

Syphilis: a fresh look at an old foe

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To members of the public, syphilis is likely to conjure up notions of an historic venereal scourge, which has long since disappeared. However, in this special issue of *Sexual Health* dedicated to syphilis, we confront the reality that in 2015 this infection remains a very real and pressing public health problem. How is it that an infection that is curable with a single shot of penicillin, and after 70 years shows no signs of penicillin resistance, is resurgent worldwide? It is timely to take a fresh look at *Treponema pallidum* and what we should be doing to mitigate its spread, morbidity and mortality. What do surveillance data from various countries tell us? What public health interventions should be prioritised? What is the optimal clinical management? We present a series of articles that aim to address these questions by reviewing published data so as to provide an evidence base to help inform decision-making.

A fitting start on the way to answering how syphilis might best be controlled or indeed eliminated is to revisit how syphilis is transmitted between individuals and how this can be prevented. Stoltey and Cohen take us through the literature on syphilis transmission and provide estimates on the likelihood of transmission between sexual partners and via other modes of transmission such as mother to child.¹ Peterman and Furness detail the evidence for the effectiveness or otherwise, of specific public health interventions that have attempted to curb syphilis in the community.² These remind us of one of the core principles that has underpinned previous control efforts, namely, the detection of the infectious stages of syphilis and treatment to stem further transmission. Both these reviews are comprehensive and underscore the fact that some pieces of the syphilis transmission and control puzzles remain missing. For instance, the per act probabilities of syphilis transmission for each of the different sexual practices thought to transmit syphilis remain elusive. Such estimates would help to refine mathematical models that have helped elucidate what we need to accomplish programmatically to bring about declines in syphilis and also help rationalise preventive strategies. For example, when considering syphilis control among men who have sex with men (MSM), how

important is oral sex in transmission and how should this be dealt with when preventative messages often focus on condoms for anal sex to prevent HIV? At a time of ever tightening health and research budgets, the question of how scarce funds are best distributed for maximal return should be addressed.

Over the last three decades, the global economic and political order has transformed profoundly and with this upheavals in societies and health systems have occurred. These have contributed to an unwelcome reappearance of syphilis in several regions. Previous reports have shown that during the 1990s, following the collapse of the former Soviet Union, rates of syphilis in the Russian Federation and former Eastern Bloc countries climbed dramatically.³ More recently, rapid urbanisation and social changes have been the backdrop to a large increase in syphilis cases in China. In this issue, the epidemiology of syphilis is reviewed across a diverse range of countries and subpopulations.

Men who have sex with men are a primary risk group for both HIV and syphilis in most high-income countries and have increasingly been recognised as a risk group for these infections in low- and middle-income countries. The intersection of HIV and syphilis within populations of MSM should not be forgotten, as syphilis is a driver of new HIV infections.⁴ Solomon and Mayer retrace the story of syphilis as experienced by MSM over time, with particular reference to the US.⁵ Using national surveillance data, Read *et al.* track trends in syphilis notifications from high income countries and show that since 2000, worryingly, syphilis epidemics among MSM have been getting worse, not better, and account for an increasing proportion of notifications.⁶ Social networking via the Internet appears by all accounts to have facilitated the transmission of syphilis through sexual networks of MSM. Coughlan *et al.* describe an outbreak of syphilis among young MSM in New Zealand where networking via the Internet appears to have furthered transmission but where the Internet was also harnessed to help contain it.⁷ Given the burgeoning use of online applications for MSM seeking sex,

often with anonymous counterparts, a clearer understanding of how these applications work and how they can be utilised to achieve public health goals is needed.

