affiliations

[1] Syphilis Diagnostic Unit, National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB

[2] Cadham Provincial Public Health Laboratory, Winnipeg, MB

[3] Department of Medical Microbiology and Infectious Diseases, University of Manitoba, Winnipeg, MB

***Correspondence:**
raymond.tsang@phac-aspc.gc.ca

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Keywords: infectious syphilis, point-of-care tests

Introduction

Infectious syphilis has been on the rise in North America since the early 2000s (1,2). In recent years, the increase has been substantial: in Canada, the rate of infectious syphilis has increased about 3.4-fold within 10 years from just under five cases per 100,000 population in 2009 to about 17 cases per 100,000 population in 2018 (3). Also, a shift in increasing rates of infectious syphilis in females of reproductive age (15 to 39 years) has been observed in both the United States (US) and Canada (2,4), leading to an increase in congenital syphilis in both countries. The reasons behind the increase in syphilis cases in Canada have been discussed recently (5), and may include better access to testing, increased sensitivity of enzyme immunoassays employed in the screening of syphilis, lapse in the practice of safe sex and changes in the social behaviour coupled with availability of social media platforms to facilitate recreational sexual encounters. To combat this increase, education to increase better awareness of syphilis, more timely and in-depth surveillance data to allow interventions to be developed that can target at risk behaviours or different at-risk ethnic groups, and better testing methods that can provide immediate results to allow for earlier treatment and contact tracing, have also been suggested (6).

Syphilis has been described as a great imitator (7); clinical and laboratory diagnosis of infectious syphilis can be challenging. The most rapid and confirmatory diagnostic test for infectious syphilis is dark-field microscopy, which looks for motile spirochetes in clinical specimens, but this method is now almost non-existent

in Canada due to the required technical expertise and the relative insensitivity of the method. Conventionally, syphilis is diagnosed serologically by measuring antibodies to both treponemal antigens (e.g. using chemiluminescent microparticle immunoassay, CMIA, which detects IgG and IgM antibodies) and non-treponemal antigens (e.g. using either rapid plasmin reagin, RPR, or Venereal Disease Research Laboratory, VDRL, tests). Patients with active or infectious syphilis show positive results with both the treponemal and non-treponemal tests while patients with past syphilis show positive results only with the treponemal test. Although these conventional serological tests and the newer molecular polymerase chain reaction diagnostic methods are accurate and sensitive, the results are not available rapidly enough to allow clinical decisions on both treatment of patients and contact tracing. Furthermore, there are currently no licensed commercial nucleic acid amplification tests for syphilis on the market.

While point-of-care tests (POCTs) for syphilis have been developed in the early 2000s and have been in use in a number of resource limited countries that lack the laboratory infrastructure, equipment and qualified personnel to carry out conventional laboratory tests, their use in resource rich countries are less well defined. Indeed, the US Centers for Disease Control and Prevention and the American Association of Public Health Laboratories, in consultation with other sexually transmitted disease experts, concluded in 2017 that there was insufficient data to recommend the use of POCT for routine syphilis testing in the US (8).

By October 2, 2020, the US Food and Drug Administration licensed two syphilis POCT kits (9): the Syphilis Health Check POC assay (Diagnostic Direct LLC, Stone Harbor, New Jersey or Trinity Biotech, Jamestown, New York) and the DPP POCT for HIV and Syphilis serology (Chembio Diagnostic System, Medford, New York). However, some evaluations of these test kits were based on small numbers of positive samples as well as serum specimens obtained by venipuncture rather than finger-prick whole blood, which is the specimen of choice for POCT (due to ease of obtaining specimen). Using finger-prick whole blood specimens, the Syphilis Health Check POCT had a sensitivity of 100% (with seven positive samples) when compared to consensus reference testing of RPR and treponemal enzyme immunoassay. This sensitivity decreased to 77.8% (with 18 positive samples) when compared with Syphilis Health Check POCT done with serum in the laboratory, and to only 50.0% sensitivity (with 16 positive samples) when compared with the treponemal enzyme immunoassay (10). Difficulty in reading the Syphilis Health Check POCT has also been reported for those specimens considered positive in the POCT but negative by consensus reference testing. A 2016 study that reported high sensitivity (94.7%) and specificity (100%) for the DPP POCT for HIV and Syphilis serology, the results for the syphilis component of the POCT were based on testing serum specimens and comparing the data to that obtained by the *Treponema pallidum* (*T. pallidum*) particle agglutination test (11). Currently, no syphilis POCT has been licensed in Canada.

In this study, our objective was to evaluate two syphilis POCTs (one has treponemal antigen and another that has both treponemal and non-treponemal antigens) to detect infectious syphilis and report on their preliminary performance based on studies done in the laboratory using serum samples with known syphilis serological test results.

Materials and methods

Patient serum samples and testing by conventional syphilis serology

One hundred serum samples from individual subjects, identified as either syphilis positive or syphilis negative at the Cadham Provincial Public Health Laboratory (Winnipeg, Manitoba), were provided in a blind fashion (regarding the syphilis test results) to the National Microbiology Laboratory for evaluation by POCT. Samples were defined as syphilis positive if tested positive by CMIA for antibodies to treponemal antigens. Samples were defined as syphilis negative when CMIA testing gave negative results. Qualitative RPR was performed on CMIA positive samples, followed by a quantitative VDRL test at the Cadham Provincial Public Health Laboratory. Both RPR and VDRL are considered as non-treponemal tests that detect non-treponemal antibodies, and positive results of either the RPR or VDRL tests (and in the presence of positive CMIA results) are indicative of active or infectious syphilis. Also, a different non-treponemal (VDRL) test was used to confirm the RPR qualitative results to increase the specificity of the non-treponemal test data.

Point-of-care test

Since there are no POCT kits licensed for sale in Canada, we obtained permission from Health Canada Special Access Program before the DPP® Syphilis Screen and Confirm Assay (ChemBio Diagnostic Systems, Inc., Medford, New York) and the Reveal™ Rapid TP Antibody test (MedMira Laboratories, Inc., Halifax, Nova Scotia) were purchased directly from the suppliers. The Reveal Rapid TP Antibody POCT detects antibodies to synthetic peptides that resemble *T. pallidum* recombinant antigens and can be used with serum, whole blood or plasma samples (12). The DPP Syphilis Screen and Confirm POCT detects antibodies to both treponemal and non-treponemal antigens in serum, whole blood or plasma specimens (13).

Two qualified laboratorians at the National Microbiology Laboratory carried out independent testing on each of the 100 serum samples with both POCT kits according to the manufacturers' instructions. Results were read manually and recorded as reactive, weakly reactive or very weakly reactive, even though any intensity of colour change in the test zone is considered reactive according to the package insert for both the Reveal Rapid TP Antibody POCT and the DPP Syphilis Screen

and Confirm POCT. We chose to score the test results in more detail since reading intensity of colour change is subjective and difficulties in reading some syphilis POCTs have been described by others. Weakly reactive and very weakly reactive results were determined by comparison with the reactions given by the controls as well as other reactive samples obtained in the same run. When discordant results were obtained by the two independent operators, the test was repeated a second time by both operators and if the results matched on the second test, they were then used. In no circumstances, were any major discordant results encountered, such as reactive by one operator and non-reactive by another operator.

After the 100 samples have been tested by both operators using the two POCTs, results were provided to the investigators at the Cadham Provincial Public Health Laboratory, who then disclosed the CMIA, RPR and VDRL results to the investigators at the National Microbiology Laboratory to perform the analysis. The sensitivity (percent of infectious syphilis samples tested positive), specificity (percent of samples without infectious syphilis tested negative), false positive rate (percent of samples without infectious syphilis tested positive) and false negative rate (percent of infectious syphilis samples tested negative) of the POCTs for detection of infectious syphilis were calculated.

Results

Characteristics of clinical samples

Of the 100 samples provided for POCT evaluations, 80 were reactive or positive by CMIA (sample over cut-off, S/CO, values ranged from 1.11 to 27.11, mean=15.68, median=16.81) and 20 were non-reactive or negative (S/CO values ranged from 0.03 to 0.14, mean=0.61, median=0.05). The 20 negative CMIA samples did not undergo further testing and were regarded as syphilis negative for both active and past infections. The 80 CMIA positive samples were further divided into 40 that were non-reactive by RPR (which suggested absence of active syphilis infections but with treated past syphilis infections) and 40 that were RPR reactive (which suggested active syphilis infections). Among the 40 CMIA positive and RPR reactive samples, six were only weakly reactive by RPR. Of these six RPR weakly reactive samples, five were tested by VDRL to give reactive results with an undiluted sample. The remaining CMIA positive, RPR weakly reactive sample was VDRL reactive at 1:2 dilution. Of the 34 CMIA positive and RPR reactive samples, 14 had low or no VDRL titres (n=7 with VDRL titres of 1:2, n=6 with VDRL titres of 1:4, and n=1 was VDRL reactive at undiluted), while 20 samples were found to have VDRL titres of at least 1:8.

Performance of Reveal Rapid *Treponema pallidum* Antibody and DPP Syphilis Screen and Confirm tests

Table 1 shows the results of the Reveal Rapid TP Antibody POCT and the DPP Syphilis Screen and Confirm POCT on the three categories of serum samples (no syphilis infection, past syphilis infection and active syphilis infection). Sera from subjects with no evidence of current or past syphilis infection were found to be non-reactive by both POCTs. Only ten of the 40 samples categorised as having past syphilis infections were reactive in the Reveal Rapid TP Antibody POCT. The DPP Syphilis Screen

Table 1: Results of two syphilis point-of-care test kits showing number of reactive and non-reactive reactions on 100 serum specimens with known conventional syphilis serological findings

Syphilis status[a]	Number of specimens	Reveal Rapid *T. pallidum* Antibody point-of-care test[b]				DPP Syphilis Screen and Confirm point-of-care test[c] presented as treponemal/non-treponemal reactions							
		R[d]	(R)[d]	NR[e]	(NR)[e]	R/R[d]	(R/R)[d]	R[d]/NR	(R/NR)[d,e]	NR[e]/R[d]	(NR/R)[d,e]	NR[e]/NR[e]	(NR/NR)[e]
No syphilis	20	0	0	20	20	0	0	0	0	0	0	20	20
Past syphilis	40	10	4	30	36	1	0	18	13	0	0	20[f]	26[f]
Active syphilis[g]	40	38	36	2	4	35	27	5	8	0	0	0	5
With VDRL titer greater than 1:4	20	20	20	0	0	20	19	0	0	0	0	0	1
With VDRL titer 1:2 to 1:4	13	12	11	1	2	10	7	3	3	0	0	0	3
VDRL undiluted or RPR WR[h]	7	6	5	1	2	5	1	2	5	0	0	0	1

Abbreviations: NR, nonreactive; R, reactive; RPR, rapid plasma reagin; RPR WR, rapid plasma reagin weakly reactive; VDRL, Venereal Disease Research Laboratory
[a] No syphilis, chemiluminescent microparticle immunoassay (CMIA) negative; past syphilis, CMIA positive but RPR nonreactive; active syphilis, CMIA positive and RPR or VDRL reactive
[b] MedMira Laboratories, Inc., Halifax, Nova Scotia
[c] ChemBio Diagnostic Systems, Inc., Medford, New York. DPP Syphilis Screen and Confirm point-of-care test results were presented as treponemal/non-treponemal reactions
[d] R=reactive included weakly reactive and very weakly reactive reactions; (R)=conservative reading regarding very weakly reactive reactions as non-reactive. We chose to score the test results in more detail since reading intensity of colour change is subjective and difficulties in reading some syphilis point-of-care tests (POCTs) have been described by others
[e] NR=non-reactive; (NR)=conservative reading and included very weakly reactive reactions
[f] Not including one sample that gave inconclusive result by DPP Syphilis Screen and Confirm point-of-care test
[g] The 40 active syphilis samples were subdivided into three categories: strongly reactive VDRL titres (greater than 1:4); weakly reactive VDRL titres (1:2 to 1:4) and VDRL reactive only with undiluted serum or qualitative RPR weakly reactive
[h] One sample RPR weakly reactive and VDRL titer 1:2; one sample RPR reactive and VDRL reactive undiluted; and five samples RPR weakly reactive and VDRL reactive undiluted

and Confirm POCT detected antibodies to the treponemal antigen in 19 of the 40 samples from subjects with past syphilis infection; only one sample was reactive for both treponemal and non-treponemal antigens, while the remaining 20 were non-reactive for both antigens.

The percentage of samples from those with active syphilis and reactive by both Reveal Rapid TP Antibody and DPP Syphilis Screen and Confirm POCTs are correlated to the quantitative non-treponemal test results, and this is particularly evident with the DPP Syphilis Screen and Confirm POCT (Table 1).

If very weakly reactive reactions were read conservatively as non-reactive (shown in parentheses in Tables 1 and **Table 2**), fewer samples from those with active and past syphilis infections were found to be reactive in both POCT. Twenty samples when tested by the Reveal Rapid TP Antibody POCT test gave either weakly reactive (n=12; three were past syphilis samples and nine were active syphilis samples) or very weakly reactive (n=8; six were past syphilis samples and two were active syphilis samples) reactions. In the DPP Syphilis Screen and Confirm POCT, 12 samples gave weakly reactive (n=1; past syphilis) or very weakly reactive (n=11; six past syphilis and five active syphilis) reactions in the treponemal antigen, while nine samples (n=8 active syphilis and one past syphilis) gave very weakly reactive results in the non-treponemal antigen (data not shown).

Table 2: Performance of Reveal Rapid TP Antibody point-of-care-test and DPP Syphilis Screen and Confirm point of care test to detect active or infectious syphilis based on laboratory evaluation of 100 serum samples defined by traditional syphilis serological assays[a]

Performance characteristics of syphilis point-of-care test	Reveal Rapid *T. pallidum* Antibody[b] point-of-care test[c]		DPP Syphilis Screen and Confirm[d] point-of-care test[c]	
Overall sensitivity[e]	95.0%	(90.0%)	87.5%	(67.5%)
Sensitivity[f]	100%	(100%)	100%	(95.0%)
Sensitivity[g]	92.3%	(84.6%)	76.9%	(53.8%)
Sensitivity[h]	85.7%	(71.4%)	71.4%	(14.3%)
Specificity	83.3%	(93.3%)	98.3%	(100%)
False positive rate	16.7%	(6.7%)	1.7%	(0%)
False negative rate	5.0%	(10.0%)	12.5%	(32.5%)

[a] Traditional syphilis serological assays included chemiluminescent microparticle immunoassay (CMIA) followed by rapid plasma regain (RPR) and/or Venereal Disease Research Laboratory (VDRL) on those CMIA-positive
[b] MedMira Laboratories, Inc., Halifax, Nova Scotia
[c] Weakly reactive and very weakly reactive reactions were regarded as reactive (results were read conservatively with very weakly reactive reactions regarded as non-reactive). We chose to score the test results in more detail since reading intensity of colour change is subjective and difficulties in reading some syphilis point-of-care tests (POCTs) have been described by others
[d] ChemBio Diagnostic Systems, Inc., Medford, New York
[e] Overall sensitivity was based on 40 samples tested CMIA positive and RPR reactive or weakly reactive. The 40 active syphilis samples were subdivided into three categories: with strongly reactive VDRL titres (greater than 1:4); weakly reactive VDRL titres (1:2 to 1:4), and VDRL reactive only with undiluted serum or qualitative RPR weakly reactive
[f] Based on 20 samples tested CMIA positive, RPR reactive and VDRL titres greater than 1:4
[g] Based on 13 samples tested CMIA positive, RPR reactive and VDRL titres 1:2 to 1:4
[h] Based on n=7 samples tested CMIA positive, either RPR weakly reactive and/or VDRL reactive at undiluted

Table 2 compares the performance characteristics of the two syphilis POCTs for the 100 serum samples that were categorized as syphilis naive, past treated syphilis, active, or infectious syphilis. Sensitivity of both POCT for detection of infectious syphilis appeared to be affected by the quantitative non-treponemal test results of the samples. Both POCT gave 100% sensitivity in samples with VDRL titres of greater than 1:4, but sensitivity decreased stepwise in samples with lower VDRL titres (Table 2), and the DPP Syphilis Screen and Confirm POCT appeared to be affected more by samples with VDRL titres of 1:2 to 1:4 or lower. While the Reveal Rapid TP Antibody test has a higher sensitivity for detection of active syphilis, the DPP Syphilis Screen and Confirm assay has a better specificity.

