Epidemiology of Infectious Syphilis in Ottawa

Recurring Themes Revisited

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ABSTRACT

Objectives: To describe the epidemiology of an outbreak of infectious syphilis in Ottawa.

Methods: A retrospective chart review of infectious syphilis cases in Ottawa from 2001-2006.

Results: Rates of syphilis have risen more than tenfold. The epidemic was centered in men, with the majority of cases (83.5%) occurring among men who have sex with men (MSM). These individuals differed from the general MSM population residing in Ottawa in their being older, more likely to be HIV positive, and more sexually promiscuous. Inconsistent condom use by MSM engaged in either oral or anal sex was pervasive. Thirty-seven percent of MSM reported sexual encounters with men from Montreal and Toronto. Visceral manifestations of syphilis, including neurosyphilis, were more common in persons co-infected with HIV. As a result, this subgroup was more likely to have received an extended antibiotic treatment regimen. There was a substantial delay between serological diagnosis and treatment. Less than half of treated cases returned for a six-month evaluation.

Conclusions: Multiple sexual partners, unprotected oral sex, and increased age among MSM were the predominant risk factors contributing to this syphilis epidemic. Co-infection with HIV modified the clinical presentation of syphilis, necessitating a more intensive diagnostic and therapeutic approach. The interconnection of urban sexual networks has likely contributed to the dynamics of local syphilis transmission and suggests that effective interventions will require a coordinated national approach.

Key words: Syphilis; epidemiology; HIV

The oscillations in the incidence of infectious syphilis since the late 1950s¹ in the United States have vividly illustrated the dynamics of the host-pathogen relationship. These periodic fluctuations in syphilis rates² have been attributed to host perturbations, such as changes in population-wide immunity³ and in sexual practices, as evidence of alterations in the virulence of the pathogen, *Treponema pallidum*, have been lacking. A similar epidemiological pattern has been observed in Canada, in which the incidence of syphilis declined throughout the late 1990s, with rates as low as 0.4 cases/100,000 in 1997,⁴ before recent presaging outbreaks in Calgary and Vancouver.^{4,5}

The re-emergence of syphilis has important implications for HIV infection. Syphilitic chancres significantly increase HIV sexual transmission, including during 'low risk' sexual acts such as oral sex.⁵ In addition, the increasing number of syphilis infections, with its short incubation time and early detection relative to HIV, may represent a harbinger of rising HIV infections.⁶ Similar speculations attend the rise in gonococcal infections.⁷⁻⁹

Conventional antibiotic treatment for HIV co-infected individuals is controversial with support for both traditional and augmented regimens.¹⁰⁻¹⁵ As the presence of HIV infection modifies the clinical expression of syphilis, an expanded diagnostic approach has been advocated, such as the adoption of lumbar puncture to exclude neurosyphilis in HIV co-infected patients.¹⁶

In this study, we sought to identify features contributing to the recent upsurge in infectious syphilis in Ottawa between 2001 and 2006. Our results indicate that potential therapeutic interventions rely upon an understanding of local and regional transmission dynamics operating in tandem.

METHODS

A retrospective chart review was conducted of syphilis cases occurring between January 2001 and June 2006 in the Ottawa-Carleton region, a metropolitan centre with a population of approximately one million. Patient records were analyzed at the Ottawa Sexual Health Center (SHC), a public health clinic, and at the

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Infectious Diseases Clinic at the Ottawa Hospital General Campus. Cases were defined as individuals with a clinical picture consistent with either primary, secondary or early latent syphilis¹⁷ and positive serological tests for syphilis, or seropositive individuals identified through contact tracing. HIV status was assigned based on a reactive serological immunoassay, self-reporting or documentation of antiretroviral treatment. Demographic characteristics were collected from questionnaires routinely used at the SHC, and from medical transcriptions and contact tracing reports.

Treatment start dates and treatment regimens were recorded directly from chart records. Treatment success was defined as a fourfold decrease in serum RPR (rapid plasma reagin) titers six months after treatment.¹⁸ Re-infection was diagnosed as the presence of new clinical signs, new epidemiological contact tracing and any RPR titer rise. In such cases, re-infection was recorded as a new infection.

