Can syphilis be eradicated from the world?

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With the description of the complete genome sequence of *Treponema pallidum*, the declining rates of primary and secondary syphilis in many developed countries, and the continuing development of easier, cheaper, and more reliable diagnostics, the goal of worldwide syphilis eradication may be achievable. Although syphilis is easy to detect and cure given adequate access to and utilization of healthcare, many barriers exist on the way to its elimination and ultimate eradication. This review discusses current opinions regarding the plans, prospects and obstacles to worldwide syphilis eradication. Curr Opin Infect Dis 14:41–44.

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Abbreviation

STD sexually transmitted diseases

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Introduction

Over the past century, several ancient diseases have been eradicated, but syphilis is not among them. Syphilis continues to plague humans. Although the characteristics of this disease deem it susceptible to elimination and ultimate eradication, it persists and sometimes thrives in underprivileged communities. Recent discoveries, however, may give hope to eradication efforts. The developing polymerase chain reaction technology and the description of the complete genome sequence of *Treponema pallidum* will hopefully advance diagnostic ability, the knowledge of pathogenesis, and vaccine development. If these milestones can be reached, worldwide eradication may be possible.

Epidemiology

Syphilis is not homogeneously distributed. According to the World Health Organization 1996 global estimates, over 12.2 million cases of syphilis exist worldwide [1]. Geographically, the vast majority of new cases occur in the developing world, which reflects the global distribution of population [2]. In many developing countries, as much as 10% of the population may be infected. As these estimates are based on prevalence data, they are biased by convenience sampling, small sample sizes, and inconsistent diagnostic criteria.

Until recently, endemic transmission was nearly eliminated in western Europe. For example, in Sweden during World Wars I and II, the incidence of primary and secondary syphilis increased dramatically among both men and women, but with the introduction of penicillin the rates plummeted [3]. Increases were again noted in the late 1960s, with the advent of the sexual revolution, and again in the 1970s among men who have sex with men. Since the advent of AIDS and the adoption of safer sexual practices, rates have remained low. Similar trends were reported in England and Wales, Germany, Denmark and Canada. However, since 1995, recent outbreaks in Europe and the United Kingdom have been attributed to both new imported sources and the resurgence of endemic foci [4–6].

Eastern Europe has experienced alarming increases in primary and secondary syphilis rates since the fall of the 'iron curtain' in 1990. From 1990 to 1997 the annual number of reported syphilis cases increased 50-fold [7]. According to reports of positive syphilis serological tests, the trends in prevalence of syphilis have been documented across several if not most socioeconomic groups. Similar outbreaks have been reported in the Baltic States,

Ukraine and several central Asian countries [8,9]. With the migration of sex workers across borders, the importation of cases into areas where syphilis was considered virtually eliminated has become problematical.

From the late 1950s until the late 1980s, syphilis and other sexually transmitted diseases (STD) appeared to have been virtually eradicated from the People's Republic of China [10]. In the 1930s and 1940s, an estimated 10% of the population had syphilis, with a 50% prevalence among some rural minorities [11]. In the 1950s under Mao's regime, a campaign to eradicate STD began, which included intensive training of public health workers, mass screening, STD campaign propaganda that targeted the disease as the enemy rather than the patient, and eradication of prostitution. By 1964, only 26 new cases of syphilis (0.004%) were detected. However, since the 1980s when China once again allowed westerners to visit in large numbers, the incidence of STD, including syphilis, has increased [12].

Over the past 60 years in the United States, syphilis rates have fluctuated. As with other developed countries, syphilis rates were high during World War II and peaked at 76 cases per 100 000 in 1947. With the introduction of penicillin and intensive public health control efforts, the rates fell to a nadir of four cases per 100 000 in 1955. The decline in cases, however, was also accompanied by a decline in federal, state, and local appropriations for disease control and a decreased emphasis on clinical disease recognition. Consequently, the near-elimination syphilis rates of the 1950s have been followed by cyclic national epidemics with 7–10 year cycles. From 1965 to 1982, the ratio of male to female syphilis cases increased steadily, and high rates of syphilis occurred predominantly among men who have sex with men. The predominance of male cases decreased with the advent of AIDS and the adoption of safer sexual practices. In the late 1980s, a sharp increase of primary and secondary cases occurred among heterosexuals and was related to drug use activity, in particular crack-cocaine and the exchange of sex for drugs or money. Currently, incident syphilis rates are less than four cases per 100 000, and half of these new cases are confined to 28 distinct geographical counties [13]. The elimination of syphilis is feasible and a national elimination plan is underway. In this context, according to the Centers for Disease Control and Prevention [14], syphilis elimination will require strategic rebuilding or enhancing and the coordination of key components of the public health infrastructure for infectious diseases, concentrating such efforts in a relatively small number of US communities.