Reproducibility of point-of-care test results between two independent operators

For the Reveal Rapid TP Antibody test, 91% of the results from both operators agreed while for the DPP Syphilis Screen and Confirm Assay, 94% and 95% of the results on the treponemal and non-treponemal components showed concordance between the two operators.

There were nine minor discrepancies between the two operators when testing the Reveal Rapid TP Antibody test, with operator #1 scoring nine samples as weakly reactive and operator #2 scoring seven as reactive and two as very weakly reactive. For the DPP Syphilis Screen and Confirm Assay, there were five discrepant results for the non-treponemal component, with operator #1 scoring them as reactive and operator #2 scoring them as very weakly reactive. For the treponemal component of the DPP Syphilis Screen and Confirm Assay, there were six discrepant results with operator #1 scoring them as reactive and operator #2 scoring them as very weakly reactive.

Discussion

This laboratory study indicated that both the Reveal Rapid TP Antibody and the DPP Syphilis Screen and Confirm POCTs had overall sensitivity and specificity of 85.0% or better, with the Reveal Rapid TP Antibody POCT showing an overall better sensitivity (95.0%) and DPP Syphilis Screen and Confirm showing better specificity (98.3%) for detection of infectious syphilis. Sera from subjects without current or past syphilis infection gave very clear-cut non-reactive results with both POCTs. Because the test samples were not random samples collected from the population, no attempt was made to extend the current results to calculate the positive and negative predictive values of these POCTs.

Most syphilis POCT kits on the market use treponemal antigen to detect anti-treponemal antibodies and only a handful of kits employ both treponemal and non-treponemal antigens that can simultaneously detect anti-treponemal as well as non-treponemal antibodies. Tests that detect anti-treponemal antibodies alone

cannot be used to differentiate subjects with active or past infections because anti-treponemal antibodies tend to persist for a long time after the active infection disappears following successful treatment. Antibodies to both treponemal and non-treponemal antigens are indicative of active and infectious syphilis because antibodies to non-treponemal antigens usually show a gradual drop in titres and eventually disappear some months after the active infection is clear with treatment.

Although the Reveal Rapid TP Antibody POCT uses antigen(s) that represents T. pallidum proteins, and the DPP Syphilis Screen and Confirm POCT also has a treponemal antigen component, results suggested that both POCT favoured the detection of infectious syphilis rather than treated past syphilis. Antibodies to the treponemal antigen were detected in only 25.0% and 48.7% of serum samples from subjects with past syphilis when measured by the Reveal Rapid TP Antibody POCT and the DPP Syphilis Screen and Confirm POCT, respectively. In our study, when compared to results obtained by CMIA, the sensitivity of the treponemal component of the DPP Syphilis Screen and Confirm POCT to detect treponemal antibodies was 100% with serum samples from active syphilis cases but was only 48.7% with serum samples from past syphilis cases. The sensitivity of the Reveal Rapid TP Antibody POCT to detect treponemal antibodies was 95.0% in those with active syphilis but was only 25.0% in those with past syphilis.

This study shows the two POCT evaluated have good sensitivity and specificity for the detection of infectious syphilis. However, in those with low non-treponemal antibody titres, their performance may be compromised, thus confirming the findings by others for this category of active syphilis patients (10,14,15). Of the two POCTs evaluated, the Reveal Rapid TP Antibody POCT may be affected less by the low non-treponemal antibody titres and was able to maintain reasonable sensitivity of 92.3% to 85.7% (to detect infectious syphilis) even in samples with VDRL antibody titres of 1:2 to 1:4 or only reactive in undiluted sera.

In the Reveal Rapid TP Antibody POCT, 25.0% of the CMIA positive samples were found to give either weakly or very weakly reactive results. In the DPP Syphilis Screen and Confirm POCT, 11.3% and 15.0% of the CMIA positive samples were found to give either weakly or very weakly reactive results to the non-treponemal and treponemal components, respectively. Both weakly reactive and especially very weakly reactive results may lead to difficulty in reading these tests in actual field use by non-trained operators. Also, the use of finger-prick whole blood specimens can potentially make reading the results even more difficult. Both training and clear guidelines on how to read POCT results may be required. Some POCT come with an electronic reader (11), and this may avoid inconsistencies in reading results between samples and operators. Another potential challenge in the implementation of POCT in sexually transmitted infection clinics or rural areas is related to the de-centralized syphilis testing and the resultant difficulties in the capturing of test results by public health for surveillance purpose and for the subsequent development of public health intervention policies.

One of the reasons that has been put forward to explain the recent increase in syphilis infection in Canada (in both urban and remote or rural locations) is the inequity of accessibility within the healthcare system, including the testing facilities for infections (5,6). Vulnerable populations, whether living in urban or rural areas, can be hard to reach due to homeless or unstable housing, mistrust in the healthcare system or lack of accessible testing facilities in remote localities. Alternate testing approaches, such as the use of POCT, may help to meet the need created by the circumstances of these at-risk populations. Current POCT provide only qualitative results of positive or negative findings, and the lack of quantitative result on antibody titres may prevent their use for monitoring response to treatment as well as differentiating repeated or reinfections from past infections. This contrasts with the current practice of using a quantitative non-treponemal test result (such as RPR or VDRL titres) to monitor for either a decrease in antibody titres as proof of positive response to treatment or a rising antibody titer in the case of no response to treatment or an occurrence of reinfection.

Limitations

There are several limitations in the interpretation of this study. First, serum samples collected for conventional syphilis serology were used instead of finger prick whole blood specimens, which will likely be the sample of choice when these tests are used in the field. Secondly, these assays were done in a controlled laboratory environment by trained laboratory staff with experience in carrying out clinical diagnostic tests; therefore, actual performance of these POCT in the field or in a real-world situation may differ. Another limitation is the small number of samples tested, especially in the subcategories of active syphilis cases with different VDRL titres and, as such, the sensitivity data may be inaccurate. Finally, the usefulness or performance of a POCT would also depend on the setting or prevalence of the disease where the POCT will be deployed.

Conclusion

The two POCT evaluated in this laboratory study appeared to show promising results for detection of infectious syphilis especially in those with non-treponemal antibody titres equal to or greater than 1:4, but not for detection of past syphilis. Further evaluations in the field will be required in order to confirm the findings in this preliminary study. Field evaluations and clinical studies will offer further experience in the use of syphilis POCT that may ultimately contribute towards better control of infectious and congenital syphilis. Data from this kind of study may also be useful for potential future licensure of such test kits in Canada.

Authors' statement

RSWT — Designed the study, analysed the results, prepared the first draft
DS — Designed the study
MS — Carried the test and analysed the results
KH — Carried the test and analysed the results

All authors commented and approved the manuscript for submission.

Results and opinion stated in this manuscript are those of the authors and they do not necessarily represent the position of neither the National Microbiology Laboratory nor the Public Health Agency of Canada.

Competing interests

None.

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Congenital syphilis re-emergence in Winnipeg, Manitoba

Peter Benoit[1]*, Lana Tennenhouse[2], Alicia Lapple[1], Gillian Hill-Carroll[1], Souradet Shaw[2], Jared Bullard[2,3], Pierre Plourde[1,2]

Abstract

Background: Infectious syphilis rates have been increasing in Winnipeg, Manitoba among individuals during their childbearing years. Untreated or inadequately treated prenatal infection often results in congenital syphilis, with devastating consequences to fetal health and survival. The objective of this study was to review public health surveillance data regarding congenital syphilis incidence and birthing parent risk factors in Winnipeg from 2018 to 2020.

Methods: Data extracted from a population-based surveillance database maintained by the Winnipeg Regional Health Authority Public Health investigations for all 2018–2020 probable or confirmed cases of early congenital syphilis or syphilitic stillbirth were reviewed. Rates of congenital syphilis were calculated per 1,000 live births. Descriptive analyses were performed to describe birthing parent age, neighbourhood of residence, intravenous substance use, Child and Family Services involvement, access to prenatal care and obtainment of adequate prenatal treatment.

Results: There were eight cases of confirmed/probable congenital syphilis in 2018, 22 cases in 2019 and 30 cases in 2020. Average birthing parent age was 26.5–27.0 years. The majority (66.7%) of birthing parents lived in inner city neighbourhoods with known infectious syphilis outbreaks. Over 50% of birthing parents did not receive any prenatal care, or the care received consisted of inadequate treatment or follow-up. Reinfection among birthing parents who did receive prenatal care was suspected in an additional 23.3% of cases.

Conclusion: Congenital syphilis rates in Winnipeg have increased dramatically. Public health and healthcare provider efforts to address the needs of the community are vital for promoting access to safe and effective prenatal care.

Affiliations

[1] Population and Public Health Program, Winnipeg Regional Health Authority, Winnipeg, MB

[2] Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB

[3] Cadham Provincial Laboratory, Manitoba Health and Seniors Care, Winnipeg, MB

***Correspondence:**
pbenoit2@wrha.mb.ca

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Keywords: congenital syphilis, surveillance, prenatal care, health inequity

Introduction

Rates of syphilis have been increasing in Canada; more than doubling between 2016 and 2020 (1), with the most dramatic increases observed in the Prairie Provinces. During the same period, rates of congenital syphilis have increased 10 to 15-fold, as a consequence of large heterosexual outbreaks of syphilis primarily in the Prairie Provinces.

Congenital syphilis occurs via vertical transmission of the spirochete *Treponema pallidum* from a pregnant person to a fetus during pregnancy. Manifestations range from asymptomatic infection to spontaneous abortion, stillbirth, and multisystem involvement with severe consequences for infant health (2). Risk of transmission to the fetus is high, with estimates of 70%–100% among untreated pregnant persons with primary or secondary syphilis, 40% in early latent syphilis and less than 10% in late latent syphilis (3). However, congenital syphilis is almost entirely preventable with adequate prenatal treatment, defined as benzathine penicillin G at least 30 days prior to delivery (4). Screening for infectious syphilis at the first prenatal care appointment is considered standard of care across Canada. Further screening may be considered in high risk/outbreak populations (3). Lack of access to prenatal care has been found to be a large modifiable risk factor for congenital syphilis in the United States (5). Given that the consequences of congenital syphilis are significant, and that effective screening and treatment are available, the occurrence of congenital syphilis cases is an

important metric to assess the success of our public health and healthcare systems. If functioning optimally, we should see no cases of congenital syphilis.

In Winnipeg, there had been no recorded cases of congenital syphilis since 1977, and more recently the first case detected in Manitoba was in 2015 (in a northern community), with the first case in Winnipeg in 2018. However, there has since been a dramatic increase in infectious syphilis, with an age-standardized rate of 79.5 and 140.4 cases per 100,000 individuals in Winnipeg in 2018 and 2019, respectively (*unpublished data, Pierre Plourde*). This represents an 81% increase in cases in 2018 over 2017 and a further almost doubling of cases in 2019. While the majority of cases previously affected men who have sex with men disproportionately, the rate of heterosexual transmission has increased with women comprising 47% of infectious syphilis cases in Winnipeg in 2018 and 54% of cases in 2019 (*unpublished data, Pierre Plourde*), with the first signals of increased transmission in heterosexual women observed as early as 2015 (6). Similar trends of increasing infectious syphilis incidence among women have been noted in other Canadian provinces, including British Columbia and Alberta (7,8). The presence of missed or inadequately treated infectious syphilis among those who are in their childbearing years represents a failure of the healthcare system and signifies the critical importance of intensifying public health and healthcare provider efforts aimed at prevention of congenital syphilis, in collaboration with community-based agencies involved in outreach to pregnant individuals.

Our objective was to review public health surveillance data regarding congenital syphilis incidence in Winnipeg from 2018 to 2020, and to describe the characteristics of pregnant persons giving birth to infants with congenital syphilis. The years 2018–2020 were chosen as a time horizon, as prior to 2018 there were no reported cases of congenital syphilis in Winnipeg for over 40 years.

Methods

Data source

Reported cases of congenital syphilis in the surveillance database of the Winnipeg Regional Health Authority were reviewed from January 2018 to December 2020. Winnipeg is the largest city in Manitoba, with a population of about 700,000 in 2016 (9) and 8,675 live births in 2018 and 8,560 live births in 2019, as recorded in the Winnipeg Regional Health Authority Healthy Parenting and Early Child Development program database (*personal communication, Dr. Christopher Green, University of Manitoba*).

All cases of infectious and congenital syphilis are reportable to Public Health at the provincial level. Cases are classified as Winnipeg cases using postal code of most recent known address, or as individuals known to be living in Winnipeg for the duration of the pregnancy without a Winnipeg address on file. Cases are managed by public health nurses who complete investigation forms, collect sociodemographic characteristics of the individual, and supplement the public health record with relevant clinical notes. For congenital syphilis investigations, public health records are maintained separately for the birthing parent and infant. These records are stored in a population-based surveillance database.

Reported cases of possible congenital syphilis are classified by Manitoba Public Health into confirmed or probable early syphilis, and starting in 2019, also include classifications of confirmed or probable syphilitic stillbirth. Based on the case definitions provided by Manitoba Health and Seniors Care (see **Annex**), classification of cases is established by the joint input of a public health nurse and paediatric infectious disease specialist, followed by the review of a medical officer of health.

Measures

Case investigation public health data reviews for both birthing parent and infant were performed for all confirmed or probable cases of congenital syphilis in Winnipeg between January 2018 and December 2020. At least two individuals reviewed each record independently. Data on the following birthing parent's characteristics were collected: 1) age (years); 2) neighbourhood of residence (Winnipeg Downtown, Point Douglas, or other); 3) intravenous substance use over the past year (yes, no); 4) Child and Family Services involvement (yes, no); 5) adequate prenatal treatment defined as receipt of at least one course of benzathine penicillin G 2.4 million units at least 30 days prior to delivery (yes, no, or unknown); and 6) receipt of any prenatal care (none, some but did not receive adequate treatment, some but high risk of re-exposure or reinfection in third trimester not adequately treated, some and treated adequately, or unknown).

Analysis

Means, medians, interquartile ranges, frequencies and percentages were used to describe the birthing parent characteristics of the study population. The birth rate of infants with congenital syphilis per 1,000 live births was calculated for each year in the surveillance period, using the estimated total number of live births per year in Winnipeg as the denominator (estimated as 8,600 for 2020).

Ethics

Research ethics approval was not required for analysis and reporting of routinely collected public health surveillance data.

Results

There were 60 cases of confirmed or probable congenital syphilis in Winnipeg from 2018 to 2020 (**Table 1**, **Figure 1**). Eight of these cases occurred in 2018, 22 in 2019 and 30 in 2020. This corresponds to rates of congenital syphilis (per 1,000 live births) of 0.9 in 2018, 2.6 in 2019 and 3.5 in 2020.

