A Review of Sexually Transmitted Infections in Australia – Considerations in 2018

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ABSTRACT

Sexually transmitted infections (STIs) bear a high burden of disease and, subsequently, high health costs globally. Chlamydia, gonorrhoea, syphilis, and trichomoniasis contribute to nearly one million infections every day worldwide. Sexually transmitted infections continue to be the most frequently notified condition to the Australian National Notifiable Diseases Surveillance System and the numbers continue to increase. Australia has achieved several significant successes in reducing STIs and blood-borne viruses (BBV) including the significant decrease in genital warts in those less than 30 years old since 2007 following the launch of human papillomavirus vaccines in women, the virtual elimination of mother to child transmission of HIV, and the increased uptake of successful hepatitis C treatment following the availability of direct acting antiviral treatment on the Pharmaceutical Benefits Scheme.

However, several challenges remain, including the ongoing rise of chlamydia, gonorrhoea, and syphilis over the last five years; the emergence of antibiotic resistance; and the increasing disparity in the prevalence of STIs and BBV in men who have sex with men, young people, and Aboriginal and Torres Strait Islander people, and challenges in the delivery of services to rural and remote Australia.

In this paper, we aim to provide a snapshot of the current landscape and challenges for chlamydia, gonorrhoea, mycoplasma, syphilis and HIV infections in Australia. *Acad Forensic Pathol.* 2018 8(4): 938-946

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INTRODUCTION

Sexually transmitted infections (STIs) bear a high burden of disease and, subsequently, high health costs globally. Chlamydia, gonorrhoea, syphilis, and trichomoniasis contribute to nearly one million infections every day worldwide (**Table 1** and **Figure 1**) (1). Sexually transmitted infections continue to be the most frequently reported condition to the Australia

lian National Notifiable Diseases Surveillance System (NNDSS) and the numbers continue to increase (2). Australia has achieved several significant successes in reducing STIs and blood-borne viruses (BBV) including the significant decrease in genital warts in those less than 30 years old since 2007 following the launch of human papillomavirus (HPV) vaccines in women (3), the virtual elimination of mother to child transmission of human immune deficiency virus (HIV)

Table 1: World Health Organization (WHO) Regional Estimates of New Cases of Four Curable Sexually Transmitted Infections. Estimated Numbers of Incident Cases In Millions In 2012, By WHO Region (1).

WHO Region	Chlamydia	Gonorrhea	Syphilis	Trichomoniasis
Region of the Americas	24.7	11.0	0.9	27.4
European Region	8.9	4.7	0.4	3.8
African Region	12.0	11.4	1.8	37.4
Eastern Mediterranean Region	10.5	4.5	0.5	15.6
South-East Asia Region	13.8	11.4	0.9	13.2
Western Pacific Region	60.9	35.2	1.0	45.3

Figure 1: World Health Organization (WHO) regions (1).

(2), and the increased uptake of successful hepatitis C treatment following the availability of direct acting antiviral treatment on the Pharmaceutical Benefits Scheme (PBS) (4).

However, several challenges remain, including the ongoing rise of chlamydia, gonorrhoea, and syphilis over the last five years, the emergence of antibiotic resistance, the increasing disparity in the prevalence of STIs and BBV in Aboriginal and Torres Strait Islander people (5), and challenges in the delivery of services to rural and remote Australia. Thus, Australia has a National Sexually Transmissible Infections Strategy to provide guiding principles in the continued efforts to reduce morbidity and mortality from STIs and BBVs (6).

In this paper, we aim to provide a snapshot of the current landscape and challenges for some of the common STIs in Australia.

DISCUSSION

Chlamydia

Chlamydia infection by *Chlamydia trachomatis*, an obligate intracellular bacteria, continues to be the most common infection notified to the NNDSS (2). Chlamydia infections manifest differently depending on the different serovars. Serovars D-K predominantly cause infection in the genital tract, pharynx, and rectum whilst serovar L has the potential to cross into the lymphatic system and cause systemic infections, called lymphogranuloma venereum (LGV) (7). Chlamydia infections can remain asymptomatic, though common presentations include dysuria and discharge. The gold standard for diagnosing chlamydia is a nucleic acid amplification test (NAAT), though “real time” qualitative methods with ability to generate faster results have proved equivalent to standard assays (8).