Testing for syphilis – screening of asymptomatic individuals and diagnosis of infectious lesions – has been a key component of control programs. A central strategy of the Australian national response to syphilis in gay men has been to link serological screening of syphilis to blood tests taken to monitor HIV. While this is logical given syphilis is overrepresented among HIV-positive MSM, implementing such an apparently simple strategy in the real world, even in a resource-rich setting, is a work in progress.⁸ Trubiano and Hoy present data showing improved detection of syphilis using this approach in a hospital infectious diseases service.⁹

Maternal infection and mother-to-child transmission of syphilis can lead to miscarriage, stillbirth or serious newborn sequelae. Yet congenital syphilis is preventable if maternal infection is detected early enough and treated. Given serological screening for syphilis and treatment with penicillin are both inexpensive, each baby infected with syphilis is tragic and avoidable. Sadly, increases in congenital syphilis cases have all too often reflected depleted health systems and fragmented antenatal care. In 2008, the stark statistic that more than one baby was born per hour with congenital syphilis in China was reported in the media.¹⁰ Ye *et al.* provide recent data on the number of congenital syphilis cases from Guangzhou, the capital of Guangdong province, where in rural areas women sometimes first present to antenatal services at delivery, again highlighting barriers to effective syphilis screening in the real world.^{11,12} The World Health Organization (WHO), which has estimated that nearly 2 million pregnant women are infected with syphilis each year, has called for the elimination of mother-to-child transmission of HIV and syphilis, and has set a minimum target of 95% of pregnant women tested for syphilis and 95% of pregnant women seropositive for syphilis treated.^{13,14} Serruya *et al.* comment on the state of antenatal screening for syphilis in Latin America and the Caribbean and reveal major deficiencies in the reporting of relevant perinatal surveillance data despite regional countries approving the WHO plan.¹⁵ These troubling reports suggest that the WHO targets are ambitious and may be difficult to achieve in countries that are most affected. But they are worthy targets nevertheless.

Point-of-care tests for syphilis offer the prospect of improved syphilis screening in resource-limited and remote settings where laboratory facilities and qualified laboratory staff are hard to find or non-existent. Furthermore, they are advantageous where follow up of patients requiring treatment is low. Bristow *et al.* review the performance characteristics of currently available point-of-care tests for syphilis.¹⁶ Encouraging developments include the improved performance of tests, the development of tests that distinguish between active and previously treated syphilis, and dual point-of-care tests for HIV and syphilis. Dual testing at point-of-care should be made available in settings with limited laboratory capacity, together with the necessary health service supports to further the WHO HIV/syphilis elimination plan.

William Osler once remarked ‘know syphilis in all its manifestations and relations, and all other things clinical will be added unto you’. While this may not hold true today, the

protean clinical manifestations of syphilis continue to intrigue and confound, and questions over optimal clinical management still exist, particularly in HIV-positive individuals. Tipple summarises published reports on how syphilis may present differently in HIV-positive patients, while Cresswell and Fisher tackle the controversial question as to whether syphilis ought to be treated differently in patients with HIV.^{17,18} Ho and Spudich delve into the complex area of neurosyphilis and critically review its diagnosis and management in the context of HIV, including the thorny issue of when lumbar punctures are indicated.¹⁹

Turning to the biology of *T. pallidum*, Ma *et al.* detail the typing methods that have been used to characterise different strains and make a case for the development of more discriminatory genotyping methods.²⁰ These would potentially pave the way for typing that would have clinical utility such as information on the source of infection and predicting treatment response.

We hope this special issue convinces readers that much more needs to be done to tackle the re-emergence of syphilis. At the very least, this should include more robust surveillance systems and the implementation of health service models that ensure optimal access to testing and treatment of at-risk populations including expectant mothers and MSM, both HIV-positive and HIV-negative. However, these measures alone are unlikely to be enough. It has become clear that the extent and intensity of existing responses have not been sufficient. Perhaps these shortcomings reflect a view that syphilis, being curable and a relatively uncommon sexually transmissible infection, is low down on the priority list. But this should not be so. More investment and research is sorely needed for the biomedical prevention of syphilis including trials of syphilis prophylaxis.^{21,22} Work on a syphilis vaccine should be stepped up.²³ The potential benefits of a vaccine could be profound: consider the impact that HPV vaccination has had in countries that have introduced it. We were unable to find an author from the syphilis vaccine development field to contribute to this issue; this is indicative of the state of research in this area. Evaluations of the potential health economic benefits of investing in various strategies are required. Our rise to the challenge of syphilis should be emphatic, collaborative and interdisciplinary, and include scientists, researchers, health providers, affected communities, funding agencies, governments and the non-government sector. In pondering what this response might look like, we could take a leaf or two from the pages of success stories in the global response to HIV.

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