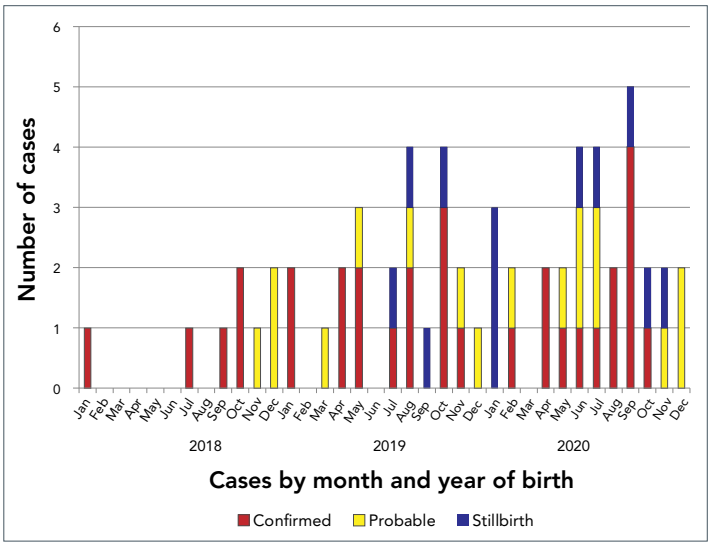
Table 1: Congenital syphilis incident cases and risk factors in Winnipeg, Manitoba from 2018–2020

Characteristic	2018 (N=8)		2019 (N=22)		2020 (N=30)	
	n	%	n	%	n	%
Adverse birth outcome						
Confirmed early congenital syphilis	5	62.5	13	59.1	13	43.3
Probable early congenital syphilis	3	37.5	5	22.7	9	30.0
Lab-confirmed syphilitic stillbirth	N/A	N/A	1	4.5	6	20.0
Probable syphilitic stillbirth	N/A	N/A	3	13.6	2	6.7
Pregnant person's age (years) at delivery, mean/median (interquartile range)	26.6/27	23–30	27.0/26	22–30	26.5/25	22–31
Neighbourhood of residence						
Downtown	3	37.5	10	45.5	10	33.3
Point Douglas	3	37.5	9	40.9	5	16.7
Other	2	25.0	3	13.6	15	50.0
Risk factors						
Intravenous substance use over the past year	4	50.0	9	40.9	3	10.0
Child and Family Services involvement	4	50.0	8	36.4	4	13.3
Adequate treatment 30 days or more prior to delivery						
Yes	0	0.0	6	27.3	2	6.7
No	8	100.0	14	63.6	25	83.3
Unknown	0	0.0	2	9.1	3	10.0
Prenatal care						
None	3	37.5	7	31.8	14	46.7
Some, but did not receive adequate treatment	3	37.5	3	13.6	3	10.0
Some, but high-risk re-exposure or reinfection in third trimester not adequately treated	2	25.0	4	18.2	8	26.7
Some, treated adequately	0	0.0	6	27.3	2	6.7
Unknown	0	0.0	2	9.1	3	10.0

Abbreviation: N/A, not available

Median birthing parent age ranged from 26.5 to 27.0 years for each calendar year throughout the surveillance period. The majority of birthing parents lived in two specific neighbourhoods of Winnipeg (Downtown and Point Douglas), both of which are considered to be in the city's inner core and have historically been associated with sexually transmitted infection outbreaks (5,10). These inner-city neighbourhoods are known to have higher rates of poverty, racialized populations and crime. They are also well studied in terms of mortality data and are known to have a significantly lower life expectancy in contrast with the rest of Winnipeg. Intravenous substance use over the past year was reported in 50.0% of birthing parents in 2018, 40.9% in 2019 and 10.0% in 2020. Child and Family Services were involved with 50.0% of cases in 2018, 36.4% in 2019 and 13.3% in 2020. Of the 16 birthing parents who reported intravenous substance use, 11 (69%) named crystal methamphetamine.

Figure 1: Early congenital syphilis in Winnipeg, Manitoba by month/year of birth, 2018–2020



Over 50% of birthing parents did not receive any prenatal care or received only limited prenatal care (usually one visit) with inadequate follow-up and treatment. On average from 2018 to 2020, 23.3% of birthing parents received prenatal care; however, a reinfection or high-risk re-exposure was suspected to have occurred in the third trimester. None of the birthing parents received adequate treatment during pregnancy in 2018, although this increased to 27.3% in 2019, then declined again to 6.7% in 2020.

Discussion

In 2007, the World Health Organization published the goal of decreasing congenital syphilis rates to 0.5 cases or less per 1,000 live births (11). With increasing cases of congenital syphilis each year and a rate of 3.5 cases per 1,000 live births in 2020, Winnipeg is far from meeting this goal. Young birthing age, residence in select inner city neighbourhoods with large infectious syphilis outbreaks, intravenous substance use and involvement with Child and Family Services emerged as possible birthing parent co-factors in this population. This strongly suggests that poverty and social structural disadvantages play a significant role in the occurrence of congenital syphilis.

Lack of access to adequate prenatal care during pregnancy was present in over 50% of those assessed during the surveillance period. Inequities in prenatal care access are a known issue in Winnipeg, with research indicating that 15%–21% of pregnant persons residing in Winnipeg's inner core received inadequate

prenatal care from 2004–2005 to 2008–2009 (12). Those who are most vulnerable may have trouble accessing the healthcare system for a variety of reasons, including lack of transportation, language difficulties, concern for healthcare provider prejudices arising from racism and lack of knowledge about the healthcare system (13). Therefore, effective approaches to the management of rising rates of congenital syphilis must take into account the unique needs of the community. In Alberta, a program was implemented that provided prenatal care to street-involved individuals with the goal of determining the feasibility of decolonizing prenatal care by performing outreach through inner city community members (14). Study participants reported high satisfaction rates with the program, and particularly emphasized their appreciation that care providers were supportive and non-judgmental. In Winnipeg, collaborative efforts between public health and Indigenous community organizations are underway with the goal of establishing Indigenous-led approaches to sexually transmitted and bloodborne infection management; however, challenges in securing funding for Indigenous-led sexually transmitted and bloodborne infection strategies continue to be a significant challenge.

A subset of the population who did receive prenatal care were suspected to have been re-exposed to infectious syphilis sometime after their first negative prenatal screens. Several individuals were treated with documented reduction in serologic response during pregnancy, followed by serologic evidence of reinfection (i.e. rising titres after titres had decreased). It is also possible that some individuals with negative syphilis serology at first prenatal visit had already developed infectious syphilis at the time of initial screening, but were too early in their infection to have developed a detectable immune response. A report from New York City indicated that about one-third of their cases of congenital syphilis occurred during pregnancies that initially screened negative (15). These results highlight the importance of repeat infectious syphilis screening during pregnancy among those living in communities with known outbreaks and other risk factors. In light of increasing congenital syphilis rates, since early 2019, healthcare providers in Winnipeg have been advised to test all pregnant individuals for infectious syphilis at 28 weeks gestation and at delivery in addition to routine first prenatal visit screening.

Data on ethnicity was not collected consistently during the surveillance period. This represents an important missed opportunity. Racialized groups have been found to disproportionately bear the burden of congenital syphilis, with a report indicating that 85% of those who gave births to infants with congenital syphilis in Los Angeles were either Latin American or African American (16). In Canada, it is known that Indigenous individuals have barriers to accessing safe healthcare due to experiences of racism in a colonialist system (17). This highlights the importance of systematically collecting data on ethnicity in future surveillance of congenital syphilis to help ensure that subsequent interventions and care models are provided in culturally safe and appropriate manners. Collaboration with Indigenous and other racialized groups would be vital for ensuring this data is collected and reported in a respectful and non-stigmatizing way.

Strengths and limitations

This surveillance data had strengths and limitations. Data on ethnicity was not collected consistently. Data on intravenous substance use was collected through surveillance data chart review and was reliant on clients self-reporting this activity. As a result, it is possible that intravenous substance use was under-reported. Some potential outcomes of congenital syphilis such as spontaneous abortion were not captured. As well, syphilitic stillbirths were not included in the surveillance database in 2018 and possibly in early 2019, which could have resulted in an underreporting of congenital syphilis. Finally, changes in public health case investigation forms and methods of data entry over the surveillance period may have led to possible inconsistencies in birthing parent characteristic data reporting between the years. A strength of the study includes the use of population-based data with rigorously defined classifications of congenital syphilis cases. Also, the current co-director of the provincial public health laboratory, where all congenital syphilis cases are tested, is a paediatric infectious disease specialist, which should ensure maximal accuracy in the classification of cases.

Conclusion

Congenital syphilis rates are increasing in Winnipeg, alongside the increase in infectious syphilis rates among individuals during their childbearing years. Lack of access to prenatal care emerged as a major risk factor for congenital syphilis. The importance of repeat screening for infectious syphilis during pregnancy in high-risk populations was also demonstrated. Addressing systemic barriers to prenatal care and implementing appropriate culturally safe care models informed by the needs of the community may be effective interventions to contend with increasing congenital syphilis rates. Future studies and interventions should emphasize a community-based research approach, where early community involvement is a key priority to connect with individuals at highest risk. This will allow researchers to learn more about key factors that increase the risk of congenital syphilis and provide access to resources in a way that is most accessible for those who traditionally do not access key resources such as prenatal care. Without these changes in approach, traditional colonialist interventions may not be effective to address rising congenital syphilis rates.

Authors' statement

PB — Analyzed and interpreted the surveillance data, drafted first copy of the manuscript, data analysis and manuscript revisions
LGT — Analyzed and interpreted the surveillance data, drafted first copy of the manuscript, data analysis and manuscript revisions

AL — Investigation, provided clinical expertise, and provided manuscript revisions
GHC — Investigation, provided clinical expertise, and provided manuscript revisions
JB — Investigation, provided clinical expertise, and provided manuscript revisions
SYS — Provided academic and methodologic expertise, data analysis, and manuscript revisions
PP — Conceptualized the project, supervised

All authors contributed equally to this surveillance analysis.

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Competing interests
None.

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Annex: Manitoba Health and Seniors Care congenital syphilis case definitions

Laboratory-confirmed case—early congenital syphilis (within two years of birth)

- Identification of *T. pallidum* by dark-field microscopy, direct fluorescence antibody, or detection of *T. pallidum* DNA by nucleic acid amplification test (e.g. polymerase chain reaction; PCR) in an appropriate clinical specimen, or equivalent examination of material from nasal discharges, skin lesions, placenta or umbilical cord, or autopsy material of a neonate (up to four weeks of age)

OR

- Reactive serology (treponemal and nontreponemal) from venous blood (not cord blood) in an infant/child with or without clinical, other laboratory, or radiographic evidence consistent with congenital syphilis* but who has one or both of the following:
  - Rising syphilis serologic titres upon follow-up where there is evidence that the mother had a syphilis infection during pregnancy
  - Titres greater than or equal to fourfold higher than those of the mother when collected at the same time or within a week, in the immediate post-natal period

OR

- Reactive serology (treponemal and nontreponemal) from venous blood (not cord blood) in an infant/child with clinical, other laboratory, or radiographic evidence consistent with congenital syphilis* whose mother was seropositive or PCR positive for syphilis during pregnancy or at delivery

OR

- A child who does not meet the above criteria but has persistently reactive treponemal serology between 18 and 24 months of age (regardless of maternal treatment status and infectious status)

* Includes any evidence of congenital syphilis on physical examination (e.g. hepatosplenomegaly, consistent rash, condyloma lata, snuffles, pseudoparalysis), evidence of congenital syphilis on radiographs of long bones, a reactive cerebrospinal fluid (CSF) Venereal Disease Research laboratory test (VDRL), an elevated CSF cell count or protein without other cause.

Probable case—early congenital syphilis (within two years of birth)†

- Reactive serology (treponemal and nontreponemal) from venous blood (not cord blood) in an infant/child **without** clinical, laboratory, or radiographic manifestations of congenital syphilis whose mother had:
  - Untreated or inadequately‡ treated syphilis at delivery

OR

  - Evidence of reinfection or relapse in the pregnancy following appropriate treatment (e.g. rising nontreponemal titres at least four-fold higher)

† A persistent treponemal serologic reaction at 18–24 months of age confirms the diagnosis of congenital syphilis. An absent serologic reaction (both treponemal and nontreponemal tests) at, or before, 18–24 months of age excludes the case (i.e. it is no longer probable case).

‡ Inadequate treatment consists of any non-penicillin therapy or penicillin administered during pregnancy but less than 30 days before delivery, or despite treatment there has been an inadequate drop in nontreponemal titres. Note: the type of penicillin administered is important; it is usually benzathine penicillin in pregnancy, with the exception of treatment for neurosyphilis.

Laboratory-confirmed case—syphilitic stillbirth

- A fetal death that occurs after 20 weeks gestation with laboratory confirmation of infection (i.e. detection of *T. pallidum* DNA in an appropriate clinical specimen, direct fluorescent antibody or equivalent examination of material from placenta, umbilical cord or autopsy material).

Probable case—syphilitic stillbirth

- A fetal death that occurs after 20 weeks gestation where the mother had untreated or inadequately treated syphilis prior to delivery OR whose mother had evidence of reinfection or relapse in pregnancy following appropriate treatment (such as rising titres), with no other cause of stillbirth established

Source: https://www.gov.mb.ca/health/publichealth/cdc/protocol/syphilis.pdf

A descriptive study of syphilis testing in Manitoba, Canada, 2015–2019

Souradet Shaw[1]*, Pierre Plourde[2,3], Penny Klassen[4], Derek Stein[3,4]

Abstract

Background: In 2018, Manitoba had the highest reported rate of infectious syphilis in Canada, at over three times the national average. Infectious syphilis in Manitoba is centred on young, marginalized heterosexual couples in Winnipeg's inner-city. Subsequently, a public health crisis involving congenital syphilis emerged in Manitoba, just prior to the coronavirus disease 2019 pandemic. Testing and screening (in the case of pregnancy) for syphilis is thought to be an effective measure to reduce the incidence of syphilis and its sequelae. The aim of this study is to describe syphilis testing practices in the general population and amongst pregnant women, during a period of shifting syphilis epidemiology.

Methods: We used population-based syphilis testing data from Cadham Provincial Laboratory (Winnipeg, Manitoba) for 2015 to 2019. Directly age-standardized rates are reported, and Poisson regression used to model the determinants of testing rates. Rates of prenatal screening are also reported.

Results: From 2015 to 2019, a total of 386,350 individuals were tested for syphilis. The rate increased annually, from 462 per 10,000 population in 2015 to 704 per 100,000 in 2019, while the female-to-male ratio decreased from 1.8 to 1.6. Prior to 2019, the majority of pregnant women (approximately 60%) were screened once, during the first trimester; however, 2019 saw more women having more than two tests during the course of their pregnancy.

Conclusion: An overall increase in the number of individuals tested was observed, reflecting the increased rate of syphilis in Manitoba. Prenatal screening patterns shifted in 2019, likely in response to rising congenital syphilis numbers.

Affiliations

[1] Institute for Global Public Health, Department of Community Health Sciences, University of Manitoba, Winnipeg, MB

[2] Population and Public Health, Winnipeg Regional Health Authority, Winnipeg, MB

[3] Department of Medical Microbiology, University of Manitoba, Winnipeg, MB

[4] Cadham Provincial Laboratory, Winnipeg, MB

***Correspondence:**
souradet.shaw@umanitoba.ca

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Keywords: syphilis, testing, prenatal, surveillance

Introduction

Over the last decade, North America has seen an increase in the burden of infectious syphilis, the sexually transmitted infection caused by the bacterium *Treponema pallidium* (*T. pallidium*) (1–3). Between 2014 and 2018, crude infectious syphilis rates in Canada increased by 153%; from 7 to 17 per 100,000 population (4). Similarly, in the United States, total case counts for infectious syphilis in 2018 (N=35,063) were the highest observed since 1991, for a rate of 11 per 100,000 population; for an increase of 70% since 2014 (2). Although the resurgence of infectious syphilis was first observed primarily amongst gay, bisexual and other men who have sex with men (gbMSM) globally, the epidemic has subsequently spread to heterosexual populations marked by structural issues such as substance use, incarceration and poverty. This has resulted in a notable increase amongst women (2,5), which poses serious challenges to public health in terms of prevention, intervention and follow-up (5,6).

Sequelae of syphilis include neurosyphilis, which can be present during any stage of syphilis (4,7), and congenital syphilis–with potentially catastrophic outcomes for the infant which can also occur in pregnant individuals (8–10). Any occurrence of congenital syphilis in high-income countries is considered a sentinel event and is considered to be a "needless tragedy" (8,11). Increased congenital syphilis cases have been observed across North America (2,4,12,13), as the incidence of congenital syphilis is associated with the prevalence of infectious syphilis in women of reproductive age (2).

Evidence supports the screening of pregnant women as a highly effective and cost-efficient method to reduce the incidence of congenital syphilis (14,15). Screening and testing of non-pregnant adult and adolescent populations vulnerable to syphilis has also been recommended (16). In vulnerable populations, mathematical modelling has shown that syphilis screening programs with high coverage and intensity can reduce incidence (17), while suboptimal screening for syphilis has been associated with higher equilibrium incidence (18). Although studies have demonstrated high rates of prenatal screening in high-income countries, like the United States, high rates of screening may not be generalizable to broader (non-insured) populations, or to other countries (19). Thus, screening remains a recommended tool in the public health approach against syphilis; however, there is a dearth of population-based studies on actual rates of syphilis screening and testing, and how they may have changed in response to growing syphilis epidemics.

In 2018, Manitoba reported the highest rate of infectious syphilis in Canada, at 61 per 100,000 population (4), and was also on track to have the highest number of congenital syphilis cases (20). Given the lack of population-based studies on syphilis screening and test rates, along with increases in infectious syphilis and concern regarding its sequelae, we sought to describe syphilis testing practices in the general population, and amongst pregnant women during a period of shifting syphilis epidemiology.