RESULTS

One hundred and two cases of infectious syphilis were reviewed. The rate of infection in the Ottawa-Carleton region increased from 0.6 cases/100,000 in 2001 to 2.8 cases/100,000 in 2003 and remained steady thereafter. The male to female ratio was 19:1. The majority of infected men (83.5%) were MSM or bisexual. Heterosexual transmission accounted for 18.6% of cases. All but four cases resided in Ottawa. Three quarters of individuals were born in Canada and the country of origin of the remainder was diverse. Two thirds of the cases were between the ages of 31 and 50 years with three quarters of the MSM population in this age group (Figure 1).

Concurrent HIV infection was present in 44 (43.1%) cases with the highest proportion found in MSM compared to that in the heterosexual cohort (48% versus 21%, respectively)(Figure 2). However, the HIV status was unknown in 42% of heterosexuals and 16% of MSM. MSM reported a higher annual number of sexual partners than heterosexual cases (Figure 3) and the number of sexual partners per year in MSM increased with age over 30 years. Oral-genital contact was the predominant form of sexual practise in MSM (Figure 4).

Figure 1. Distribution of cases by age in years

Figure 2. HIV status of cases of infectious syphilis

Figure 3. Number of sexual partners per year of patients with infectious syphilis

Approximately one half of epidemiologically linked sexual partners resided outside of Ottawa (data not shown).

Secondary syphilis was the predominant clinical expression of disease as 57 (59%) of cases presented with this clinical manifestation (Figure 5). HIV co-infected patients were more likely to exhibit visceral signs of secondary syphilis including hepatitis, meningitis and retinitis, compared to HIV-negative individuals. A chancre was present in all of the 29 cases of primary syphilis irrespective of the HIV status.

The elapsed time between the dates of serological confirmation and the initiation

of treatment were recorded for 87 of the 102 cases. The length of time between diagnosis and treatment did not correlate with the stage of syphilis. Patients presenting to the Infectious Diseases Clinic at the Ottawa Hospital were more likely to receive treatment at the initial assessment.

Benzathine penicillin G was the sole antibiotic administered to 33 (89%) HIV uninfected patients and to 17 (40%) patients concurrently infected with HIV. With the exception of 5 cases (4 HIV co-infected and 1 HIV negative) who received a combination of benzathine penicillin G and doxycycline, the use of doxycycline

Figure 4. Sexual practices of cases of infectious syphilis

Figure 5. Syphilis stage at presentation and HIV status

was confined to penicillin-allergic patients (3 HIV negative and 9 HIV co-infected cases). Of the 37 HIV-negative individuals, 27 (81%) were treated with one dose of intramuscular benzathine penicillin G 2.4 million units and 3 with a 14-day course of oral doxycycline 100 mg bid. In contrast, only 6 (14%) HIV-positive patients received either regimen. Of the 42 HIV-positive individuals, 20 (48%) were treated with an extended regimen of either three weekly intramuscular injections of benzathine penicillin G (total of 7.2 million units) or with a prolonged 28-day course of oral doxycycline 100 mg bid. The majority (65%) of these 20 individuals presented with secondary syphilis.

Lumbar puncture was performed in 19 neurologically asymptomatic patients with HIV infection with a serum RPR titer $\geq 1:32$, or a CD4 cell count <350 cells/ μ L irrespective of titer.^{19,20} Twelve (63%) of these patients were diagnosed with neurosyphilis,²⁰ reflected by either a positive CSF VDRL titer or CSF pleocytosis. All were treated with a minimum two-week

course of either intravenous penicillin G 4 million units Q4H or ceftriaxone 2 gm daily. Seven individuals received an additional three weekly intramuscular injections of benzathine penicillin G. Overall, 27% of HIV-positive cases were diagnosed with neurosyphilis.²⁰