Challenges

In Australia, the rate of notification of chlamydia continues to increase, particularly in the 20 to 29-year-old age group (Figure 2) (9). Notifications continue

to be higher in females compared to males, though this has been thought to reflect increased testing in females compared to males. Treatment of chlamydia with azithromycin and doxycycline remains effective (10), but the ongoing challenges remain in awareness of asymptomatic carriage of infection, identification of risk, and access to testing services within these high risk populations. An unpublished survey of young people in Queensland (aged <25 years) showed that 75% had ever been sexually active, but only 31% had ever had an STI test, and only 11% consider themselves at risk of contracting an STI. Moreover, several studies have shown a high reinfection rate, with a study in the UK demonstrating an annual redetection rate of 18.5 per 100 person years (11).

Gonorrhoea

Neisseria gonorrhoeae is the causative agent for gonorrhoea. It causes greater than 100 million cases per year worldwide with an estimated total lifetime direct medical cost of care in the US of up to USD 243 million (12). In addition, it has been implicated as a synergistic risk for the acquisition of HIV infection. In Australia, rates of gonorrhoea continue to rise, but unlike chlamydia, more males are diagnosed with the infection at a ratio of 3:1 (3).

Challenges

Within the last decade, antibiotic resistant *Neisseria gonorrhoeae* has become a major public health threat. This includes resistance to sulphonamides, tetracyclines, fluoroquinolones, and cephalosporins (Figure 3) (13). Most recently, in March 2018, two cases of gonorrhoea in Australia demonstrated *in vitro* resistance to both first line combined antibiotics prompting a worldwide alert for increased surveillance and action (14). This highlights the importance of effective surveillance programs (15), the ongoing need to continue to culture and perform antibiotic susceptibility in an era of NAAT testing, ongoing research to determine new and effective antibiotic regimens, and the need for genotype tests which are able to quickly determine antibiotic susceptibility (16). New prevention paradigms, such as vaccines are also required (17).

Mycoplasma

Mycoplasma genitalium (*M. gen*) was initially described in 1981. To date, it remains the smallest free-living bacterium (580 kB genome). It is a slow growing and fastidious organism with no cell wall, creating challenges in testing and treatment. *Mycoplasma genitalium* infections are associated with urethritis in men and in women cause endometritis, pelvic inflammatory disease, tubal infertility, and cervicitis. It remains debatable whether *M. gen* is the causative agent for proctitis in men, though it is of concern that

a study in Australia has found that the anorectum is the most common site detected for *M. gen* in men who have sex with men (MSM), with an anorectal prevalence of 8.9% (18).

Challenges

Testing platforms by NAAT for *M. gen* have only been licenced in Australia since 2016 and are primarily offered in larger laboratories (19). The validity of the tests remains restricted to samples for urogenital sites, despite reported high prevalence of infection in

Figure 2: Chlamydia notification rate per 100 000, 2007-2016, by year and age group (9).

anorectal sites (18). The associations for disease and complications of *M. gen* are well established in women (20), but less so in men, which creates a debate as to whether it is an infection that should be screened for routinely in asymptomatic patients.

A further challenge is the rapid emergence of resistance of *M. gen* to effective antibiotics. *Mycoplasma genitalium* resistance can be acquired and transmitted, with the 23S RNA mutation, which confers resistance to macrolides, and topoisomerase IV target mutations, which confer quinolone resistance (21). The increasing reports of a high prevalence of macrolide resistance *M. gen* makes treatment options difficult due

to cost and availability of antibiotic options (Figure 4) (18, 22, 23). In Australia, there are no coordinated surveillance system for *M. gen*, unlike chlamydia and gonorrhoea infections. Therefore, the level of evidence is limited to retrospective observational cohorts from individual clinics. The availability of routine or reflex testing for antibiotic resistance by genotyping has also been limited to larger laboratories or research studies, with long lag times to appropriate antibiotic prescribing. Furthermore, treatment with moxifloxacin is currently recommended if macrolide resistance is suspected (24), but it is currently not licenced for the treatment of *M. gen* in Australia (25) and, therefore, access remains limited and costly.