Methods

Data sources

All syphilis testing in Manitoba is performed at Cadham Provincial Laboratory (CPL). Testing for sexually transmitted and bloodborne infections is provided free of charge for Manitobans (21). For routine syphilis screening and diagnosis, a reverse algorithm is used at CPL. Screening consists of an initial chemiluminescent assay for IgG and IgM antibodies to Treponemal antigens. Positive screening results are further tested by quantitative Rapid Plasma Reagin or Venereal Disease Research Laboratory testing for infectious syphilis. New positive cases receive an additional *T. pallidum* particle agglutination test as a confirmatory test. Manitoba also offers a prenatal screening program, which offers serological screening for a number of sexually transmitted and bloodborne infections.

In response to the growing number of congenital syphilis cases, provincial guidelines for syphilis screening of pregnant persons were revised to recommend screening at the first visit, 28–32 weeks, and delivery for all pregnant persons and monthly screening for persons with newly diagnosed syphilis that was treated during the current pregnancy. In addition, guidelines recommend screening for other sexually transmitted and bloodborne infections in the first trimester, including HIV, gonorrhea, chlamydia, and hepatitis B and C, when indicated.

Definitions

Routine testing

The laboratory received date was used to pull all syphilis tests from January 1, 2015 to December 31, 2019; this date was used to define year of testing. An individual was counted once in a calendar year, with the earliest test used as the index date; age at index date was used to define age groups. Population data were provided by Manitoba Health, Seniors and Active Living. The crude testing rate was calculated using the appropriate mid-point population as the denominator; the number of individuals was counted in the numerator. Cases missing any information on sex, age and region were excluded from analyses (accounting for less than 1% of the cases). Where appropriate, rates were stratified by regional health authority (RHA), administrative geographic areas constructed for the purposes of healthcare delivery. In Manitoba, there are a total of five RHAs (with 2020 populations reported) (22): Winnipeg Regional Health Authority (WRHA; n=791,284); Southern Health-Santé Sud (SH-SS: n=211,896); Prairie Mountain Health (PMH; n=172,641); Interlake-Eastern Regional Health Authority (IERHA; n=133,834); and Northern Regional Health Authority (NRHA; n=77,283).

Prenatal testing

Frequency of prenatal syphilis testing was based on the number of unique women giving birth per year, based on the date of delivery. For any given year, the number of women tested during each trimester was "back-calculated" using the date of delivery, with gestational age on the delivery record used to calculate trimesters. Weeks 0–13 were used to denote the first trimester; weeks 14–27 the second and 28 or more weeks the third trimester. The age of the mother was that on the date of delivery.

Analyses

For analyses describing routine syphilis testing, rates were age-standardized to the Canadian population from the 2012 Census; 95% confidence intervals (95% CI) were generated (23). Poisson regression models, with the logarithm of the population entered as an offset, were used to produce unadjusted and adjusted rate ratios and 95% CIs. Age group, sex and year of test were included in regression models. Crude annual rate of change was calculated using Poisson regression models. For prenatal screening, the number of women in Manitoba, by RHA and age group, was used in the denominator for age-specific calculations. The 95% CIs were estimated using the exact binomial distribution. Only women between 10 and 59 years of age were included in the numerator and denominator for prenatal screening calculations.

Results

In the five-year period from 2015–2019, a total of 485,808 syphilis tests were performed at CPL, representing 386,735 individuals tested. Excluding those with missing information

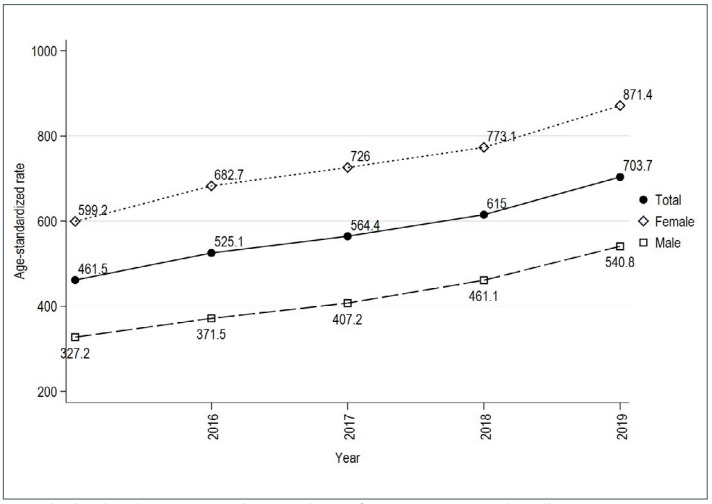
(on geography, sex and age), a total of 475,231 tests were performed on 386,350 unique individuals. Increases in testing were observed every year (**Table 1** and **Figure 1**). In 2015, a total of 62,252 individuals were tested (age-standardized rate: 461.5 per 10,000 population [95% CI: 457.8–465.1]); this increased to 94,578 individuals in 2019 (703.7 per 10,000 population; 95% CI: 699.2–708.2). This amounted to an annual increase of 10.5% over the study period ($p<0.0001$), while the annual female-to-male testing ratio decreased from 1.8 to 1.6. The ratio of samples to patients increased an average of 17% (from 1.15 to 1.35) from 2015 to 2019. **Figure 2** shows changes in age-standardized testing rates by RHA, over the study period. Although at the provincial level rates increased from 2015 to 2019, this increase was heterogeneous across RHAs; the largest increases were observed in NRHA and WRHA, while the rates in SH-SS stayed relatively similar across the study period.

Table 1: Frequency, age-standardized rates (per 10,000 population) and 95% CI, all syphilis testing performed at Cadham Provincial Laboratory, by sex, Manitoba (2015–2019)[a]

Determinants	Female			Male			Total			Female-to-male ratio
	Number	Age-standardized		Number	Age-standardized		Number	Age-standardized		
		Rate	95% CI		Rate	95% CI		Rate	95% CI	
Year										
2015	40,333	599.2	593.4–605.1	21,919	327.2	322.9–331.6	62,252	461.5	457.8–465.1	1.83
2016	45,952	682.7	676.5–689.0	24,842	371.5	366.9–376.2	70,794	525.1	521.2–529.0	1.84
2017	48,831	726.0	719.6–732.5	27,182	407.2	402.4–412.1	76,013	564.4	560.4–568.5	1.78
2018	51,967	773.1	766.5–779.8	30,746	461.1	456.0–466.3	82,713	615.0	610.8–619.2	1.68
2019	58,499	871.4	864.3–878.5	36,079	540.8	535.2–546.4	94,578	703.7	699.2–708.2	1.61
Total	245,582	730.5	727.6–733.4	140,768	421.6	419.2–423.8	386,350	573.9	572.1–575.7	1.73
Rate of change[b]	N/A	9.1%	8.8%–9.4%	N/A	13.1%	12.6%–13.5%	N/A	10.5%	10.3%–10.8%	N/A

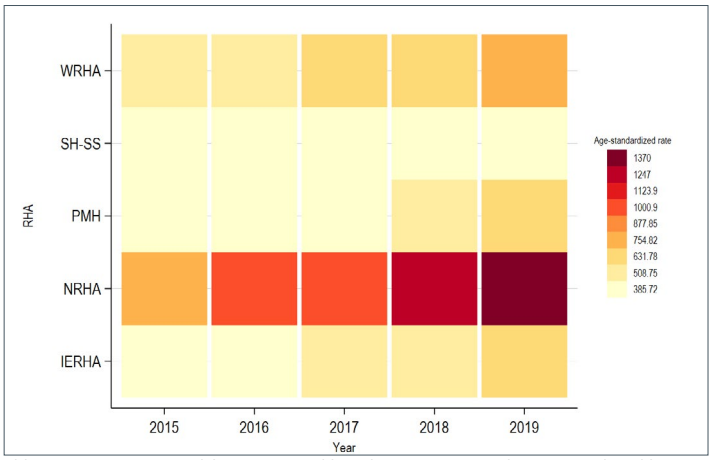
Abbreviations: CI, confidence intervals; N/A, not applicable
[a] Counts include total number of tests performed. 2012 Canadian population (from Statistics Canada) used as standard population
[b] Calculated by Poisson Regression using crude rates

Figure 1: Age-standardized rates[a] (per 10,000 population), individuals tested for syphilis in Manitoba, by sex and year (2015–2019, N=386,350)[b]



[a] Standardized to the 2012 Canadian population (from Statistics Canada). All rates per 10,000 population
[b] Counts include unique individuals tested for syphilis that year

Figure 2: Heatmap of age-standardized rates (per 10,000 population), individuals tested for syphilis in Manitoba, by Regional Health Authority and year (2015–2019, N=386,350)



Abbreviations: IERHA, Interlake-Eastern Health Authority; NRHA, Northern Regional Health Authority; PMH, Prairie Mountain Health; RHA, Regional Health Authority; SH-SS, Southern Health-Sante Sud; WRHA, Winnipeg Regional Health Authority

Results from multivariable Poisson regression demonstrated that adjusted for all other variables in the model, males tested at slightly more than half the rate of females (adjusted relative risk [ARR]: 0.57, 95% CI: 0.56–0.57; **Table 2**); the number of individuals tested for syphilis in 2019 increased by 50%, compared with 2015 (ARR: 1.52, 95% CI: 1.50–1.53); and testing rates amongst those 25–29 years of age were twofold higher relative to those 15–19 years of age (ARR: 1.99, 95% CI: 1.97–2.02). A time by sex interaction (not shown) revealed a significant interaction between year and sex ($p<0.0001$), suggesting that the proportion of men testing, relative to women increased over time.

Over the course of the study period, approximately 77,000 women received a prenatal syphilis test, with the annual number of tests stable at around 15,500 women per year (not shown).

Table 3 shows age and region-specific prenatal screening test rates; the per capita screening rate amongst women 10–59 years of age was 294.2 per 10,000 (95% CI: 292.2–296.3) from 2015 to 2019. Screening rates were highest in NRHA (487 (95% CI: 476–497) per 10,000), and lowest in IERHA (262 [95% CI: 256–269] per 100,000). There was a gradient in age-specific rates across RHAs, with the highest age-specific rates in the 25–39 year old age group, with the exception of NRHA. Within NRHA, the highest age-specific rate was seen in the 15–24 year old age group, at 1,184 (95% CI: 1,148–1,220) per 10,000. This was the highest age-specific prenatal syphilis screening rate across all age group and RHA-strata in our study. Through a series of Venn diagrams, **Figure 3** shows the distribution of prenatal tests, by trimester. Up until 2018, the majority of women who delivered received only one prenatal syphilis screening test, and this test was done during their first

Table 2: Crude rate (per 10,000 population), unadjusted and adjusted relative risks and 95% CI from Poisson regression, determinants of syphilis testing, Manitoba (2015–2019)

Determinants	Crude rate		URR	95% CI	ARR	95%CI
Sex						
Female	719.6	716.7–722.2	Ref	N/A	Ref	N/A
Male	417.5	415.3–419.7	0.58	0.58–0.58	0.57	0.56–0.57
Year						
2015	458.8	455.2–462.4	Ref	N/A	Ref	N/A
2016	521.7	517.9–525.6	1.14	1.13–1.15	1.14	1.13–1.15
2017	560.2	556.2–564.2	1.22	1.21–1.23	1.22	1.21–1.23
2018	609.6	605.4–613.7	1.33	1.32–1.34	1.33	1.31–1.34
2019	697.0	692.5–701.4	1.52	1.51–1.53	1.52	1.50–1.53
Age group						
Younger than 15	37.3	36.2–38.3	0.04	0.04–0.05	0.04	0.04–0.05
15–19	841.8	833.1–850.5	Ref	N/A	Ref	N/A
20–24	1,491.0	1,480.2–1,502.0	1.77	1.75–1.79	1.77	1.75–1.79
25–29	1,694.0	1,682.5–1,705.6	2.01	1.99–2.04	1.99	1.97–2.02
30–39	1,208.6	1,201.5–1,215.7	1.44	1.42–1.45	1.42	1.40–1.44
40-49	467.8	463.2–472.5	0.56	0.55–0.56	0.55	0.54–0.56
50 or older	168.3	166.7–170.0	0.20	0.20–0.20	0.20	0.19–0.20

Abbreviations: ARR, adjusted relative risk; CI, confidence intervals; N/A, not applicable; Ref, reference; URR, unadjusted relative risk

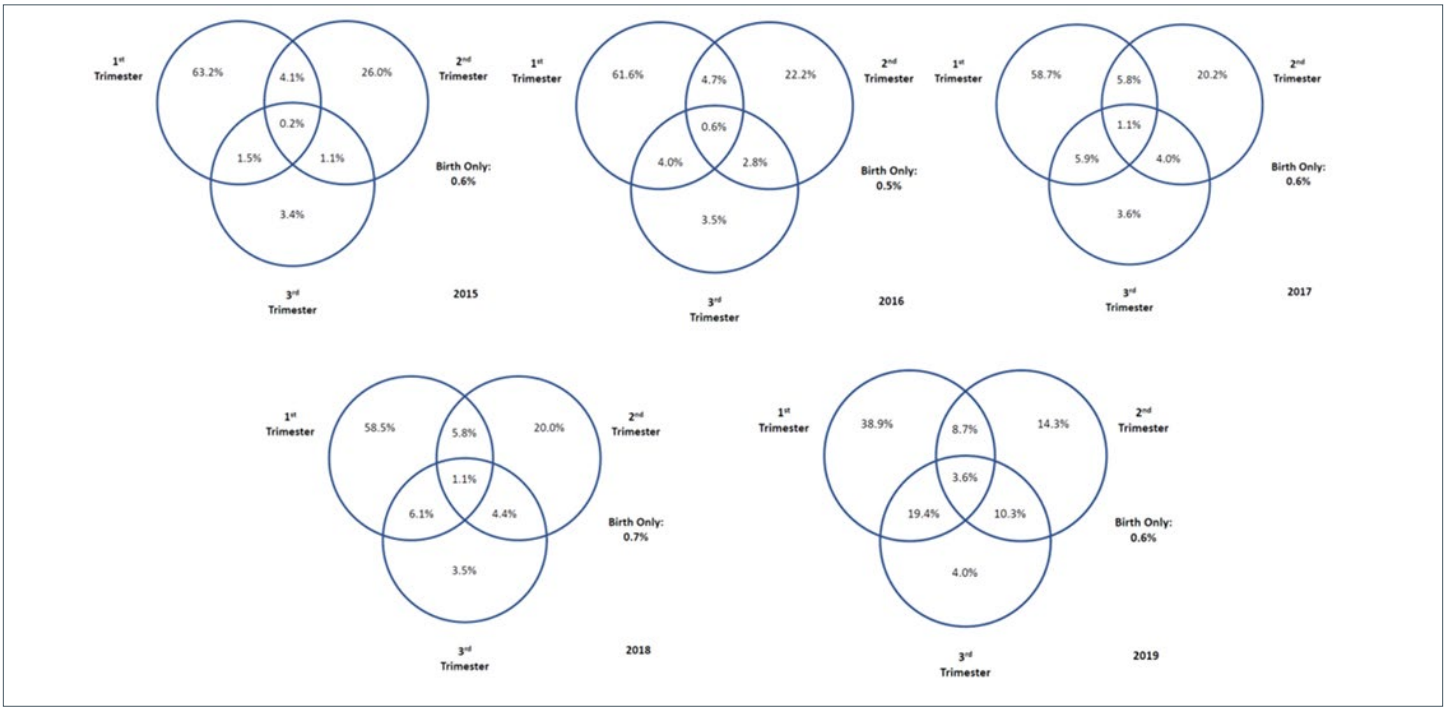
Table 3: Frequency and age-specific rates (per 10,000) of prenatal syphilis testing, Manitoba women (10–59 years old), by age group and Regional Health Authority (2015–2019)[a]

Age group (years)	WRHA			PMH			IERHA			NRHA			SH-SS		
	Number	Rate	95% CI	Number	Rate	95% CI	Number	Rate	95% CI	Number	Rate	95% CI	Number	Rate	95% CI
Younger than 15	33	1.0	0.7–1.5	11	1.4	0.7–2.5	13	2.3	1.3–4.0	59	10.6	8.1–13.7	13	1.1	0.6–2.0
15–24	6,465	264.3	258.0–270.7	2,386	464.5	446.4–483.0	1,936	500.4	478.9–522.6	3,595	1,184.0	1,147.8–1,220.8	3,679	529.0	512.5–545.9
25–39	32,912	766.2	758.2–774.2	6,704	819.0	800.3–838.0	4,155	782.3	759.6–805.5	4,387	1,107.1	1,076.4–1,138.4	9,289	945.9	927.6–964.3
40 or older	1,107	21.5	20.3–22.8	152	14.5	12.3–17.0	101	11.3	9.2–13.7	101	24.2	19.7–29.4	275	22.8	20.2–25.6
Total	40,517	268.9	266.3–271.5	9,253	292.0	286.2–297.9	6,205	262.2	255.8–268.7	8,142	486.5	476.2–496.9	13,256	329.7	324.2–335.3

Abbreviations: IERHA: Interlake-Eastern Health Authority; NRHA: Northern Regional Health Authority; PMH: Prairie Mountain Health; SH-SS: Southern Health-Sante Sud; WRHA: Winnipeg Regional Health Authority

[a] Counts include unique individuals screened for syphilis that year

Figure 3: Prenatal syphilis testing patterns, by trimester and year of infant birth, Manitoba women 2015–2019



trimester; from 2015 to 2018, this proportion ranged between 59%–63%. During this period, approximately 1% received at least one screening test in all three trimesters. A substantial shift in testing patterns was observed in 2019, with only 39% of women now receiving a screening test during their first trimester. The proportion receiving testing in the first and third trimesters increased from 1.5% in 2015 to 19% 2019. Similarly, the proportion receiving tests in both the second and third trimesters increased from 1.1% to 10% between 2015 and 2019. Finally, approximately 3.6% of women aged 10–59 years of age and who delivered in 2019 had a prenatal syphilis test in all three trimesters, a 20-fold increase from 2015.