Successful treatment of syphilis was defined as a fourfold decrease in RPR titers six months post-therapy,^{18,21} therefore this analysis was confined to patients who completed the six-month serological evaluation. Only 49 of the 102 cases met this criterion. The extent of follow-up did not differ in the HIV-positive and HIV-negative groups. Twenty-eight (67%) of the 42 HIV-positive patients completed follow-up. Twenty-three (78%) of these individuals received either an extended therapy regimen or an intravenous β -lactam antibiotic, and only three cases (13%) failed treatment, including one person who received intravenous penicillin. Similarly, only one HIV co-infected patient receiving conventional regimens did not achieve serological success. Two of the treatment failures were

felt to be due to unrecognized CNS infection. Less than half of HIV-negative individuals had 6-month follow-ups. The majority (71%) received conventional therapies and five patients failed treatment. One HIV-negative individual was deemed serofast, defined as a case whose titers did not decline irrespective of treatment and symptomatic resolution, and consequently this result were not included. The small number of patients returning for the six-month evaluation precluded a meaningful assessment regarding whether treatment failure was associated with a specific antibiotic regimen.

DISCUSSION

The rate of infectious syphilis in Ottawa has risen sharply, increasing greater than tenfold from 0.2 cases/100,000 between 1997-99 (Ottawa Public Health, data not published) to 2.8 cases/100,000 in the interval from 2003-06. As in previous studies,^{1,22} a disproportionate number of these cases were male. Although cases of infectious syphilis treated outside of these two clinics were not included in the analysis, the magnitude of the epidemic was likely captured in our study as the SHC tracks all reactive serologic tests for syphilis in the Ottawa-Carleton region.

The median age of men in this study was 40 years, which is 2.5 years older than the median age of men in Ottawa,²³ indicating that an older age group is primarily affected by this epidemic.^{1,24} The shift in age demographics may be explained by the unique risk factors present in these men. Qualitative research revealed that older men are less likely to insist on condom use due to fear of rejection from younger sexual partners.²⁵ Older MSM also have a higher incidence of isolation and depression which is associated with risky sexual practices.²⁵ Our findings support these observations as MSM over 30 years of age had a higher number of sexual partners and a higher incidence of unprotected anal sex.

The MSM community is less defined by geographic borders, as infected men are known to travel between cities to meet sexual partners.^{7,25-27} Movement between Montreal, Toronto, and Ottawa was common within the Ottawa MSM population. The parallel increase in the number of cases of infectious syphilis in Quebec²⁸ and

Toronto (T. Wong, personal communication) suggests that increased interconnectivity of an underlying network of sexual contacts in these three cities has contributed to the dynamics of both local and regional syphilis transmission.

Such a synchronization of syphilis rates across wide geographical areas has been attributed to progressive recruitment of a non-immune susceptible population interacting with an infected core group.²⁹ Data from the Ontario Men's Survey³⁰ supports the existence of such a group of highly sexually active individuals as the behaviour of the MSM diagnosed with syphilis are clearly distinct from the general MSM population. Similarly, the conduct of men with syphilis in our study exhibited a stronger history of previous sexually transmitted infections in which the prevalence of HIV and other STIs was ten- and twofold more prevalent, respectively (data not published). In addition, MSM infected with syphilis were more sexually promiscuous, with only 21.3% reporting fewer than 5 partners in the past year compared to 56% of the general Ottawa MSM population.

The low prevalence of condom use was notable. Within the heterosexual population, vaginal sex was the sole source of transmission reported in two thirds of cases and only about 10% of individuals used condoms consistently. Among MSM, the high prevalence of unprotected oral sex, largely regarded as an HIV-safe alternative to anal sex, is recognized as an independent mode of syphilis transmission⁶ and is likely a contributor to spread in the Ottawa epidemic. Indeed, over one third of MSM with syphilis reported consistent use of condoms with anal sex, indicating that these cases were infected likely by oral sex. The overall high rate of unprotected sex correlates with previous reports that also demonstrate an increasing prevalence of unsafe sexual practices among MSM,^{22,25,26,31} attributed to faith in anti-retroviral therapies and to mental fatigue arising from years of protected sex to reduce the risk of HIV.^{32,33}