Requirements for disease control

Over the past century, syphilis was almost eliminated in several countries, but managed to resurge. In 1937, Thomas Parran, Surgeon-General of the United States, in his book 'Shadow on the Land' [15] presented certain fundamentals of successful European syphilis control programmes, which included organized treatment, the repression of commercialized prostitution, and case finding and case holding. Using this model, Parran proposed a formula for syphilis control that included case finding through serological screening, prompt therapy for infected individuals, the identification of people exposed to infectious syphilis, mandatory serological screening of potential transmitters, and public education regarding the infection and its consequences. This formula was adopted in the United States during national elimination programmes in the 1940s and again in the 1960s. Although these programmes reduced rates substantially, neither succeeded in eliminating sustained syphilis transmission. As near-elimination levels have been followed by cyclic national epidemics that arise every 7–10 years, control of syphilis at low levels does appear to be feasible. Currently, incidence rates are under four per 100 000 population and cases appear to be limited to discreet areas. The United States Public Health Service once again is targeting syphilis for national elimination. Although the disease appears to be controllable, can it now be eliminated?

By disease profile, syphilis should be susceptible to elimination. It only affects humans; there is no animal reservoir. Its incubation period is within 9–90 days, which allows sufficient time to interrupt transmission by rapid prophylactic therapy of sexual contacts. Serological diagnosis, although not perfect, is inexpensive and widely available. Infection is treatable with a single, inexpensive penicillin injection and no antimicrobial resistance has yet been reported.

Barriers to elimination and eradication

Many barriers must be overcome before syphilis can be eliminated and then eradicated. At the population level, the spread of syphilis, as with any STD, depends upon the average number of new cases of infection generated by an infected individual. Individuals with syphilis are most contagious to their sexual partners during the primary and secondary stages of their disease, which may last as long as 6 months to a year. The faster the infected person seeks diagnosis and receives treatment, the faster the disease can be controlled. However, the time to diagnosis of a case varies between and among populations, and is dependent upon complex individual, social, cultural and economic factors. For example, among the first steps to seeking care for sexually transmitted infections is self-perception of risk and the recognition of disease symptoms. Undoubtedly, a factor contributing to the persistence of syphilis is the often-painless presentation of its genital ulceration in the primary stage of infection and the protean manifestations of its

secondary stage. Men tend to present earlier in the disease process for evaluation and therapy, but unfortunately women present later in the disease and are often diagnosed when they are less contagious to their sexual partners [16].

In both developing and developed nations, the stigma associated with seeking care for any STD may be prohibitive. The successful, albeit short-lived, eradication of STD in the People's Republic of China, despite its historical, political and economic differences from most other countries, has important messages for global STD prevention [10]. The China experience demonstrates that public health campaigns can have a dramatic impact on STD, and that STD control can only be achieved by sustained elevation in the status of women. As with proposed global AIDS prevention strategies, the promotion of information and education, generation of appropriate social service resources, identification of social support networks, recognition of prostitution and provision of other means of support to women will prevent the spread of other STD, especially syphilis [17].

Even if no stigma exists, there may be a lack of available and appropriate care facilities. Inadequate medical education of healthcare providers to recognize and treat syphilis promptly, as well as inadequate sex education and health information of the affected communities compound elimination problems. Existing care facilities may be extremely stressed, with urbanization and migration of populations as a result of poverty, famine or war. The potential for further stigmatization and ill will generated by poorly articulated targeting on the basis of race/ethnicity or place of residence are substantial [18].