Discussion

According to the Public Health Agency of Canada, while Canada as a whole showed a 153% increase in infectious syphilis rates between 2014 and 2018, Manitoba showed a 560% increase during the same time period (4). A recent study observed increasing rates of syphilis amongst women in Winnipeg as early as 2014, with outbreaks among young women associated with living in the inner-city, substance use and being co-infected with chlamydia (5). At the time of the study, although 24% of the women reported being pregnant, no congenital syphilis cases were detected (5). Subsequent to this study, Manitoba reported its first case of congenital syphilis in over 50 years in 2015 and another case was identified in 2017 (4). Congenital syphilis cases in Manitoba grew dramatically since that time, with at least 30 cases reported in 2020 in Winnipeg alone, for a crude rate of 3.5 per 1,000 live births (13).

Manitoba Health, Seniors and Active Living recommended that all pregnant women be screened for syphilis during their first prenatal visit (24); however, vertical transmission of syphilis can occur despite existing prenatal screening programs, as women can become infected between testing and delivery, and a diagnosis of syphilis may be missed by clinicians due to its non-specific clinical manifestations (12,14). Our results show a recent and substantial change in prenatal screening practice, with the proportion of women having only one test during pregnancy decreasing from 93% in 2015 to 57% in 2019. Conversely, the proportion of women having two or more tests increased from 7% in 2015 to 43% in 2019. Given the expanding syphilis epidemic in Manitoba, an even larger increase in screening rates in the third trimester could lead to the detection of more cases of congenital syphilis. Of some concern is the persistent proportion of women whose health records indicated the only prenatal screening they received was at the time of delivery. This proportion ranged from 0.5%–0.7% in any given year and over the course of the study period, amounted to approximately 400 women. Furthermore, recent evidence suggested a significant impact of the coronavirus disease 2019 (COVID-19) pandemic on testing rates and clinic visits for sexually transmitted and bloodborne infections in North America (25–27); for syphilis, this may have resulted in an increasing proportion of undiagnosed syphilis, leading to increased congenital syphilis. Monitoring of prenatal syphilis screening rates is thus critical to the goal of eliminating congenital syphilis. The United States Centers for Disease Control and Prevention suggested testing be offered in a variety of modalities, including walk-in clinics, telehealth and self-testing kits (28). Given the availability of population-based

testing data in Manitoba, future research should explore the impact of the COVID-19 pandemic on testing rates of syphilis and other sexually transmitted and bloodborne infections, and describe whether certain sub-populations were more likely to be impacted. The shift from gbMSM to heterosexual transmission of syphilis likely played a role in the declining female-to-male ratio, with both gbMSM and heterosexual men more likely to test for syphilis. This was supported by the year by sex interaction being statistically significant in regression models; monitoring trends in syphilis testing in males, before and after the arrival of COVID-19 will be an important surveillance objective.

Aside from congenital syphilis, another consequence of infectious syphilis is neurosyphilis, with the rise in incident syphilis infections in Manitoba expected to produce an increase in the number of neurosyphilis cases. A review of neurosyphilis cases in Alberta, Canada found approximately 30 cases of early and late neurosyphilis annually between 2015 and 2016 (7). Program data from CPL have reported 23 and 28 (up to September 2019) lab-detected neurosyphilis cases in 2018 and 2019, respectively, based on reactive cerebrospinal fluid–Venereal Disease Research Laboratory tests conducted with non-bloody cerebrospinal fluid (*Stein, personal communication*). Landry *et al*. found clear socio-demographic differences between those diagnosed with early and late neurosyphilis (7). Early neurosyphilis cases were more likely to be male, to be born in Canada, to be Caucasian and to report having sex with other men; in contrast, late neurosyphilis cases were also more likely to be male, but to be born outside of Canada and to identify as heterosexual (7). Future surveillance efforts to detect neurosyphilis are highly recommended.

Strengths and limitations

A strength of our study was that it was population-based; thus, testing rates were not restricted to certain sub-populations. Limitations include limited demographic, clinical and epidemiological information; further research should link individuals to other administrative healthcare datasets. Due to limitations in accessing incident syphilis rates, testing rates were not compared with incidence of syphilis by RHA; however, NRHA and WRHA have historically reported the highest rates of infectious syphilis (29).

Conclusion

Our results demonstrate that the number of individuals testing for syphilis increased between 2015 and 2019. Within Manitoba, increasing incidence of infectious syphilis received significant media exposure, while public health alerted practitioners to the necessity of syphilis screening (4); both media and public health communications likely contributed to increased testing rates. Future research should explore whether testing and screening are reaching the most appropriate populations, especially given the increases in congenital syphilis cases observed in Winnipeg.

Authors' statement

SYS — Conceptualized analyses, performed statistical analysis, and wrote the first draft of the manuscript
PJP — Interpreted findings and revised the manuscript critically for intellectual content
PK — Designed the extraction process, acquired data, performed initial statistical analyses and contributed to manuscript revisions
DS — Conceptualize analyses, interpreted findings and revised the manuscript critically for intellectual content

Each author met the ICMJE criteria for authorship. All authors approved the final version of the manuscript.

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Competing interests

None.

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Lessons from management of syphilis in Nunavut, Canada, 2012–2020

Ameeta E Singh[1]*, Kethika Kulleperuma[2], Jenny Begin[2], Jessica DeGuzman[3], Diane Sammurtok[4], Obed Anoee[4], Theresa Koonoo[2], Jasmine Pawa[2,5]

Abstract

Background: Nunavut, part of Inuit Nunangat, is a geographically vast territory in northern Canada, with a population of over 38,000 people. Most (85%) of the population identify as Inuit. Nunavut has experienced a significant rise in heterosexual infectious syphilis cases since 2012. Management of communicable diseases, including syphilis, is challenging due to high staff turnover and long delays in specimen transport times. Social determinants of health are also an important contributor. The aim of this study is to describe the epidemiology and program elements for infectious syphilis from 2012–2020 and to highlight beneficial interventions.

Methods: Syphilis is a notifiable disease in Nunavut with all cases reported to the Territorial Department of Health. Cases were staged by a medical consultant. Data were analyzed and released in public reports as part of the public health program.

Results: From 2012 to 2020, 655 infectious syphilis cases were reported, with 53% of reported cases among females. Infection rates were highest in 20 to 39-year-olds. There was significant variability in reported cases over this time period by geographic region, with the majority of infectious cases reported from the Kivalliq region. Despite 48 reported cases in pregnancy, no confirmed congenital syphilis cases were identified. Program staff identified strengths of the response as well as ongoing needs, such as plain language resources available in multiple languages.

Conclusion: Despite the logistical challenges with syphilis management in the territory, the overall outcomes have been positive, with no confirmed congenital cases identified. We attribute this to a coordinated effort by multiple partners including key actions by public health nurses and community health representatives.

Affiliations

[1] Division of Infectious Diseases, University of Alberta, Edmonton, AB

[2] Government of Nunavut, Department of Health, Iqaluit, NU

[3] Government of Nunavut, Department of Health, Rankin Inlet, NU

[4] Government of Nunavut, Department of Health, Arviat, NU

[5] Dalla Lana School of Public Health, University of Toronto, Toronto, ON

***Correspondence:**
ameeta@ualberta.ca

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Keywords: syphilis, Canada, Arctic region, epidemiology, public health, Community Health Representative

Introduction

Nunavut, part of Inuit Nunangat, is a geographically vast northern territory in Canada with a population of over 38,000 people, of whom 85% identify as Inuit (1). Nunavut has experienced a significant rise in heterosexual infectious syphilis cases over the last few years. Prior to 2012, five or fewer cases per year were identified; in 2016–2018, more than 100 cases per year were identified; far higher than the national rate. In 2017, the Department of Health contracted an infectious diseases specialist to assist with the outbreak. Following a 2017 review of syphilis prevention and control in the territory, several changes were made to the syphilis program in Nunavut including the revision of territorial syphilis guidelines, additional training for healthcare and public health staff, enhanced prevention activities by community health representatives (CHR) and staging and assistance with management and follow-up of all syphilis cases by the medical consultant. Since many pregnant women are transferred out of territory (especially from the Kivalliq region) for delivery, the medical consultant has endeavoured to prepare summary letters on all cases with positive syphilis serology to facilitate care in the receiving province.

Syphilis management in Nunavut is particularly challenging for several reasons, including the vast geographic area with triage of cases requiring complex care to three different provinces in Canada, the remote locations of many communities resulting in long delays in specimen transport times and inconsistent staffing. Social determinants of health are relevant not only to syphilis but to the overall health status of Inuit. Work by Inuit Tapiriit Kanatami, Canada's National Inuit Organization, flagged the importance of self-determination and of building on the strengths of Inuit culture and language (2). Despite these challenges, through the efforts of community members and health staff, we have not observed some of the adverse outcomes reported in other jurisdictions, such as higher rates of congenital syphilis cases.

Our objective was to describe the epidemiology of infectious syphilis in Nunavut and to describe the factors that may have contributed to the observed outcomes. This work is conducted and shared as part of public health practice, including program planning and evaluation, not as formal research.

Methods

Healthcare infrastructure and flow

A variety of public governmental, non-governmental resources and published literature were accessed to describe the flow of healthcare and public health services in Nunavut and to outline the roles and responsibilities of health personnel in Nunavut.

Syphilis testing

Similar to other Canadian jurisdictions, symptomatic persons access diagnostic services while asymptomatic individuals may be offered syphilis testing as a part of screening or case finding (via contact tracing and notification) processes. Syphilis is a notifiable disease in Nunavut, with all cases reported to the territorial Department of Health. Serologic tests are used to diagnose syphilis in Nunavut using a reverse sequence algorithm. The initial screen is with a syphilis enzyme immunoassay (Architect Syphilis TP Chemiluminescent Microparticle Immunoassay, Abbot Laboratories, Abbott Park, Illinois, United States). A positive enzyme immunoassay is followed by a quantitative rapid plasma reagin (RPR BD Macro-Vue™ RPR test, Becton Dickinson Microbiology Systems, Mississauga, Ontario, Canada) and the first time a syphilis enzyme immunoassay is positive, it is confirmed using a *Treponema pallidum* particle agglutination assay (TPPA; Serodia®-TPPA, Fujirebio Diagnostics Inc, Seguin, Texas, United States). Syphilis is treated as per the Nunavut sexually transmitted infection treatment guidelines (3) and positive results are reported to local, territorial and national public health authorities as per the territorial notifiable disease guidelines (3).

Case reporting and classification

All cases of syphilis in Nunavut are reported by healthcare providers to the Regional Communicable Disease Coordinator (RCDC) and territorial epidemiology team using a standardized case definition form. The following information is routinely entered into a surveillance database: name; date of birth; sex; geographic region; healthcare number; reason for testing; ethnicity; details on prior syphilis history; pregnancy status; results of syphilis laboratory tests; treatment provided date; and staging. Although routinely collected on the case definition form, the following information is not routinely entered into the database: presence or absence of symptoms; risk factors; and partner information. Completed forms were sent to a medical consultant over the study period and staging was completed using Nunavut Case Definitions (see Supplemental Table: Nunavut Surveillance Case Definitions for Syphilis) (3). Confirmation of case staging is then returned to the RCDC and territorial epidemiologist, who work closely with the Territorial Communicable Disease Specialists (TCDS) and Public Health Officers as required. Contact tracing and other public health preventive measures are conducted as per territorial guidelines.

Data collection and analysis

National and territorial infectious syphilis case counts are extracted from the national notifiable disease dataset and territory's syphilis surveillance database, respectively. National and Nunavut regional population data is extracted from Statistics Canada (4) and Nunavut Bureau of Statistics, respectively. All rates are standardized using the 2011 standard population. Data are analyzed using Microsoft Excel and released in public reports as part of the public health program.

Results

Healthcare infrastructure and flow of services

Syphilis diagnosis, management and prevention: The roles and responsibilities of the range of health personnel who provide clinical and preventive services for persons potentially affected or infected with syphilis in Nunavut are summarized in **Table 1**. Nunavut's healthcare system relies heavily on shorter-term nursing contracts and locum physicians, many of whom come from outside the territory (5). Of 25 communities in the territory, three (Iqaluit, Cambridge Bay and Rankin Inlet) have full-time physicians while smaller communities are typically serviced by physicians on a rotating basis (5). For most communities, twenty-two community-based clinics, staffed primarily by community health nurses (CHNs) (registered nurses working in an expanded scope of practice), offer primary care and acute services (5). Locum staff typically stay for relatively short periods and turnover of both physicians and nurses is very high with the vacancy rate in some regions is as high as 71% (3). Through this process, medical directives for CHNs and public health nurses (PHNs) were reviewed for opportunities to better share work.

Table 1: Roles and responsibilities of healthcare staff providing prevention and care for persons potentially affected by or infected with syphilis[a]

Type of provider	Roles
Most responsible provider (e.g. registered nurse, medical doctor, midwife)	Assess individual Conduct testing Provide treatment Complete Syphilis Report Form or Syphilis Report Form for infants and STI Contact Investigation form and submit to RCDC Notify, assess and treat contacts
Public health nurse	Assess patient Conduct testing Arrange treatment Coordinate partner notification
Regional Communicable Disease Control nurse	Receive and monitor positive test results and follow-up serology for syphilis Receive Syphilis Notification Forms from MRP Ensure syphilis treatment and follow-up completed by MRP Coordinate transfer of medical information/ recommendations to MRP Consult with STI Medical Consultant as needed for management of cases Ensure syphilis staging completed by STI Medical Consultant and submitted to TCDS and epidemiologist
Community Health Representative	Promotes health and wellbeing in the community by responding to community public health needs and supporting regional and territorial public health priorities by assisting individuals to develop skills and knowledge through providing public health information and education for heath
Territorial STI Medical Consultant	Providing expert clinical advice and support to the Department of Health and individual practitioners regarding the management of STIs, especially syphilis including: Staging, treatment and follow-up Support for the territorial communicable disease program on the topic of STIs and controlling the syphilis outbreak Consultation on difficult or complicated syphilis cases Developing consultation letters for prenatal women diagnosed with syphilis Consultation and recommendations for follow-up of the infants born to syphilis positive mothers
Epidemiologist	Analyses and interprets syphilis data Develops reports
Territorial Communicable Disease Specialist	Coordinate out of province transfer of information for cases and contacts Works with MOHs/PHOs on territorial protocols
Medical Officer of Health(s)/Public Health Officer(s)	Provides public health expertise to support the key operations of health protection, disease prevention and health promotion Provides leadership and expertise to the public health unit, including health protection and the population health unit Establishes and maintains public health standards and best practices as well as advocates for the preservation and improvement of the health of Nunavummiut

Abbreviations: MOH, Medical Officer of Health(s); MRP, Most Responsible Provider; PHN, public health nurses; PHO, Public Health Officer(s); RCDC, Regional Communicable Disease Coordinator; STI, sexually transmitted infection; TCDS, Territorial Communicable Disease Specialists

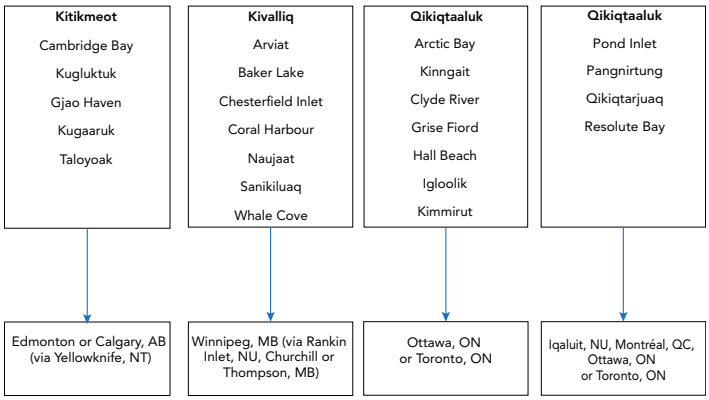
[a] This summary is focused on the care for syphilis and that there are many who work in health system roles who are not acknowledged here. This includes, but is not limited to, administrative staff; medical travel programs; policy, finance, communications and human resources team members

Community health representatives are invaluable members of the health services team (5). They have important expertise and experience in understanding the communities they work in, including being able to work in and connect with individuals in Inuktitut. A federal CHR program was implemented in 1962 by the Medical Services Branch of Health and Welfare Canada (6). Within the territorial Department of Health for Nunavut, there currently 33 available positions with 27 full-time CHRs, of whom all but two are female. While the principal role of the CHR in recent years has been to focus on health education, promotion and infection prevention, the specific role varies from community to community. In Nunavut, CHRs have been mobilized to assist with the response to syphilis since the start of the outbreak. Specific activities have included hosting information sessions at high schools, providing access to condoms and information regarding birth control options and developing health promotion materials. Other activities have included hosting health information booths, assisting with translation services and providing support in navigating the health system. In some communities, hosting monthly radio shows has facilitated the provision of information and allowed community members to phone in and ask questions.