The optimal treatment of syphilis in HIV-infected patients is controversial.¹¹⁻¹⁶ In our study, the majority of HIV-positive cases attained serologic treatment success. A high proportion of the HIV co-infected patients underwent lumbar puncture to exclude neurosyphilis.^{19,20} Two of the treat-

ment failures in the HIV-positive group were attributed to unrecognized CNS infection, in agreement with prior studies^{15,16} which demonstrated neurosyphilis relapses in HIV-positive patients previously treated with benzathine penicillin G injections. Our results support the selective performance of lumbar puncture in HIV concordant patients exhibiting laboratory features suggestive of asymptomatic neurosyphilis.¹⁹ Of note, one third (5 of 14) of HIV-negative patients failed treatment with intramuscular long-acting penicillin G for reasons that are unclear, emphasizing the importance of extended clinical and serological monitoring.³⁴ However, such extended follow-up occurred in less than 50% of cases, a finding that has been previously associated in perpetuating syphilis transmission.⁹

A significant delay between serological diagnosis and treatment has also likely contributed to maintaining the pool of infected individuals and sustaining the syphilis outbreak. Several individuals with classic secondary syphilitic rashes were repeatedly misdiagnosed and required skin biopsies for the correct etiology.

This study has several limitations. The low patient compliance with follow-up syphilis serology and the undetermined HIV status in a significant number of cases restrict judgements regarding the effectiveness of a particular therapeutic regimen and clinical outcome. A selection bias may have occurred as individuals using the SHC may have chosen this clinic for its testing anonymity and therefore represent an unbalanced number of 'high risk' individuals. Second, patients seen at the Infectious Diseases Clinic may have created a treatment bias towards augmented regimens. Finally, self-reported sexual behaviours are subject to recall and social desirability biases.

In conclusion, the syphilis epidemic in Ottawa is centered in the MSM population in which the dynamics of transmission appear to reside in a core group of infected individuals. The mobility of this population subset emphasizes the necessity for a coordinated nuanced regional-based intervention program. Unsafe sexual behaviours and the delay in recognition and treatment of infected patients underscores the need for continual education of health care professionals and of individuals engaged in high-risk sexual practices.

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RÉSUMÉ

Objectifs : Décrire l'épidémiologie d'une flambée de syphilis infectieuse à Ottawa.

Méthode : Examen d'un graphique rétrospectif des cas de syphilis infectieuse survenus à Ottawa de 2001 à 2006.

Résultats : Les taux de syphilis ont plus que décuplé. L'épidémie était concentrée dans la population masculine, la majorité des cas (83,5 %) s'étant produits chez des hommes ayant des relations sexuelles avec des hommes (HRSH). Ces sujets différaient de la population générale des HRSH vivant à Ottawa du fait de leur âge (ils étaient plus vieux), de leur probabilité accrue d'être séropositifs pour le VIH et de leur plus grande promiscuité sexuelle. L'irrégularité dans le port du condom par les HRSH pratiquant le sexe oral ou anal était omniprésente. Trente-sept p. cent des HRSH ont déclaré avoir eu des rapports sexuels avec des hommes de Montréal et de Toronto. Les manifestations viscérales de la syphilis, y compris la neurosyphilis, étaient plus courantes chez les sujets co-infectés par le VIH. Par conséquent, ce sous-groupe était plus susceptible d'avoir suivi une antibiothérapie prolongée. Nous avons observé un délai important entre le sérodiagnostic et le traitement. Moins de la moitié des cas traités se sont soumis à une nouvelle évaluation après six mois.

Conclusion : Les partenaires sexuels multiples, les rapports sexuels oraux non protégés et le vieillissement de la population des HRSH étaient les principaux facteurs de risque ayant contribué à l'épidémie de syphilis. La co-infection par le VIH a modifié le tableau clinique de la syphilis et nécessité une approche diagnostique et thérapeutique plus intensive. L'interconnexion des réseaux sexuels des villes a sans doute contribué à la dynamique de la transmission locale de la syphilis, ce qui donne à penser que des interventions efficaces exigent une approche coordonnée à l'échelle nationale.

Mots clés : syphilis; épidémiologie; VIH