Although currently available diagnostic tests and therapeutic agents are sufficient, cheap and highly effective tools to eliminate the endemic transmission of syphilis, they are not perfect. Serological tests, the mainstay of syphilis diagnosis, are often falsely negative in primary stage syphilis and can be hard to interpret in areas of the world where other endemic treponematoses, such as yaws or pinta, exist. Although cheap and highly effective, benzathine penicillin G therapy must be given by injection. Persons infected with syphilis who fear or dislike injections may therefore avoid therapy. Research to determine the efficacy of single-dose oral antibiotic therapy, such as azithromycin, to treat early syphilis is ongoing [19,20•]. If such therapies are efficacious and can be provided at low cost, injections could be avoided.

Another barrier to sustained syphilis control may be the inability to identify and promptly treat potentially infected sexual partners. Because sexually transmitted syphilis is most contagious during the primary and secondary stages, and sexually exposed persons can incubate the disease for as long as 3 months before they develop the primary stage, it is possible to disrupt disease transmission by treating all exposed persons before they become infected. Unfortunately, persons already infected with syphilis may have engaged in sexual contact with anonymous individuals, or may not want to identify their sexual contacts because of the fear of repercussions or distrust of the public health system. If a person who is diagnosed with infectious syphilis cannot or will not identify his or her sexual contacts, one of the major components of Parran's formula for syphilis control is lacking. The immediate opportunity to interrupt disease transmission by identifying, screening and treating potentially infected individuals is missed. In recent years, however, the effectiveness of this linear partner notification, treatment and counseling method to evaluate and control the transmission of syphilis has been questioned because patients have not been able or willing to name their sexual contacts [21,22]. Some experts have recommended that partner notification should take on a new epidemiological dimension [23]. The use of specific populations, rather than infected individuals, as the units for syphilis intervention may be a means for overcoming problems with naming and locating sex partners. Historically, this epidemiological 'cluster' approach produced a lower yield of infected, previously untreated patients than following up those specifically named as sex partners, but it still identified a relatively high percentage of persons who might not have been reached in any other way. Research is currently underway to investigate the utility of identifying, screening and treating social networks rather than sexual networks as a method of syphilis control.

Conclusion

The challenge to eradicate endemic syphilis globally is herculean, but with continued effort and scientific advances eradication may be possible. Elimination, however, precedes eradication. Globally, endemic syphilis thrives in underprivileged population groups in remote areas with little or no access to healthcare. As proposed by the US Centers for Disease Control and Prevention Syphilis Elimination Plan [24•], the design challenge for syphilis elimination will be to pursue efficiently the elimination of one microbe predominantly through integrated or 'horizontal' strategies that reduce STD in a general way and that more broadly enhance community health in the distressed communities in which syphilis persists [14]. Successful strategies for elimination exist, new therapies and diagnostic tests are being evaluated. Perhaps the most exciting development that makes eradication possible is the sequencing of the *Treponema pallidum* genome [25]. This landmark project will promote vaccine development, and thus help to

promote syphilis elimination to the international community.

However, to go from elimination to eradication, involvement of all levels of government, the entire community, and the medical, educational, industrial, and social work sectors is essential [17]. Dr Raymond A. Vonderlehr, who was Chief of the Venereal Diseases Division of the United States Public Health Service, spent the great majority of his professional career in the struggle to eradicated syphilis, In 1962 at the World Forum of Syphilis and Other Treponematoses, he warned public health professionals:

'It is a well understood precept in a free society that the price of liberty is eternal vigilance. And, if we in our time are to free this nation of syphilis infection, we must remain ever steadfast in our will and determination to see this current struggle through to a successful conclusion. If we have learned anything from the past, it is the fact that syphilis will not just go away because we would wish it so. We should now be aware and ever remain aware that this highly contagious disease will require our eternal vigilance and vigorous effort when the trend line of syphilis incidence inevitably approaches the end point of eradication. For it will be in this critical period that pressures will develop from many quarters to cease and desist the great impetus that is now being built up. Unless there is raw courage, rare determination, and a united will, the forces of reaction and complacency will gain the upper hand and history will again be repeated.'

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