Persons requiring additional medical services are typically transported out of territory, sometimes via another in-territory location, as summarized in **Figure 1**.

Syphilis testing: Specimens from the Kitikmeot region were submitted to DynaLife Laboratories (Edmonton, Alberta) and from the Qikiqtaaluk and Kivalliq regions to the Qikiqtani General Hospital Laboratory (Iqaluit, Nunavut). Since transport from remote communities only occur on certain days of the week depending on flight schedules and may require a transfer of specimens at another in-territory hub, the time to test results can be very prolonged. In smaller communities, the time to

Figure 1: Examples of patterns of patient travel from Nunavut to out of territory destinations[a]



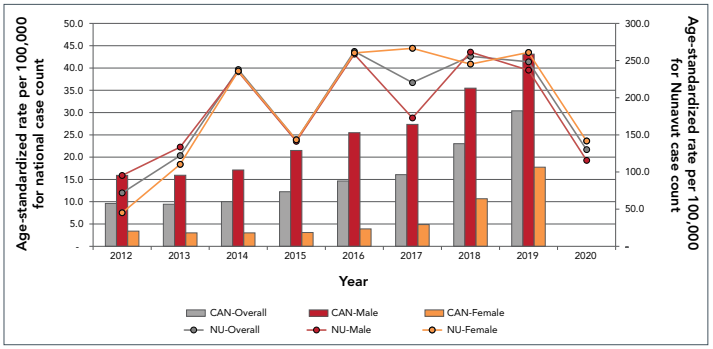
Abbreviations: AB, Alberta; MB, Manitoba; NU, Nunavut; NT, Northwest Territory; ON, Ontario; QC, Québec
[a] See reference (7)
Note: The above is not an exhaustive list of communities in Nunavut but provides examples of travel patterns. It is also important to note that the community names may be out of date (for example Kinngait was formerly known as Cape Dorset)

syphilis test results often varies from 8–12 days and can be up to a few weeks. In addition, pregnant women who required transport outside of territory were often tested or re-tested in the receiving province resulting in a variability in test results, especially the RPR, due to differences in testing algorithms and types of tests used.

Epidemiology

A total of 655 cases were reported in Nunavut from 2012–2020, with 95% of reported cases among persons of Inuit ethnicity (similar to the general population with 85% identifying as Inuit). The age-standardized rates of infectious syphilis by sex in Nunavut and Canada (**Figure 2**) show territorial rates well above the national rates for both males and females. In contrast to the national rates, where age-standardized rates were much higher among males, the territorial age-standardized rates were similar for males and females. **Figure 3** shows the age-standardized rates of infectious syphilis in Nunavut by region and year and highlight the geographic spread and relative case growth across the territory and the three regions. Since there were five or fewer annual cases reported before 2012, with the observation of increased infectious cases in 2012 (more than 20 cases), the outbreak was declared in 2012 with cases first reported in Iqaluit (**Figure 4**). Initially the outbreak was centered in the Qikiqtaaluk region and then shifted to the Kivalliq region. Since new infectious cases continue to be observed, the outbreak is currently considered to be ongoing. Qikiqtaaluk had more than 50% of the total Nunavut population and has been reporting cases since 2012, with notable fluctuations over time. Case growth is Kivalliq region increased dramatically in 2016 but appeared to be declining since then. Overall, 53% (n=349) of cases were reported among females with the overall male-to-female ratio in Nunavut of 0.9 (range 0.7-1.0) (**Table 2**). The staging of cases was classified as primary in 54% (n=356), secondary in 18% (n=117), early latent in 27% (n=175) and unknown in 1% (n=7).

Figure 2: Age-standardized rates of infectious syphilis by sex in Nunavut and Canada, 2012–2020



Abbreviations: CAN, Canadian; NU, Nunavut

Figure 3: Age-standardized rates of infectious syphilis in Nunavut by region and year, 2012–2020 (n=655)

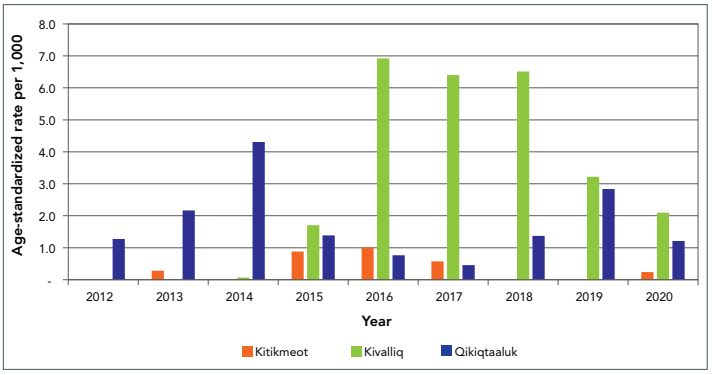
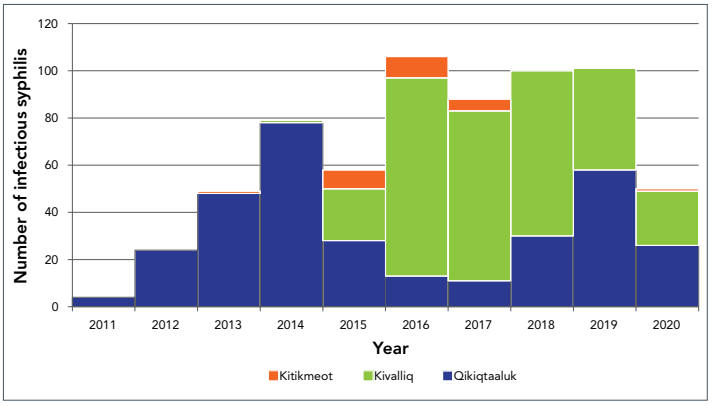


Figure 4: Epidemiological curve of infectious syphilis in Nunavut by region, 2011–2020



Cases were distributed across all age groups with the majority of cases between 20 and 39 years of age. During this time, 48 pregnant women were diagnosed with infectious syphilis in Nunavut, with over 66% cases in the Kivalliq region, over 30% in the Qikiqtaaluk region and fewer than 5% in Kitikmeot region (exact case counts are not available due to low reported numbers). All pregnant women were treated in accordance with Nunavut guidelines (3). With regards to neonatal outcomes, 40 of the infants were classified as non-cases (maternal transfer of antibodies only), four were either therapeutic/

Table 2: Infectious syphilis cases[a] in Nunavut by year, sex, male-to-female ratio, age group, syphilis stage and region, 2012–2020

Description	Region			
	Nunavut	Kitikmeot	Kivalliq	Qikiqtaaluk
Total case count	655	24	315	316
2012	24	0	0	24
2013	49	<5	<5	48
2014	79	<5	<5	78
2015	58	8	22	28
2016	106	9	84	13
2017	88	5	72	11
2018	100	0	70	30
2019	101	0	43	58
2020	50	<5	20+	26
Sex				
Female	349 (53%)	14	176	159
Male	306 (47%)	10	139	157
Male-to-female ratio	0.9	0.7	0.8	1.0
2012	1.7	0	0	0.6
2013	1.2	<5	<5	0.8
2014	0.8	<5	<5	1.2
2015	0.9	1.7	0.8	1.2
2016	0.9	0.8	1.4	0.4
2017	0.6	4.0	1.8	0.8
2018	1.0	0	1.1	0.9
2019	0.9	0	0.8	1.3
2020	0.7	<5	1.9	1.4
Age group				
Younger than 15 years	5 (1%)	<5	<5	<5
15–19 years	92 (17%)	7	65	38
20–24 years	110 (22%)	5	89	49
25–29 years	143 (22%)	9	59	79
30–39 years	147 (24%)	<5	64	93
40 and older	158 (14%)	<5	35	55
Staging				
Primary	356 (54%)	13	178	165
Secondary	117 (18%)	<5	49	64
Early latent	175 (27%)	7	88	80
Documentation error	7 (1%)	0	0	0

[a] Case counts fewer than five were not reported

spontaneousabortion or stillbirth (not due to syphilis), three cases of probable congenital syphilis cases and one case was awaiting follow-up information at the time of writing. Of the cases classified as maternal transfer, 23 (57%) of the pregnant women were treated before 20 weeks gestation and four (10%) after 30 weeks gestation.

Discussion

After observing little or no endemic transmission of syphilis, Nunavut has experienced a significant rise in infectious syphilis cases since 2012, with numbers/rates peaking in 2016 and remaining stable each year until 2019. This increase was followed by a decline in 2020. The reason for the observed decline in 2020 was not clear as syphilis testing data were not available for the observed time period, but numbers/rate are anticipated to have declined due to reduced interactions with the healthcare system in the territory related to the coronavirus disease 2019 (COVID-19) pandemic. Similar trends were reported in other jurisdictions (8). Another possible explanation is that the prevention measures enacted during the COVID-19 pandemic, such as stay-at-home recommendations and closing of non-essential businesses, may have resulted in a change in sexual behaviour related to physical distancing and therefore a true decline in cases (8).

The outbreak of infectious syphilis was principally transmitted heterosexually in contrast to the overall Canadian rate, which is higher among males. Consequently, 48 pregnant women were diagnosed with infectious syphilis during the study period, with approximately 2/3 from the Kivalliq region. The women with infectious syphilis during pregnancy from the Kivalliq region were typically flown to Winnipeg at 34–36 weeks gestation and remained there until delivery. Most of the pregnant women from the Kivalliq region were from very small communities (fewer than 2,000 individuals) that may have a small community health centre with variable levels of medical staff support and services. The main hub, Rankin Inlet, has a birthing centre with midwives who provide support for uncomplicated deliveries but since infants born to mothers treated for infectious syphilis during pregnancy require assessment for congenital syphilis by experienced paediatricians, all these women were transferred to Winnipeg for delivery. In addition, the birthing centre in Rankin Inlet is presently closed due to staffing considerations. Women who were diagnosed with infectious syphilis after 20 weeks gestation were transferred to Winnipeg for monitoring as treatment may result in a Jarisch Herxheimer reaction, which can result in the premature onset of labour (9). Pregnant women in the Qikiqtaaluk region are routinely transferred to Qikiqtani General Hospital for treatment (at greater than 20 weeks gestation) and delivery. Interestingly, two recent retrospective case series of pregnant women diagnosed with syphilis and treated in Winnipeg and Alberta reported no serious maternal

or fetal events following treatment (10,11). Nunavut medical travel accounts for 20% of health expenditures in Nunavut due to the relative absence of roads and the reliance on air travel (7); this is relevant in the context of pregnant women >20 weeks gestation with infectious syphilis who are routinely transferred to a major centre for treatment. The Winnipeg and Alberta studies, while small, do not support the routine practice of admission to hospital for treatment of infectious syphilis in late pregnancy. Given the small retrospective nature of the studies, however, these studies may not have identified a subset of women who may be at risk for serious adverse events.

With regards to the neonatal outcomes of infectious syphilis in pregnancy, we found no cases of confirmed congenital syphilis. Vertical transmission of syphilis occurs in all stages of syphilis and in each trimester of pregnancy, but risk of transmission increases with earlier syphilis stage and later gestational age (9). Fetal infection occurs in more than 50% of untreated early syphilis (9). The low rate of adverse neonatal outcomes observed in Nunavut can be attributed to multiple factors including the routine testing of all/majority pregnant women for syphilis in the early pregnancy and prompt treatment if syphilis is diagnosed. The majority (or perhaps all) of the women undergo syphilis testing, often in early pregnancy, due to the small size of the communities and also the women will typically access services as they usually require transfer out of most communities for delivery. Studies have consistently shown that early and adequate maternal treatment during early pregnancy confers the lowest rates of congenital syphilis and adverse pregnancy outcomes (12,13). In addition, Nunavut syphilis guidelines recommend routine re-screening for infectious syphilis at 24–28 weeks gestation, thus enabling the earlier identification and treatment of reinfection. In addition, to minimize the impact of the laboratory variation in RPR results, all infectious syphilis cases returning from out of territory have a repeat RPR collected upon return so that this result can be used to inform future follow-up.

All members of the health services team play important roles in the care and prevention of persons with syphilis. While front line providers (such as CHNs) are critical in doing the initial assessments and coordinating treatment, the RCDC is essential in ensuring that the treatment and serologic follow-up occur and that partner(s) are contacted and offered testing and treatment. The RCDC, in consultation with the territorial syphilis medical consultant, also ensures that relevant medical information is relayed to other providers who may be involved in the care of the patient. The TCDS consultant (who is often also a nurse) ensures that relevant information is relayed for clients for out-of-territory care and follow-up, and works with the Medical Officer of Health(s)/Public Health Officer(s) on territorial protocols. The territorial epidemiologists' role is to provide accurate and timely epidemiologic data, which is essential for program planning. Nunavut has experienced a high turnover of both permanent and locum temporary health services staff over the years and this has been particularly challenging during the syphilis surge and the COVID-19 pandemic. The update of Nunavut syphilis guidelines, one-page algorithms and protocols has helped with to ease these transitions.

The role of the CHRs cannot be underestimated. To quote the Royal Commission on Aboriginal Peoples: "One of the most successful programs involving Aboriginal people in promoting health of Aboriginal people is the community health representative program" (14). In many northern and isolated communities including in Nunavut, the turnover of health professionals, is extremely high; the CHR provides the only continuity of care in some communities. "The CHRs are the people that the community members trust and relate to in terms of health information and services." (14). There is a paucity of data in Canada on the impact of the role of CHRs in the prevention and control of communicable diseases, including syphilis. Perhaps the closest analogy in the published literature is the impact of the role of peer workers. A systematic review found that peer education interventions are associated with a three-fold increase in HIV testing with a consistent impact on behavioural change for over 24 months (15). Peers provide informational, emotional and affiliation support for utilization of testing services (16).

Discussions about communicable disease specifically and health status more broadly need to be considered in the context of social determinants of health. Inuit Tapiriit Kanatami has created Inuit-focused resources to inform organizations and government, including public health practice, on key social determinants of health for Canadian Inuit (2). In discussing health challenges faced by Inuit, researchers and others need to be mindful of the strength, richness and wealth of knowledge encompassed in Inuit culture. The impact of colonialism, including residential school programs, has been far-reaching and deeply impactful (17). The first government school for Inuit opened in Chesterfield Inlet in 1951. In June 1964, it is estimated that 75% of Inuit children and youth aged 6–15 years were enrolled in these schools as of 1964 and that at least 3,000 Inuit who attended residential schools are alive today. Westernization and colonization have been identified in the literature as negative influences on sexual health because of the loss of the accumulated wisdom and knowledge of Inuit regarding the life cycle, reproductive health and family planning, as well as traditional ways of life that incorporated both practical skills and cultural principles (18,19). These have contributed to significant disruptions to family structures and relationships. Sexual abuse, including of children, is a significant concern. Organizations such as Pauktuutit have developed resources to try to support individuals and organizations in addressing this (20). In a recent survey of Inuit youth, most did not report using the Internet for sexual health information (18) but to quote one of the CHRs, social media often provides a "wrong message" about relationships. In the same survey, parents/caregivers were reported as the preferred sources of knowledge about sexual health and relationships among youth respondents. It was also noted that most households in Nunavut do not have internet

access and only use public browsers that may inadvertently block sexual health content while intending to block pornographic content (18). In addition, social determinants of health, including inadequate, overcrowded housing and high unemployment rates, are closely connected to substance use in the territory (21). The substances most often used are alcohol and marijuana, and binge drinking is common. While little Canadian data are available, persons who use drugs are more likely to report stigma and mistrust of the healthcare system, which may contribute to decreased healthcare utilization and reluctance to identify and locate sex partners (22).