Figure 3: History of discovered and recommended antimicrobials and evolution of resistance in *Neisseria gonorrhoeae*, including the emergence of genetic resistance determinants, internationally. During the preantimicrobial era (before the 1930s), treatment consisted of, e.g., a healthier lifestyle, copaiba, cubebs, urethral irrigations, potassium permanganate, silver compounds, mercury compounds, and hyperthermia. Reproduced with permission from *Antimicrobial resistance in Neisseria gonorrhoeae in the 21st century: past, evolution, and future* (13).

SUL = sulfonamides
OFX = ofloxacin

PEN = penicillin
CFM = cefixime

SPT = spectinomycin
CRO = ceftriaxone

TET = tetracycline
AZM = azithromycin

CIP = ciprofloxacin
DOX = doxycycline

Syphilis

Syphilis, caused by the organism *Treponema pallidum*, has been recognized since antiquity (26). However, in the last decade, the number of syphilis notifications have continued to rise, particularly in MSM (27). Syphilis remains a highly contagious, systemic infection capable of causing genital ulceration, meningitis, neonatal death, and long-term cardiovascular and neurological sequelae.

Challenges

Australia currently faces an ongoing outbreak of syphilis affecting young Aboriginal and Torres Strait Islander (ATSI) people since January 2011. This outbreak, which began in northern Queensland, has continued to extend across the states to the Northern Territory, Western, and South Australia (28). While *T. pallidum* remains susceptible to penicillin treatment,

suboptimal drug levels, particularly in the central nervous system, means that benzathine penicillin delivered as an intramuscular injection remains the recommended treatment for syphilis (24), which poses as a barrier to care for those presenting to primary care. The potential long latency periods and relatively high asymptomatic carriage often leads to pitfalls in testing. Engagement with affected populations, such as MSM and ATSI peoples, remains key to raising awareness and increased testing behavior and engagement into care.

HIV

By the end of 2016, 26 444 people were estimated to be living with HIV in Australia. HIV continues to disproportionately affect MSM in Australia, with 75% of those living with HIV in 2016 identifying MSM as a likely route of transmission and an incidence of 0.85 per 100 person years (3). Through large testing

Figure 4: Prevalence of macrolide resistance in *M. genitalium* (23).

campaigns, improved access to care, and treatment and enhanced surveillance and contact tracing efforts, Australia has edged closer to the United Nations Program “90-90-90” global target for HIV (**Figure 5**) (29). Targeted campaigns for HIV testing in MSM in Australia have largely been a success with lower rates (11%) of undiagnosed HIV in MSM compared to heterosexual risk exposure and people who inject drugs (3). Access to HIV prevention strategies, such chemoprophylaxis for HIV infection (PrEP), have been well received (30) with more than 7000 patients enrolled in PrEP programmes in 2016, culminating in the listing of PrEP medication on the Pharmaceutical Benefits Programme (PBS) in April 2018, making Australia one of the first few countries to provide access to PrEP by a nationally subsidized program.

Challenges

Approximately 30% of all new HIV diagnoses in Australia are diagnosed “late” (3), meaning a CD4 count of less than 350 cells/ μ L, which confers a higher morbidity and poorer prognosis. Ongoing surveillance to identify gaps and changing trends in HIV diagnoses is important, including HIV awareness and testing efforts in migrants from neighbouring Southeast Asia and ATSI. Despite improved outcomes, people living with HIV continue to have more comorbidities than their peers (31) and continue to experience stigma and discrimination which prohibit a good quality of life (32, 33).

Access to PrEP for those at risk remains disproportionate, with further barriers for those living in more

Figure 5: The HIV diagnosis and care cascade in Australia, 2014-2016, females (29).

rural and remote communities, temporary residents to Australia who are not eligible for medication on the PBS, and those who may not identify themselves at risk of HIV infection. Furthermore, changes in trends of other STIs in the MSM community, changes in condom use, and long-term sequelae of PrEP in HIV negative patients remains largely unknown.

CONCLUSION

The control of sexually transmitted infections to reduce the burden and cost remains a challenge. Despite advances in knowledge of infections, technologies to detect pathogens, and improved treatment options, the incidence of STIs continue to grow globally. The inherent nature of asymptomatic carriage of most of these infections, cultural stigmatisation of sexual health, a disproportionate burden of disease in the young and minority populations, equity in cost and access to newer testing, and prevention technologies are only some of the current challenges. The science of STIs is only useful if it can be implemented into national policies for ongoing provision of services and, more importantly, if the affected communities remain engaged and empowered to seek care.

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