Community health representatives and other providers have commented on the importance of the choice of language when providing health services in Nunavut. Many health promotion programs in public health programs are developed by individuals whose first language is English. The majority of Nunavut residents identify Inuktitut as their first language. Language structure, vocabulary, sound systems, grammar and other considerations are important and affect meaning and communication. This is especially true when referring to health-related and sexual health concepts. Resources such as the "Tukisiviit: Do You Understand?" project with a sexual health glossary has been described as very helpful (23).

Small communities pose both benefits as well as challenges with the management of syphilis. Persons infected with syphilis may be concerned about the privacy of their health information in small communities and as such, may avoid coming to the local health centre where a relative may be working. In addition, access to medical services at most mines is limited which may result in a delay in diagnosis and treatment of cases and contacts. The remote nature of many communities results in a very long lag between specimen collection and the reporting of results. This can lead to ongoing transmission of the infection as well as disease progression. One of the ways that this delay could be mitigated is with POCT for the detection of syphilis. Currently there is no Health Canada approved point-of-care test (POCT) syphilis available. A Canadian Institutes of Health Research-funded initiative has commenced in Nunavut and Nunavik (a region comprising the northern third of the province of Québec) to evaluate the acceptability, performance and utility of a dual syphilis POCT (24); however, this work has been delayed due to the COVID-19 pandemic and staffing considerations. Improving the education of those at risk of acquiring the infection is also important and, at the request of the CHRs, work is underway to develop educational posters that include Inuktitut translations of text and visual displays of syphilitic lesions. We anticipate that this and other such education interventions will promote the utilization of sexually transmitted infection services in communities as similar peer-led initiatives have been successful in other settings (25–27). The utility of mobile health interventions, such as text message reminders for testing, has not been evaluated in Nunavut but such initiatives have been shown to increase syphilis and HIV testing, link persons to services and achieve behavioural change (28–32).

Ongoing work is needed to continue to improve community engagement, to deliver healthcare and public health services in a way as consistent with truth and reconciliation goals as possible, to incorporate more information on the CHRs and culturally-appropriate approaches to healthcare into the academic literature, and to end the current syphilis outbreak. Improved information on the experiences of individuals accessing healthcare and public health services is also needed.

Conclusion

Despite the logistical challenges with syphilis management in the territory, the overall outcomes have been positive, with no confirmed congenital cases identified. We attribute this to a coordinated effort by multiple partners including key actions by PHN and CHR.

Authors' statement

AS — Conceived of the report, drafted and revised the paper
JP — Conceived of the report
KK — Analysed and interpreted the data

All authors reviewed drafts and contributed to revision of the manuscript.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

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Exploring management of antenatally diagnosed fetal syphilis infection

Margot Rosenthal[1]*, Vanessa Poliquin[1]

Abstract

Background: The incidence of syphilis among Canadian women of childbearing age has risen dramatically in the past decade, with a resurgence of infants born with congenital syphilis. While guidelines exist to guide maternal infection during pregnancy, there is little evidence available to guide management in situations where the developing fetus is found to be severely affected.

Case review: Our patient presented in the second trimester of her pregnancy as syphilis contact. Positive serologic tests (venereal disease research laboratory titre of 1:64) and a chancre suggested primary infection. Ultrasound demonstrated a fetus at 19+3 weeks gestation with hydrops fetalis and a markedly abnormal brain. Amniocentesis confirmed congenital syphilis infection on polymerase chain reaction testing. After nine days of intravenous penicillin G, the fetal status had worsened, and the family ultimately chose a medical termination of the pregnancy.

Discussion: Evolving ultrasound technology has allowed us to identify severely affected fetuses, who may historically have been delivered stillborn. Following routine syphiliotherapy with benzathine penicillin, these abnormal ultrasound features may take weeks or months to reverse, which poses a challenge in prognostication and counselling. Case reports data suggests intensive treatment with intravenous penicillin may be effective in severe cases where fetal hydrops is present.

Conclusion: This case highlights the potential morbidity of fetal syphilis infection and underscores the paucity of current literature. Information sharing will be essential to build a modern knowledge base on treating this ancient disease.

Affiliation

[1] Department of Obstetrics, Gynecology and Reproductive Sciences, Max Rady College of Medicine, University of Manitoba, Winnipeg, MBty of Toronto, Toronto, ON

***Correspondence:**
umrose32@myumanitoba.ca

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Keywords: syphilis, fetal syphilis, pregnancy, ultrasound findings

Introduction

Syphilis infections among Canadian women of childbearing age has risen dramatically in the past decade, with resurgence of affected pregnancies and infants born with congenital syphilis (1). Vertical transmission from transplacental passage of spirochetes occurs in 50%–80% of untreated patients, with transmission rates highest with primary and secondary infections (2). Affected gravidas are at increased risk of stillbirth and preterm delivery (3). Antenatal treatment with intramuscular benzathine penicillin G is highly effective at preventing congenital syphilis (4). In a minority of cases, sequelae of fetal infection can be detected by ultrasound (5). There is a paucity of evidence available to guide clinicians caring for these affected pregnancies.

Case presentation

We present the case of a 29-year-old G4P3 (fourth pregnancy; three deliveries) female called to care in her rural community in Manitoba, Canada as a syphilis contact. She presented pregnant with an unsure last menstrual period, with no significant medical or surgical history. Given her risk as a sexual contact, she was treated for syphilis empirically with one dose of intramuscular benzathine penicillin G. She complained of worsening back pain and weakness over several weeks with increasing difficulty moving her neck, prompting transfer to our tertiary care setting for further evaluation and management.

A painless, shallow ulcerated vulvar lesion was identified at the posterior fourchette, which was swabbed and ultimately positive for *Treponema pallidum* (*T. pallidum*) deoxyribonucleic acid on

polymerase chain reaction (PCR) testing. Her clinical symptoms raised concern for neurosyphilis as she had a positive Jolt test suggesting meningeal irritation although Brudzinsky and Kernig's signs were negative. Strength in the lower extremities was objectively decreased. She did not have a fever or skin rash.

She was admitted to the antepartum unit at Winnipeg's Health Sciences Centre and co-managed by the Infectious Disease, Reproductive Infectious Diseases and Maternal Fetal Medicine services. A lumbar puncture was performed, and antibiotic therapy initiated with intravenous penicillin G (24 million units per day divided every four hours in accordance with neurosyphilis dose recommendations). The cerebrospinal fluid showed low protein (0.12 g/L) and normal glucose levels, with a normal total nucleated cell count of $1x10^6$/L. Uninfused computed tomography and magnetic resonance imaging scans of the brain and spine (done without gadolinium as it is contraindicated in pregnancy) did not demonstrate acute abnormalities. She had microcytic anemia with a hemoglobin level of 77 g/L and inflammatory markers with an erythrocyte sedimentation rate higher than 140 mm/hour and a C-reactive protein level of 58 mg/L.

Maternal syphilitic infection was confirmed with serum Venereal Disease Research Laboratory (VDRL) titre of 1:64 and *T. pallidum* IgG detected by chemiluminescent microparticle immunoassay. In addition to the positive PCR result on the vulvar lesion confirming a chancre, a review of serology from a year prior confirmed this to be a primary infection. No other sexually transmitted infections were identified, and additional serologic findings are outlined in **Table 1**. The cerebrospinal fluid was negative for VDRL and all cultures (bacterial, mycobacterial and fungal) were negative.

Table 1: Maternal investigations

Test	Source	Result
Treponema pallidum Ab IgG+IgM	Serum	**Positive**
VDRL	Serum	**Reactive 1:64**
Toxoplasma gondii IgM/IgG	Serum	Negative/negative
Cytomegalovirus IgM/IgG	Serum	Negative/antibody detected
Parvovirus B19 IgM/IgG	Serum	Negative/indeterminate
West Nile virus IgM	Serum	Negative
Anaplasma phagocytophilum IgG	Serum	Negative
Treponema pallidum DNA PCR/NAAT	Vulvar lesion	**Target detected**
CSF-VDRL	CSF	Non-reactive
Treponema pallidum DNA PCR/NAAT	CSF	Target not detected
Bacterial culture	CSF	Negative
Mycobacterial culture	CSF	Negative
Fungal culture	CSF	Negative

Abbreviations: CSF, cerebrospinal fluid; DNA PCR/NAAT, deoxyribonucleic acid polymerase chain reaction/nucleic acid amplification test; IgM/IgG, immunoglobulin M/immunoglobulin G; VDRL, Venereal Disease Research Laboratory

Ultrasound performed by Maternal Fetal Medicine demonstrated a single live intrauterine pregnancy at gestational age of 19+3 weeks. The fetus was affected by severe hydrops fetalis, as demonstrated by large pleural effusions, large ascites compressing the kidneys and body wall edema (**Figure 1**). The brain was very abnormal with bright cerebrospinal fluid and streaky echoes throughout the cortex (**Figure 2**). There was polyhydramnios with a maximum vertical pocket of 8 cm, with a thickened and overtly hydropic placenta (**Figure 3**). The umbilical artery Doppler ultrasound was abnormal with an increased systolic to diastolic ratio; however, the middle cerebral artery (MCA) Doppler did not demonstrate evidence of fetal anemia (peak systolic velocity 1.37 MoM). To complete the evaluation for hydrops, amniocentesis was performed and sent for microbiologic and genetic evaluation. Results are summarized in **Table 2** and were notably positive for *T. pallidum* on PCR testing.

Figure 1: Very large ascites, echogenic clumped bowel, compressed kidneys suggestive of high intra-abdominal pressure at 19+3 weeks gestational age

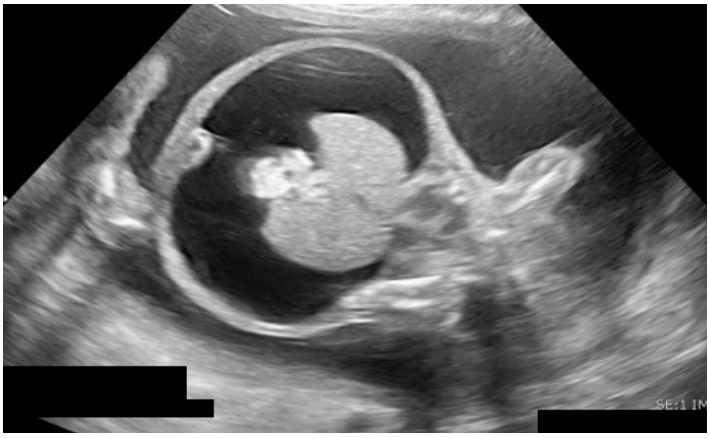


Figure 2: Marked scalp edema, very abnormal brain with bright cerebrospinal fluid, streaky echoes throughout brain matter at 19+3 weeks gestational age

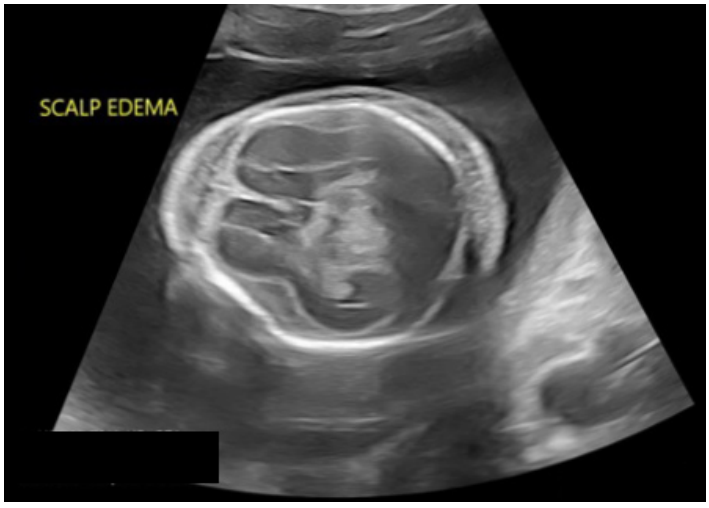


Figure 3: Enlarged, hydropic, placenta with multiple cystic lesions at 19+3 weeks gestational age

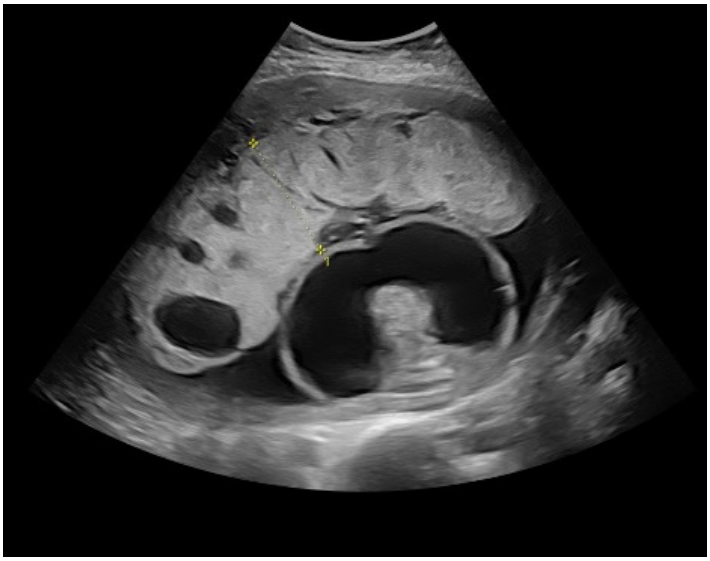


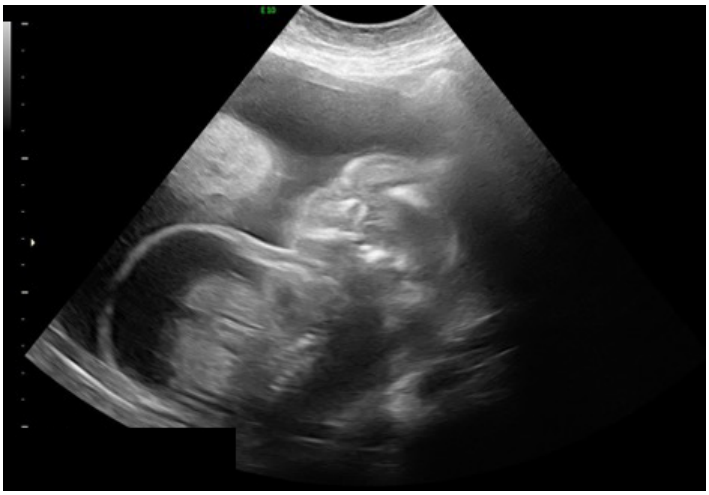
Table 2: Amniocentesis results

Test	Source	Result
Treponema pallidum DNA PCR/NAAT	Amniotic fluid	**Target detected**
Cytomegalovirus DNA NAAT	Amniotic fluid	Target not detected
Parvovirus B19 DNA NAAT	Amniotic fluid	Target not detected
Viral culture	Amniotic fluid	Negative

Abbreviations: DNA NAAT, deoxyribonucleic acid nucleic acid amplification test; DNA PCR/NAAT, deoxyribonucleic acid polymerase chain reaction/nucleic acid amplification test

Treatment was continued with intravenous penicillin in the hopes of achieving sufficient levels to treat the fetal infection. After nine days, a repeat detailed ultrasound demonstrated worsening fetal ascites. The fetus was now 20+5 weeks gestation with an abdominal circumference of 282 mm (32+2 weeks size) (**Figure 4**). The scalp edema and Doppler ultrasound results remained stable. The family was counselled in depth about options, including termination of pregnancy or expectant management with serial ultrasound and fetal magnetic resonance imaging to follow structural neurologic changes. Overall, the prognosis was thought to be poor given the extent of hydrops at early gestation and severity of the changes in the cerebral cortex. Ultimately, the family decided to proceed with termination of pregnancy. Medical induction of labour was carried out with mifepristone followed by vaginal misoprostol. A stillborn hydropic female infant was delivered, indicative of intrapartum demise, at 21+0 weeks gestation and weighing 747 g (greater than 99th centile for gestational age). The family declined an autopsy. The placenta weighed 387 g (over twice the average weight for that gestational age) with pathologic signs of decidual hemorrhage, necrosis and acute inflammation.

Figure 4: Worsening of ascites with abdomen measuring 32 weeks size at 20+5 weeks gestational age



Maternal symptoms continued to improve after delivery and intravenous penicillin was discontinued. Once able to ambulate without assistance, she was discharged home. Follow-up serology showed an appropriate treatment response with her VDRL titre down to 1:4.

Discussion

Congenital syphilis is a preventable disease. In a 2019 statement, the Society of Obstetricians and Gynecologists of Canada advocated for adequate screening in pregnancy, with enhanced three-point screening in outbreak areas (1). Treatment of syphilis in pregnancy has been shown to be highly effective at decreasing rates of congenital syphilis, syphilitic stillbirth and obstetrical complications such as preterm birth (3). The treatment of choice is intramuscular benzathine penicillin G at a dose of 2.4 million units, with a second dose administered one week later (3). A third dose in recommended for patients with late latent syphilis (3).

Given the increased risk for intrauterine growth restriction, fetal anomalies, and hydrops fetalis, additional sonographic surveillance is recommended (6). In a cohort study of seropositive women who had an ultrasound prior to treatment for syphilis, Rac *et al.* found that 30% had evidence of fetal syphilis (5). Fetal hepatomegaly was the most noted abnormality (seen in 79% of affected fetuses) with placentomegaly, polyhydramnios, ascites and evidence of fetal anemia with elevated peak systolic velocity in the MCA Doppler ultrasound was also seen (5). The authors went on to track timeline to resolution of abnormal Doppler ultrasound features and found MCA Doppler ultrasound abnormalities, ascites and polyhydramnios were the first to resolve (80% resolution within 40 days), followed by placentomegaly and hepatomegaly, which could persist until delivery. It should be noted that ultrasound findings of congenital syphilis are not commonly identified before 18 weeks gestation

as the immature fetal immune system is not yet able to mount a sufficient response (3,6).

Congenital syphilis was historically diagnosed after birth, with most infected neonates showing symptoms by the second month of life (6). Modern technologies, including ultrasound, have demonstrated an evolving role in diagnosis of fetal syphilis over the last three decades. Much of the clinical wisdom in treating syphilis predates these antenatal diagnostics, leaving the modern clinician with a diagnosis but limited evidence to guide treatment.

In our patient's case, treatment was initiated using intravenous (IV) penicillin G at neurosyphilis dosing for maternal indication. Treatment was continued in hopes of treating the fetal infection. A case report by Galan *et al.* described the use of IV penicillin G to treat syphilis-related fetal hydrops at 24 weeks gestation after an ultrasound showed worsening features 10 days after receiving intramuscular benzathine penicillin (7). Their patient showed complete resolution of sonographic findings after 10 days of IV therapy (7). A second case by Chen *et al.* reported on a patient diagnosed with secondary syphilis at 28 weeks gestation with sonographic findings of fetal hydrops and anemia and with an elevated MCA peak systolic velocity (8). Their patient was admitted and treated with IV penicillin G for 14 days to target maximal and sustained fetal levels (8). The patient underwent an ultrasound-guided cordocentesis and fetal transfusion, and showed resolution of the fetal hydrops within two weeks (8). Although both cases had relatively rapid resolution of symptoms when compared with the data from Rac's cohort, there is not enough information to draw conclusions about optimal therapy for fetal syphilis.

Our case outlines a situation that, without treatment, would almost certainly would have progressed to syphilitic stillbirth. Current obstetrical guidelines for investigation of stillbirth are vague in the recommendations for infectious screening, with many local hospitals developing their own protocols (9). This leads to possibility of missed diagnoses of syphilis during investigation of non-immune fetal hydrops and stillbirth, with implications at the level of both patients and greater public health.

Conclusion and call to action

This case highlights the potential severity of fetal syphilis infection and underscores the paucity of current literature to guide management of a severely affected fetus in the antepartum period. Information sharing will be essential to build a modern knowledge base on the treatment of this resurging infection. We urge obstetrical care providers to increase infectious screening and keep syphilis on the differential when investigating severe complications.

Authors' statement

The authors have no conflicts of interest to disclose.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

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Delayed diagnosis of maternal and congenital syphilis: An unrecognized epidemic?

Zachary Dionisopoulos[1], Fatima Kakkar[2], Ana C Blanchard[2]*

Abstract

Syphilis is an infection caused by *Treponema pallidum* spirochetes. The diagnosis of this sexually transmitted disease may be missed, partly due to the painless nature of genital ulcers in its primary stage. Women in Canada are screened for syphilis in their first trimester of pregnancy, but late pregnancy testing is not done in all provinces to date; therefore, undetected vertical transmission of syphilis may occur. This case emphasizes the importance of recognizing congenital syphilis in infants and young children with unexplained growth problems and biochemical and hematological abnormalities. Congenital syphilis remains a rare diagnosis, but in the context of increased syphilis rates in Canada during recent years, clinicians should consider this diagnosis in infants presenting with compatible clinical manifestations.

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Affiliations

[1] Paediatrics Residency Program, Department of Paediatrics, CHU Sainte-Justine, Université de Montréal, Montréal, QC

[2] Division of Infectious Diseases, Department of Paediatrics, CHU Sainte-Justine, Université de Montréal, Montréal, QC

***Correspondence:**
ana.blanchard@umontreal.ca

Introduction

Congenital syphilis can be challenging to diagnose, as it may mimic other conditions. In addition, clinicians may not consider congenital syphilis due to the rarity of this diagnosis and because women are screened for syphilis in first trimester of pregnancy. Here, we report the case of an infant with intrauterine growth restriction (IUGR) and known congenital cytomegalovirus infection who presented with persistent anemia, thrombocytopenia and liver enzyme elevation. This case highlights the need to have a high index of suspicion in infants presenting with these findings and raises important questions about the need for third trimester screening in pregnant women in Canada.

Case

A two-month-old infant was admitted to hospital for evaluation of bicytopenia and hepatitis in September 2021. He was born to a G1P1 21-year-old-mother. In the first trimester, she had negative HIV, hepatitis B and C virus and syphilis serologies. She was rubella immune and had negative chlamydia and gonorrhea urine screens. The pregnancy was complicated by oligohydramnios and IUGR in the third trimester. The baby was born prematurely at 35+1/7 weeks of gestation by vaginal delivery, with Apgar scores of 9-10-10. Birth parameters confirmed IUGR with a birth weight of 1,910 kg (z score -1.48, centile 6.97), a length of 46 cm (z score -0.09, centile 46.47) and a head circumference of 31 cm (z score -0.86, centile 19.53). As part of his IUGR workup, salivary and urine cytomegalovirus (CMV) polymerase chain reaction (PCR) tests were done at day zero and day five of life and were found to be positive at 33,884,416 and 3,801,894 copies/mL respectively. The infant had a normal complete blood count and liver enzyme panel at that time. A transfontanellar ultrasound showed small colloidal parenchymal cysts in the right caudate nucleus of unknown origin, without intracranial calcifications. A cerebral magnetic resonance imaging was normal. Ophthalmological and audiological exams were normal. Valganciclovir was initiated at a dose of 16 mg/kg/dose twice daily, with a plan to complete six months of therapy. He was discharged home at 38+4/7 weeks.

On follow-up at six weeks of age, the infant was found to have a hemoglobin level of 66 g/L, a platelet count of $77x10^9$/L and a white blood count of $10x10^9$/L. His alanine aminotransferase level was 253 U/L, aspartate aminotransferase was 254 U/L, gamma-glutamyl transferase was 256 U/L, alkaline phosphatase level was 690 U/L, albumin was 29 g/L and his coagulogram was normal. The anemia and liver enzyme abnormalities were thought to be due to valganciclovir toxicity so treatment was held. He was seen in the clinic a week later without improvement of his blood work findings; therefore, he was admitted to the Paediatrics ward for further investigation.

On admission, he was afebrile and well overall. On physical exam, he had hepatosplenomegaly and mild diffuse desquamation. He was irritable, but consolable. An extensive workup was done including blood and urine cultures, nasopharyngeal multiplex viral PCR, Epstein Barr virus, parvovirus B19, adenovirus, herpes simplex virus and CMV blood PCRs—all results were negative. He required a packed red blood cell transfusion as his hemoglobin had dropped to 57 g/L.

After 10 days in hospital, the infant developed a new onset low grade fever. Given the persistent unexplained anemia, a bone marrow aspirate was planned. On repeat questioning of the mother alone for possible infectious symptoms, she described for the first-time flu-like symptoms following delivery, as well as a sore throat and genital lesions. In addition, she presented at the time of repeat questioning a bilateral erythematous scaling papular palmar rash (**Figure 1**) on physical examination, which had appeared in the previous three weeks. Syphilis serologies were immediately ordered on the patient and his mother. They both had strongly-positive syphilis enzyme immunoassays and rapid plasma reagin of 1:64. A lumbar puncture was performed on the infant, with the cerebrospinal fluid analysis showing normal white and red blood cell counts, glucose and protein profiles as well as a negative Venereal Disease Research Laboratory test. A cerebral magnetic resonance imaging was repeated and was normal. A skeletal survey was not conclusive for congenital syphilis, but slightly enhanced periosteal reactions were noted along both femurs and the right tibia (**Figure 2**). Placental examination showed only one area of villitis of unknown significance, and no spirochetes were seen on immunochemistry stains.

Figure 1: Rash, woman with secondary syphilis, Montréal, 2021

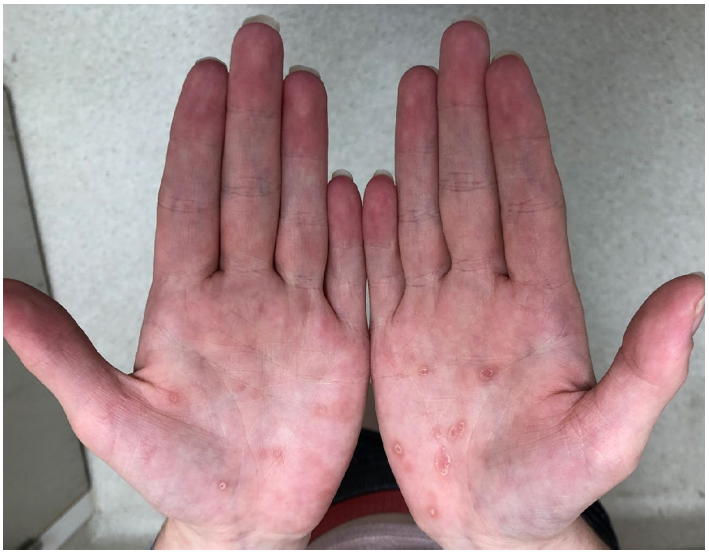
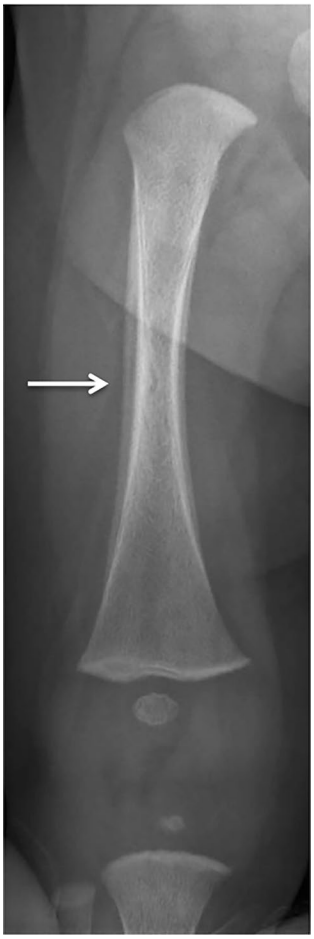


Figure 2: Radiograph of the right femur[a] of an infant with congenital syphilis, Montréal, 2021



[a] Slightly enhanced periosteal reactions were noted along both femurs and the right tibia. The right femur is shown here

The infant was treated with a 10-day course of intravenous penicillin G, with rapid resolution of his fever and his bloodwork abnormalities. A repeat rapid plasma reagin at the end of treatment was 1:32. The patient was discharged with follow-up in the Congenital Infection Clinic. His mother was referred to an adult infectious diseases clinic, where she received appropriate treatment and serological follow-up.

Discussion

The rate of syphilis in Canada increased by 85.6%, from 5.0 to 9.3 cases per 100,000 population, from 2010 to 2015. Although this rate was higher in males than in females and was thought to be largely attributable to men who have sex with men, there was a 27.8% increase among females with individuals aged 20–39 years having the highest rates (1). In a recent report, national rates of syphilis increased by 124% between 2016 and 2020, with the largest increase occurring among females (740%). Nearly a third of cases occurred in women (versus only 8% in 2016) (2). In addition, the incidence of congenital syphilis has been rising in recent years in Canada, with cases increasing from

2.5 per 100,000 women aged 15–39 years in 2016 to 39.7 per 100,000 women aged 15–39 years in 2020 (2). This alarming rise in syphilis amongst Canadian women and their infants calls for urgent attention, as has already been recently reported in the United States and Australia (3,4). The Canadian Paediatric Surveillance Program has recently begun a cross-sectional study across Canada to describe the epidemiology of congenital syphilis, identify risk factors in mothers of affected children and describe the investigation and management of these children (5).

Congenital syphilis occurs through vertical transmission, during pregnancy and/or birth. It may have severe consequences for the infant, including sensorineural hearing loss, neurodevelopmental disorders, musculoskeletal deformity or death (6). The risk of transmission varies to more than 80% depending on the mother's stage of disease, with a higher risk of transmission in primary and secondary stages (6). With appropriate treatment in pregnancy, the risk of congenital syphilis decreases to 1%–2% (7). Although syphilis is routinely tested for in first trimester of pregnancy, serological testing of pregnant women later in pregnancy is not currently a widespread practice across Canada. This is typically done in a targeted fashion for high-risk settings, of which the definitions may vary. Third trimester screening has been implemented in 2019 in British Columbia, due to the occurrence of two severe congenital syphilis cases (8).

Infants may be completely asymptomatic at birth (9); however, a wide array of clinical manifestations may occur in the context of congenital infection, including prematurity, small stature for gestational age, anemia, thrombocytopenia, hepatosplenomegaly and osteitis (9). Paediatricians and family doctors should be aware of these clinical manifestations, promptly suspect congenital syphilis, obtain investigations and provide rapid management to prevent late-onset disease and complications. A detailed history of symptoms and epidemiological risk factors should be obtained from mothers in complete confidentiality, as illustrated in this case, so that the opportunity for diagnosis is not missed. All children with clinical or serological evidence of congenital syphilis should be treated with penicillin G for 10 to 14 days, depending on severity of their disease. Clinical and serological follow-up of all children potentially exposed to syphilis in utero is required (9).

Of note, coinfection with CMV and syphilis in newborns remains largely undescribed in the literature. As CMV is increasingly recognized as a leading cause of congenital infection, it may be more frequently detected; therefore, there may be more cases of coinfection described in the future. The impact of coinfection on the long-term clinical outcomes of affected infants will warrant further research.

Conclusion

This case highlights the importance of considering congenital syphilis in young infants with unexplained hepatosplenomegaly, hematological and biochemical abnormalities, despite negative first trimester screening during pregnancy. Surveillance initiatives, such as that led by the Canadian Paediatric Surveillance Program, are useful to characterize the epidemiology and severity of congenital syphilis which is potentially underdiagnosed in Canadian youth. With the current resurgence of syphilis in Canada, third trimester testing of pregnant women may be considered by public health policy makers in different provinces and territories.

Authors' statement

All authors were involved in the management of the patient: ZD and ACB made the diagnosis and provided initial management and counselling And FK provided long-term clinical follow-up and management. ZD wrote the initial draft of the manuscript. ACB oversaw manuscript preparation and revisions. All authors read and approved the final manuscript.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

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Public Health Agency of Canada
130 Colonnade Road
Address Locator 6503B
Ottawa, Ontario K1A 0K9
ccdr-rmtc@phac-aspc.gc.ca

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